Indian Perspective on De-escalation from Dual Antiplatelet Therapy to Single Antiplatelet Therapy Study: A Knowledge, Attitude, and Practice Study among Indian Interventional Cardiologists

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Abstract

Background: Coronary artery disease (CAD) management is one of the most significant facets of interventional cardiology. Evidence from several clinical trials has redefined the drug management of CAD, including optimizing the duration of antiplatelet treatment regimens in the management of CAD, which is an intricate clinical issue. The available evidence indicates that East Asians have a higher bleeding risk. However, the Indian phenotype differs from that of East Asians, making this data confounding when applied to clinical decision-making among Indian patients. There is a need for a close understanding of Indian interventional cardiologists’ perceptions of complex decision-making pertaining to antiplatelet agents among Indian CAD patients in real-world clinical settings.

Aim: This Indian Perspective on De-escalation from Dual Antiplatelet Therapy to Single Antiplatelet Therapy (INDEPTH) study aims to assess the perspective of Indian interventional cardiologists regarding de-escalating from dual antiplatelet therapy (DAPT) to single antiplatelet therapy (SAPT), approach to decision-making, barriers, and related challenges in CAD management.

Methods: A cross-sectional knowledge, attitude, and practice (KAP) study survey was carried out among Indian interventional cardiologists practicing across different regions of India. A total of 209 responses were received. Descriptive statistics was used to summarize all the parameters. IBM Statistical Package for the Social Sciences (SPSS) statistics was used for biostatistical analysis.

Results: The study indicated that >90% of CAD patients received DAPT therapy immediately after percutaneous coronary intervention (PCI) (86.1%, p < 0.001). About 115 (55%) of the respondents reported using calculator-based scoring for evaluating bleeding risk in patients on DAPT therapy for the management of acute coronary syndrome (ACS) with post-PCI (p = 0.167).

Regarding the usual duration of DAPT therapy post-ACS, nearly half of the respondents, 94 (45%), said that 6–12 months is the usual duration for DAPT therapy in post-ACS patients, followed by >12 months 94 (45%) of the respondents; 17 (8.1%) of the respondents reported it is 3–6 months, and lastly up to 3 months as per four (1.9%) of the respondents (p < 0.001). A total of 128 (61%) of the respondents strongly believe that balancing bleeding with ischemic risk influenced the choice of antiplatelet agent when treating established CAD.

As per interventional cardiologists surveyed, the perfect de-escalation time frame for Indian CAD patients with high bleeding risk (HBR) is up to 3 months (35.9%, p < 0.001), 6–12 months for medium bleeding risk (48.8%, p < 0.001), and >12 months for low bleeding risk (65.6%, p < 0.001). Regarding SAPT therapy, almost one-third of the respondents, 65 (31.1%), reported that they prescribed antiplatelet therapy other than aspirin in 20–40% of their SAPT-eligible patients. Furthermore, 69 (33%) of the respondents said that they preferred to prescribe clopidogrel in 50–75% of SAPT-eligible patients. While 64 (30.5%) prescribed in 25–50%, 53 (25.4%) prescribed in <25% and 23 (11%) of the respondents prescribed the drug in >75% of the SAPT-eligible patients. (p < 0.001), "Atorvastatin + clopidogrel" is the most preferred combination of SAPT primarily for the management of CAD among the majority of interventional cardiologists [33%, 95% confidence interval (CI): 1.97–2.24, p < 0.001]. The study respondents also indicated a need for Indian-specific guidelines on de-escalating from DAPT to SAPT in CAD management.

Conclusion: The INDEPTH study indicated that the majority of CAD patients received DAPT immediately after PCI. The perfect de-escalation time frame for Indian CAD patients with "high-bleeding" risk is up to 3 and 6–12 months for "medium-bleeding" risk and >12 months for "low-bleeding" risk. One-third of respondents used clopidogrel as an antiplatelet agent in 50–75% of SAPT-eligible patients. Atorvastatin + clopidogrel is predominantly the most preferred combination of statin + SAPT for the management of CAD. Although the current international guidelines cover the Indian perspective to some extent, there is a need for Indian-specific guidelines on de-escalating from DAPT to SAPT.

Introduction

Coronary Artery Disease in India: Overview and Management

Coronary artery disease (CAD), sometimes referred to as coronary heart disease (CHD), results from decreased myocardial perfusion that causes angina, myocardial infarction (MI), and/or heart failure (HF). It accounts for one-third to one-half of the cases of cardiovascular diseases (CVD). An increasing burden of CAD in India is a major cause of concern. The prevalence of CAD in urban populations in India has been estimated between 5 and 10% and 3.3–7.4% in rural India. Hospitalizations due to CAD were reported in 10% of urban and 4% of rural populations, with an average hospitalization burden of 6.0%. Many studies have reported that Indians are more susceptible to CAD and have a higher case-fatality rate than the Western populations.

The mortality associated with CAD among Asian Indians is 20–50% higher than any other population. Various international organizations have formulated recommendations and guidelines for the management of CAD. Studies have shown that evidence-based medicine, with

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treatment according to the clinical practice guidelines (CPG), improves patient care outcomes.\textsuperscript{14,15} Multiple approaches, including medical therapies and interventional procedures, may be useful and form key pillars of intervention for optimizing treatment outcomes in CAD management.\textsuperscript{11} These include different classes of pharmacological agents such as antiplatelet agents, antianginal, antihypertensive, HF therapies, and lipid-lowering agents.\textsuperscript{16}

**Antiplatelet Therapy in Coronary Artery Disease Management**

Acute coronary syndrome (ACS) is principally driven by platelet aggregation. Dual antiplatelet therapy (DAPT) has demonstrated a reduction in recurrent ischemic events.\textsuperscript{17} Antiplatelet therapy is an essential component of the medical regimen in ACS as well as for secondary prevention. Multiple randomized trials have conclusively indicated that DAPT that includes aspirin and P2Y12 inhibitors should be taken for at least 12 months following ACS.\textsuperscript{11} Approximately, 8–10% of patients undergoing percutaneous coronary intervention (PCI) have atrial fibrillation and other indications for an oral anticoagulant.\textsuperscript{11,18} DAPT has become the cornerstone of the management of CAD. The two major guidelines by the American College of Cardiology (ACC)/American Heart Association (AHA-2016) and the European Society of Cardiology (ESC-2017) have stated class IA recommendation to initiate DAPT for a minimum duration of 12 months, post-ACS.\textsuperscript{19,20} The latest recommendations from the ACC/AHA Guidelines 2023 for the management of chronic coronary disease reemphasized the significant benefits of aspirin use in secondary prevention. The guideline suggests using DAPT in those with high thrombotic risk and low bleeding risk. The guideline recommended DAPT, which consisted of clopidogrel and aspirin for 6 months post-PCI, followed by single antiplatelet therapy (SAPT) to reduce major adverse cardiovascular event (MACE) and bleeding events (class of recommendation: 1, level of evidence: A).\textsuperscript{21}

**Challenges in Applying Antiplatelet Therapy in CAD: More than Meets the Eye**

Among antiplatelet agents, aspirin and clopidogrel (P2Y12 receptor antagonists) are widely prescribed medications in CAD.\textsuperscript{22} Recent guidelines have proposed a personalization of therapy according to the patient’s bleeding and ischemic risks, with dedicated scores designed to predict such risks.\textsuperscript{23} Factors associated with an increased risk of ischemic events include recent ACS, prior MI, diabetes, complex coronary lesions, and procedural aspects, while a history of bleeding is the principal risk factor for bleeding events. The tools to support decision-making are the DAPT score and the predicting bleeding complications in patients undergoing stent implantation and subsequent DAPT (PRECISE-DAPT) score. A high DAPT score of >2 in patients who have received a 12-month course of DAPT without experiencing ischemic or bleeding events favors prolongation to 30 months. Conversely, a high PRECISE-DAPT score of >25 at the index event signifies a high risk of bleeding and a potential benefit from shortened DAPT duration.\textsuperscript{24}

Moreover, compared with Caucasian patients, East Asian patients are considered to have a different ischemia/bleeding propensity in response to antiplatelet and antithrombotic therapy, known as the “East Asian Paradox” (i.e., more bleeding events but fewer thromboembolic events).\textsuperscript{25} This is consistent with the available epidemiological data collated from cerebrovascular events, especially those incorporating hospital-based registries in Asia. The striking clinical features of stroke in Asia include a relatively high prevalence of intracerebral hemorrhage, lacunar infarction, intracranial atherosclerosis, and stroke in young patients. Studies indicate that intracerebral hemorrhage is reported in 22% of the Asian population, as opposed to 9.8% of the Caucasian population.\textsuperscript{26} One of the plausible mechanisms explaining the East Asian paradox is the low body weight phenotype of this population.\textsuperscript{25}

However, it is noteworthy that the Indian phenotype differs from East Asians in that they have a relatively higher body weight and body mass index than some of the East Asian regional populations.\textsuperscript{27} The consistency of patterns of bleeding tendencies and events between East Asian and Indian populations have not been elaborately studied. Hence, applying this scientific evidence may pose a dilemma in clinical decision-making pertaining to the modulation of antiplatelet therapeutic strategies among CAD patients.

Moreover, in real-world settings, prolonged and potent therapy is often difficult to maintain due to the patient’s clinical characteristics and comorbidities, and the use of scores is limited by several practical challenges, such as the large overlap between factors associated with increased ischemic and bleeding events.\textsuperscript{28} Both ischemic and bleeding events may occur in post-PCI; applying medication choices and defining specific treatment duration are areas in need of more certainty with regard to their impact on individual risks in real-world settings.\textsuperscript{29} A better understanding of ischemic and bleeding risk profile, as well as individual responsiveness to antiplatelet agents, has been instrumental in defining the optimal regimen for the individual patient. In particular, the intensity and duration of aspirin and P2Y12 inhibiting therapy need to be adjusted to reduce the risk of ischemic complications while minimizing the risk of bleeding.\textsuperscript{30}

Strategies developed to mitigate the risk of bleeding include shortening DAPT duration, P2Y12 inhibitor monotherapy, and de-escalation.\textsuperscript{30} De-escalation of DAPT duration appears to be a favorable intervention, with a reduction in risk of bleeding, mostly without an increase in ischemic events, despite an increase in ischemic events reported in some studies using abbreviated DAPT.\textsuperscript{31} A great deal of uncertainty persists among clinicians and healthcare providers regarding the default time of de-escalating strategy for most patients with ACS.\textsuperscript{32} Switching between P2Y12 receptor antagonists is frequently seen in clinical practice as prasugrel and ticagrelor used early on after a PCI are de-escalated to clopidogrel maintenance to decrease the risk of bleeding and reduce treatment costs. Certain pieces of evidence show that CYP2C19 genotyping to guide this de-escalation is effective in optimizing the clinical outcomes in patients undergoing PCI.\textsuperscript{33} The interpretation and application of the evidence in the rapidly progressing field of antiplatelet therapy can be challenging.\textsuperscript{17}

**Background**

The clinical decision-making regarding de-escalation and switching of antiplatelet therapy in real-world settings is challenging, and it is based on cardiologists’ clinical acumen combined with the judicious application of scientific evidence. While the scientific evidence is available, many trials may not represent the entire diversity of patients presenting to a cardiologist due to their stringent inclusion/exclusion criteria and insufficient representation of the patient population encountered in real-world settings. The available evidence indicates that East Asians have a higher bleeding risk. This corroborates with the Asian epidemiological data pertaining to hemorrhagic cerebrovascular events. However, the Indian phenotype differs from that of East Asians, and hence, this data may be confounding when applied to clinical decision-making among Indian patients.

The Indian interventional cardiologists’ perception of de-escalation and switching to antiplatelet therapy is limited. Hence, there is
a need for a knowledge, attitude, and practice (KAP) study to assimilate practical insights regarding the applicability of antiplatelet therapies among Indian CAD patients.

**Aim of the Study**

This Indian Perspective on De-escalation from Dual Antiplatelet Therapy to Single Antiplatelet Therapy (INDEPTH) study aims to assess the perspective of Indian interventional cardiologists regarding de-escalating from DAPT to SAPT, approach to clinical decision-making, barriers, and related challenges in CAD management. The study is conducted to understand and seek practical insights regarding the use of antiplatelet agents in the Indian CAD patient population.

**Methods of the Study**

The INDEPTH study is a nationwide, cross-sectional, voluntary, questionnaire-based KAP survey conducted among practicing interventional cardiologists in India. The survey questionnaire consisted of 32 questions prepared in English under the guidance of an eminent, academically authoritative group of five interventional cardiologists in the country. As the study did not involve the collection or analysis of human data, ethics committee approval was not deemed necessary. Digital tools, such as Google Forms, were used to capture, record, and collate the study data. Statistical package software was used to analyze the data for biostatistical analysis (Statistical Package for the Social Sciences (SPSS), IBM Corp; Windows version 29).

A total of 209 responses were received, and all responses were included in the final analysis. The data were presented using frequencies and percentages for categorical variables and as means through descriptive statistics. The Chi-squared test was used to compare categorical data. A p-value of <0.05 was considered significant. A confidence interval (CI) of 95% was applied to represent the statistical significance of the results.

**Results**

**Geographical Distribution of Responses**

Upon analyzing the geographical distribution of survey responses, it was noted responses to the survey were received more from the Southern region 81 (38.7%), followed by Central 49 (23.44%), Eastern 37 (17.7%), Northern 26 (12.4%), Western 10 (4.7%), and six (2.8%) from Northeastern regions, respectively. The survey responses covered the opinions of interventional cardiologists from heterogeneous geographical locations across the country.

**Bleeding Risk Evaluation in CAD**

More than half of the respondents, 115 (55%), reported using calculator-based scoring for evaluating bleeding risk in patients who are on DAPT therapy for the management of ACS with post-PCI. Another 94 (45%) reported that they used their own clinical judgment (p = 0.167) (Table 1).

**DAPT Therapy**

The majority of the respondents, 180 (86.1%), reported that >90% of the patients received DAPT therapy immediately after PCI. However, 27 (12.9%) respondents said that around 50–90% of the patients received the same treatment after PCI (p < 0.001).

Regarding the preference for the combination of DAPT, most respondents indicated 142 (67.9%), “ticagrelor + aspirin” as the most preferred combination (CI 95%: 1.38–1.61, p < 0.001), while other respondents, 112 (53.6%), indicated “clopidogrel + aspirin” as the second preference (CI 95%: 1.93–2.12, p < 0.001), and some respondents 120 (57.4%) indicated “prasugrel + aspirin” as the third preference (CI 95%: 2.75–2.95, p < 0.001).

**Duration of DAPT Therapy**

Regarding the usual duration of DAPT therapy post-ACS, nearly half of the respondents, 94 (45%), said that 6–12 months is the usual duration for DAPT therapy in post-ACS patients, followed by >12 months according to 94 (45%) of the respondents, 17 (8.1%) of the respondents reported it is 3–6 months, and lastly up to 3 months as per four (1.9%) of the respondents (p < 0.001) (Table 2).

**Impact of Bleeding Risk in Modulating DAPT Therapy**

About 89 (42.6%) of the respondents rated bleeding as a risk “in few patients,” followed by “sometimes” by 72 (34.4%); other 33 (15.3%) of the respondents said that it is “always” a risk concern and lastly 16 (7.7%) of the respondents opined bleeding as a “rarely” a concern while prescribing DAPT for secondary prevention (p < 0.001).

Furthermore, 86 (41.1%) of the interventional cardiologists indicated that they considered shortening the duration of DAPT due to bleeding concerns “in few patients.” A total of 80 (38.3%) of the respondents considered shortening the therapy “sometimes,” while 31 (14.8%) of the respondents “frequently” considered shortening the DAPT therapy due to bleeding, and lastly, 12 (5.7%) said that they “rarely” considered it (p < 0.001). The survey response also indicated that nearly half of the respondents, 99 (47.4%),
consider reducing the dose of antiplatelet in DAPT “in a few patients” due to bleeding concerns. And 63 (30.1%) of cardiologists said they “sometimes” considered reducing the dose, and 30 (14.1%) of respondents “frequently” considered, while 17 (8.1%) of the respondents “rarely” considered reducing the dose of antiplatelet in DAPT due to bleeding (p < 0.001).

With regard to the manner in which bleeding risk influences their decision to de-escalate (earlier vs later) the antiplatelet therapy, 83 (39.7%) of the respondents said that it influences “in few patients,” followed by “sometimes” as per 72 (34.4%), then “frequently” as per 41 (19.5%) of the respondents, and lastly 13 (6.2%) said it “rarely” influenced their decision-making (p < 0.001) (Table 3).

Also, 128 (61%) of the respondents “strongly believe” that balancing bleeding with ischemic risk influences the choice of antiplatelet agent when treating established CAD. About 61 (29.2%) of the respondents pointed out that it does influence to “some extent,” while 18 (8.6%) of the respondents said it “rarely” influenced decision-making (p < 0.001).

Table 3: Impact of bleeding risk in modulating DAPT therapy

<table>
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<th>Parameters</th>
<th>Total (N = 209)</th>
<th>p-value</th>
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<td>Bleeding as a risk while prescribing DAPT for secondary prevention</td>
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<td>p &lt; 0.001</td>
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<tr>
<td>In few patients</td>
<td>89 (42.6%)</td>
<td></td>
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<tr>
<td>Sometimes</td>
<td>72 (34.4%)</td>
<td></td>
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<tr>
<td>Frequently</td>
<td>33 (15.3%)</td>
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<tr>
<td>Rarely</td>
<td>16 (7.7%)</td>
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<tr>
<td>Shortening duration of DAPT due to bleeding</td>
<td></td>
<td>p &lt; 0.001</td>
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<tr>
<td>In few patients</td>
<td>86 (41.1%)</td>
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<td>Sometimes</td>
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<td>Frequently</td>
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<td>Rarely</td>
<td>12 (5.7%)</td>
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<tr>
<td>Reducing the dose of antiplatelet in DAPT</td>
<td></td>
<td>p &lt; 0.001</td>
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<td>Rarely</td>
<td>17 (8.1%)</td>
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<tr>
<td>Influence of bleeding on the decision to de-escalate</td>
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<td>p &lt; 0.001</td>
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<td>In few patients</td>
<td>83 (39.7%)</td>
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<tr>
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<td>13 (6.2%)</td>
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De-escalation Time Frame for DAPT among Indian CAD Patients

About 75 (35.9%) of the respondents indicated up to 3 months is the perfect de-escalation time frame for Indians with high-bleeding risk, followed by 3–6 months as per 79 (35.7%), and another 52 (24.9%) of the respondents said 6–12 months and seven (3.3%) said it is >12 months (p < 0.001).

For medium bleeding risk, 102 (48.8%) of the respondents said 6–12 months as the perfect de-escalation time frame, while 66 (33%) said it is 3–6 months, 20 (9.6%) said it is >12 months and 18 (8.6%) of the respondents said it is up to 3 months (p < 0.001).

With regard to low bleeding risk, 136 (65.6%) of the respondents said that >12 months is the perfect de-escalation time frame, while 44 (21.1%) of the respondents said it is 6–12 months, 16 (7.7%) would go for 3–6 months, and 12 (5.7%) opined for “up to 3 months” (p < 0.001) (Fig. 1).

Use of SAPT Therapy

Regarding SAPT therapy, almost one-third of the respondents, 65 (31.1%), reported that they prescribed antiplatelet other than aspirin in 20–40% of their SAPT-eligible patients, 57 (27.3%) of the interventional cardiologists said that they prescribed it in 40–60% SAPT-eligible cases, 56 (26.8%) of the respondents prescribed in 20% and 31 (14.8%) of the respondents used it in >60% of the eligible SAPT patients (p = 0.006).

Choice of Antiplatelet Agents

Furthermore, 69 (33%) of the respondents said that they preferred to prescribe clopidogrel in 50–75% of SAPT-eligible patients. While 64 (30.5%) prescribed in 25–50%, 53 (25.4%) prescribed in <25%, and 23 (11%) of the respondents prescribed the drug in >75% of the SAPT-eligible patients (p < 0.001) (Fig. 2).

More than half of the respondents, 117 (55%), said that they prescribe ticagrelor in <25% of SAPT-eligible patients. And 39 (18.7%) of the respondents pointed out they prescribed the drug in 25–50% of cases, 27 (12.9%) of the respondents prescribed it in 50–75%, and 26 (12.4%) of the respondents used it >75% of the SAPT eligible patients (p < 0.001) (Fig. 3).

Considerations for SAPT Therapy

Recurrent episode/event was the “most important” consideration (CI 95%: 1.72–1.98, p < 0.001) as per 96 (45.9%) of the respondents, followed by bleeding risk as “fairly important” (CI 95%: 1.82–2.04, p < 0.001) as agreed by 85 (40.7%) of the respondents, gastrointestinal (GI) bleeding as “slightly important” (CI 95%: 2.42–2.65, p < 0.001) as per 102 (48.8%) of the respondents and frequency of administration as the “least important” (CI 95%: 3.23–3.47, p < 0.001) as per 75 (35.9%) of the interventional cardiologists who responded the survey (Fig. 4).

Recurrent of Ischemic Events

Half of the respondents, 105 (50.5%), reported that double stenting of coronary bifurcation lesions has the maximum chance of recurrence. In comparison, 64 (30.5%) said that complex lesions, 23 (11%) mentioned stenting of chronic total occlusion (CTO) lesions, and 17 (8.1%)...
stated primary PCI has the maximum chance of recurrence of ischemic events ($p < 0.001$).

**Impact of Choice of Stent on Antiplatelet Therapy**

About 91 (43.5%) of respondents pointed out that their choice of antiplatelet therapy is “sometimes” influenced by the choice of stent. While 45 (21.5%) of the respondents said it “rarely” influences treatment choice, 38 (18.2%) said it “frequently” influences decision-making, and lastly, 35 (16.7%) opined it “rarely” influences the choice of antiplatelet therapy ($p < 0.001$).

**Individuality and Ethnic Influences on Decision-making of Therapy**

About 111 (53.1%) of the respondents reported that they consider interindividual variability in $<25\%$ of patients with responses to P2Y12 inhibitors while deciding therapy regimes. In comparison, 77 (36.8%) of respondents considered it in 25–50% of patients, and 19 (9.1%) of the respondents pointed out they only considered it in 50–70% of their patients ($p < 0.001$).

With regard to Asian paradox, the respondents believed the “Asian paradox” (for bleeding risk) is relevant to Indian patients while considering DAPT; 130 (62.2%) reported it is “sometimes” applicable to Indian patients while considering DAPT, followed by “in few patients” as per 37 (17.7%) of the respondents, “very often” as per 34 (16.3%) of the respondents, and eight (3.4%) of the respondents said it is “rarely” applicable ($p < 0.001$).

**Considerations for Switching from Ticagrelor/Prasugrel to Clopidogrel**

Furthermore, 134 (64.1%) of the respondents stated major bleeding events as the “most important” consideration to switching from ticagrelor to clopidogrel ($CI\ 95\%: 1.44–1.67, p < 0.001$), adverse reactions (such as dyspnea) ($CI\ 95\%: 2.18–2.43, p < 0.001$) as “fairly important” as per 82 (39.2%) of the respondents, need for oral anticoagulation as “slightly important” ($CI\ 95\%: 2.31–2.55, p < 0.001$) as per 80 (38.3%) of the respondents, and creatinine levels as the “least important” ($CI\ 95\%: 3.18–3.42, p < 0.001$) as per 113 (54.1%) of the respondents (Fig. 5).

Major bleeding events emerged as the “most important” consideration to switch from prasugrel to clopidogrel ($CI\ 95\%: 1.17–1.34, p < 0.001$) as per 170 (81.3%) of the respondents, need for oral anticoagulation as “fairly important” ($CI\ 95\%: 2.15–2.36, p < 0.001$) as per 117 (56%) of the respondents, creatinine levels as “slightly important” ($CI\ 95\%: 2.93–3.15$) as per 81 (38.8%) of the respondents, and adverse reaction as the “least important” ($CI\ 95\%: 3.02–3.25, p < 0.001$) as per 89 (42.6%) of the interventional cardiologists (Fig. 6).

**Limitations of Newer Antiplatelet Therapies**

About 73 (34.9%) of the respondents indicated that “ambiguity about dose requirements for lower body weight and elderly with prasugrel” was the major limitation of the newer antiplatelets ($CI\ 95\%: 2.03–2.32, p < 0.001$), followed by “twice daily dosing of ticagrelor as “fairly important” ($CI\ 95\%: 2.18–2.47, p < 0.001$) as per 62 (29.7%) of the respondents, dyspnea “slightly important” ($CI\ 95\%: 2.61–2.86$) as per 83 (39.7%) of the respondents and cost stated primary PCI has the maximum chance of recurrence of ischemic events ($p < 0.001$).

**Choice of Statin and Polypills in Secondary Prevention**

About 85 (40.7%) of the respondents said that both atorvastatin and rosuvastatin as their choice of statin in secondary prevention, and another 62 (29.7%) of the respondents opined for rosuvastatin, and 61 (29.2%) preferred atorvastatin ($p < 0.001$).

**Fig. 4:** Important considerations while choosing antiplatelet for SAPT therapy

**Fig. 5:** Considerations while switching from ticagrelor to clopidogrel

**Fig. 6:** Considerations while switching from prasugrel to clopidogrel
For the combination of SAPT along with a statin, “atorvastatin + clopidogrel” was the “most preferred” combination of SAPT (95% CI: 1.77–2, \(p < 0.001\)) as per 76 (36.4%) of the respondents, followed by “rosuvastatin + clopidogrel” as the “second preference” combination (95% CI: 2–2.24, \(p < 0.001\)) as per 83 (39.7%) of the respondents, atorvastatin + aspirin as the “third preference” (95% CI: 2.51–2.82, \(p < 0.001\)) as per 73 (34.9%) of the respondents, and “atorvastatin + ticagrelor” (95% CI: 3.01–3.26, \(p < 0.001\)) as the “least preferred” combination of SAPT as per 91 (43.5%) of the respondents (Fig. 8).

**Indication Preference for Prescribing a Fixed-dose Combination of Atorvastatin + Clopidogrel**

About 69 (33%) of the respondents indicated that management of CAD was the “most preferred” for prescribing a fixed dose combination of atorvastatin + clopidogrel (95% CI: 1.97–2.24, \(p < 0.001\)), while 66 (31.6%) of the respondents reported “secondary prevention of CVD” as the second preference (95% CI: 2.11–2.36, \(p < 0.001\)), 53 (25.4%) of the respondents indicated ACS (95% CI: 2.34–2.65, \(p < 0.001\)) as the third preference, and 96 (45.9%) of interventional cardiologists rated “primary prevention” as the least preferred (95% CI: 2.73–3.06, \(p < 0.001\)) for prescribing the fixed-dose combination (Fig. 9).

**Perception Pertaining to International Guidelines**

About 166 (79.5%) of the respondents shared that current international guidelines on DAPT and SAPT “somewhat” cover the Indian perspective. However, 30 (14.4%) of the respondents felt that the Indian perspective is “always” covered, while 13 (6.2%) opined that it is “rarely” covered (\(p < 0.001\)). About 99 (47.4%) “strongly” believed that there is a need for India-specific guidelines on DAPT and SAPT. Another half of respondents, 98 (46.9%), also suggested that “it would be better” to have Indian-specific guidelines, and 10 (4.8%) went for “maybe” (\(p < 0.001\)). More than half of the respondents, 130 (62.4%), said that the current international guidance on prescribing antiplatelet therapy in established ACS is “always” friendly, and 66 (31.9%) believed that the guidelines are “sometimes” friendly (\(p < 0.001\)) (Table 4).

**Guidelines for Determining Antiplatelet Therapies in CAD**

While selecting an antiplatelet strategy for those with established ACS, 140 (67%) of the respondents reported that following the latest CPGs is their biggest consideration
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while selecting an antiplatelet strategy in ACS. About 42 (20%) of the respondents considered consulting with patients and considering a patient-centric approach, and 27 (12.9%) of the respondents considered adopting the latest clinical evidence while choosing antiplatelet in ACS treatment (p < 0.001).

**Discussion**

The present study assessed the perspective and sought practical insights among Indian interventional cardiologists on de-escalation from DAPT to SAPT therapies in real-world settings in India.

The survey responses covered the opinions of interventional cardiologists from heterogeneous geographical locations across the country.

More than half of the respondents, 115 (55%), reported using calculator-based scoring for evaluating bleeding risk in patients who are on DAPT therapy for the management of ACS with post-PCI. Another 94 (45%) reported that they used their own clinical judgment (p = 0.167). This indicates that in real-world scenarios in India, bleeding risk evaluation still remains a clinical judgment in a large number of practice settings.

The study reported that the majority of respondents indicated that >90% of the patients received DAPT therapy immediately after PCI.

Despite this majority, the survey indicated that there is a small proportion of CAD patients who do not receive DAPT immediately after PCI. This proportion of patients reflected in our KAP study seems a trend to be quantitatively on the higher side than reported in related other patient-included observational studies.

The factors for nonconsideration of the initiation of DAPT after PCI may include but are not restricted to suspected intracranial hemorrhage, a recent history of intracranial hemorrhage, severe thrombocytopenia, and active clinically significant bleeding.

A more recently published OPTICA study provided the first-in-human evidence that P2Y12 inhibitor monotherapy directly following PCI for non-ST-segment elevation ACS is feasible without any overt safety concerns and highlights the need for randomized controlled trials (RCT) comparing direct P2Y12 inhibitor monotherapy with the current standard of care.

Regarding the usual duration of DAPT therapy post-ACS, nearly half of the respondents, 94 (45%), opined that 6–12 months is the usual duration for DAPT therapy in post-ACS patients, followed by >12 months according to 94 (45%) of the respondents, 17 (8.1%) of the respondents reported it is 3–6 months, and lastly up to 3 months as per four (1.9%) of the respondents (p < 0.001). It indicates that Indian interventional cardiologists are prudent in considering the usual DAPT therapy duration of <12 months when needed.

More than three-fourths of respondents would consider shortening the duration of DAPT due to bleeding risk in certain patients (about 41.1% “in few patients” and 38.3% “sometimes”).

Importantly, 128 (61%) of the respondents “strongly believe” that balancing bleeding with ischemic risk influences the choice of antiplatelet agent when treating established CAD. This clinical challenge remains pertinent in Indian clinical practice settings while using antiplatelet treatment in CAD patients.

Almost three-fourths of respondents would consider that bleeding risk influences decisions to de-escalate (earlier vs later) DAPT therapy in certain cases (about 39.7% “in few patients,” and 34.4% “sometimes”).

About 71.6% of respondents opined for <6 months (35.9% of respondents for up to 3 months and 35.7% for 3–6 months) as the perfect de-escalation time frame for Indian CAD patients with high bleeding risk (HBR).

Valgimigli et al. and MASTER DAPT investigators earlier concluded that 1 month (abbreviated DAPT) of DAPT was noninferior to the continuation of therapy for at least 2 additional months (standard DAPT) with regard to the occurrence of net adverse clinical events and major adverse cardiac or cerebral events. The abbreviated DAPT therapy also resulted in a lower incidence of major or clinically relevant nonmajor bleeding.

In our KAP study, even among CAD patients receiving DAPT with “low bleeding” risk, 136 (65.6%) of the respondents said that >12 months is the perfect de-escalation time frame. The remaining respondents (~34.5%) preferred <12 months as the perfect de-escalation time frame in this group (“low bleeding” risk), indicating prudence among Indian interventional cardiologists toward possible consideration for de-escalation of DAPT and opportunity toward consideration of earlier initiation of SAPT in appropriate cases. A similar trend is observed among ~41.6% of interventional cardiologists, who suggested a perfect de-escalation time frame to be <6 months among CAD patients receiving DAPT with “medium bleeding” risk (Fig. 10).

The Academic Research Consortium for High Bleeding Risk (ARC-HBR) definition addresses an unmet need by providing a framework for evaluating treatment options for patients undergoing PCI at increased bleeding risk. A total of 20 clinical criteria were identified as major or minor by consensus, supported by published evidence (Table 5). Patients are considered to be at HBR if at least one major or two minor criteria are met.

Factors associated with an increased bleeding risk after percutaneous coronary intervention include age >75 years, comorbidities such as renal disease, liver disease and active cancer, anemia, low platelet count, stroke, intracranial hemorrhage (ICH), brain arteriovenous malformation (bAVM), bleeding diathesis, history of prior bleeding or transfusion, and iatrogenic such as the use of oral anticoagulants (OAC), nonsteroidal anti-inflammatory drug (NSAIDs), steroids, planned surgery on DAPT, recent trauma or surgery.

The prevalence of HBR according to ARC-HBR criteria in studies of European and Asian populations has ranged from 30 to 50%, and the incidence of major bleeding events in the HBR groups of these studies has consistently been 24% at 1 year.

Regarding SAPT therapy, almost one-third of the respondents, 65 (31.1%), reported that they prescribed antiplatelet other than aspirin in 20–40% of their SAPT-eligible patients. This implies that SAPT agents beyond aspirin are
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Table 5: Major and minor criteria for HBR at the time of PCI

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticipated use of long–term oral anticoagulation*</td>
<td>Age ≥ 75 years</td>
</tr>
<tr>
<td>Severe or end–stage CKD (eGFR &lt;30 mL/minute)</td>
<td>Moderate CKD (eGFR 30–59 mL/minute)</td>
</tr>
<tr>
<td>Hemoglobin &lt;11 gm/dL</td>
<td>Hemoglobin 11–12.9 gm/dL for men and 11–11.9 gm/dL for women</td>
</tr>
<tr>
<td>Spontaneous bleeding requiring hospitalization or transfusion in the past 6 mo or at any time, if recurrent</td>
<td>Spontaneous bleeding requiring hospitalization or transfusion within the past 12 months not meeting the major criterion</td>
</tr>
<tr>
<td>Moderate or severe baseline thrombocytopenia† (platelet count &lt;100 × 10⁹/L)</td>
<td>Long-term use of oral NSAIDs or steroids</td>
</tr>
<tr>
<td>Chronic bleeding diathesis</td>
<td>Any ischemic stroke at any time not meeting the major criterion</td>
</tr>
<tr>
<td>Liver cirrhosis with portal hypertension</td>
<td>Recent major surgery or major trauma within 30 days before PCI</td>
</tr>
</tbody>
</table>

bAVM indicates brain arteriovenous malformation; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; HBR, high bleeding risk; ICH, intracranial hemorrhage; NSAID, nonsteroidal anti-inflammatory drug; PCI, percutaneous coronary intervention; *this excludes vascular protection doses; †, baseline thrombocytopenia is defined as thrombocytopenia before PCI; §, National Institutes of Health Stroke Scale score ≥5.

Another more recently published post hoc analysis of the “Harmonizing Optimal Strategy for Treatment of Coronary Artery Diseases—Extended Antiplatelet Monotherapy” trial, aimed to evaluate the benefits of clopidogrel across high–risk subgroups, concluded that the beneficial effect of clopidogrel over aspirin monotherapy was consistent regardless of clinical risk or relative ischemic and bleeding risks compared with aspirin monotherapy. 46

Regarding the choice of antiplatelet therapy regimes, “ticagrelor + aspirin” is the preferred combination of DAPT, followed by “clopidogrel + aspirin.” 46

Recurrence of ischemic events after bleeding risk are important factors when considering SAPT agents among Indian interventional cardiologists.

The survey indicated that the choice of SAPT is influenced by balancing bleeding with ischemic risk, choice of the stent, and recommendations from the latest CPGs.

Half of the respondents, 103 (50.5%), reported that double stenting of coronary bifurcation lesions has the maximum chance of recurrence. These results seem in line with other meta–analysis evidence published by Abdelfattah et al., which included two RCTs, 10 observational studies encompassing 7,105 patients follow–up for a median duration of 42 months, reporting that for left main bifurcation PCI using second–generation drug–eluting stents (DES), a provisional stenting strategy was associated with a trend toward a lower incidence of MACE driven by statistically significant lower rates of target lesion revascularization, compared with systematic double stenting. 47

About more than one–third (about 43.5%) of respondents pointed out that their choice of antiplatelet therapy is “sometimes” influenced by the choice of stent. This implies that the choice of the stent may not always affect the decision pertaining to the choice of antiplatelet therapy.

Drug–eluting stents (DES) were introduced in interventional cardiology and have since rapidly replaced bare metal stents (BMS). DAPT was essential to avoid potentially catastrophic stent thrombosis (ST) after stenting. Premature discontinuation of DAPT was found to be a strong predictor of ST with Sirolimus–eluting stents (SES) and Paclitaxel eluting stents (PES), the first–generation DES. Due to evidence of late and very late ST events with first–generation DES, “the longer, the better” DAPT therapy evolved into being. The second–generation DES—everolimus eluting stents (EES) and zotarolimus eluting stents (ZES) and third–generation DES with biodegradable polymers (BES) are found to have lower rates of late and very late ST. A meta–analysis showed EES to have a lower risk of ST than BMS. 48 The CSI–NIC (National Interventional Council of Cardiological Society of India) data published by Kumar et al. reported 4,38,351 percutaneous coronary interventions of recurrence. These results seem in line with other interindividual variability with responses to P2Y12 inhibitors and Asian Paradox is applicable in some cases.

The proportion of Asian populations enrolled in landmark RCTs is substantially low, which limits the direct application of trial findings into clinical practice in Asian countries. Moreover, compared with Caucasian patients, East Asian patients are considered to have a different ischemia/bleeding propensity in response to antithrombotic therapy, known as the “East Asian paradox” (i.e., more bleeding...
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Consensus recommendations on switching oral P2Y12 inhibitors:

(A) Acute/Early phase

- Clopidogrel
  - C 600 mg LD
    - (24 hours after last P dose)
  - T 180 mg LD
    - (24 hours after last T dose)
- Prasugrel
  - P 60 mg LD
    - (24 hours after last P dose)
- Ticagrelor
  - P 60 mg LD
    - (24 hours after last T dose)

(B) Late/Very late phase

- Clopidogrel
  - C 75 mg LD
    - (24 hours after last P dose)
  - T 90 mg bid MD
    - (24 hours after last P dose)
- Prasugrel
  - P 10 mg MD
    - (24 hours after last C dose)
  - T 90 mg bid MD
    - (24 hours after last T dose)
- Ticagrelor
  - P 60 mg LD
    - (24 hours after last T dose)

Figs 11A and B: Consensus recommendations on switching oral P2Y12 inhibitors: (A) Switching between oral agents in the acute/early phase; in the acute/early phase (<30 days from the index event), switching should occur with the administration of a loading dose (LD) in most cases, with the exception of patients who are de-escalating therapy because of bleeding or bleeding concerns, in whom a maintenance dose (MD) of clopidogrel (C) should be considered; timing of switching should be 24 hours after the last dose of a given drug, with the exception of when escalating to prasugrel (P) or ticagrelor (T), when the LD can be given regardless of the timing and dosing of the previous clopidogrel regimen; *consider de-escalation with clopidogrel 75 mg MD (24 hours after last prasugrel or ticagrelor dose) in patients with bleeding or bleeding concerns; (B) Switching between oral agents in the late/very late phase; in the late/very late phase (>30 days from the index event), switching should occur with the administration of an MD 24 hours after the last dose of a given drug, with the exception of patients changing from ticagrelor to prasugrel therapy, for whom an LD should be considered; de-escalation from ticagrelor to clopidogrel should occur with administration of an LD 24 hours after the last dose of ticagrelor (but in patients whom de-escalation occurs because of bleeding or bleeding concerns, an MD of clopidogrel should be considered); *consider de-escalation with clopidogrel 75 mg MD (24 hours after the last prasugrel or ticagrelor dose) in patients with bleeding or bleeding concerns.

Events but fewer thromboembolic events). Coincident with consecutive RCTs in Western populations to optimize antithrombotic strategies, several such studies have now been conducted in East Asian cohorts. The clinical characteristics unique to East Asians compared to Caucasians include HBR, increased risk of hemorrhagic stroke, and GI bleeding. The plausible mechanism of the East Asian Paradox may be attributed to unique demographics, lower body weight, genetic predispositions, and differential responses to P2Y12 inhibitors. The possible optimal strategies for this population include a reduced dose regimen, short-term DAPT, and early use of P2Y12 inhibitors monotherapy.

Indian phenotype differs from East Asians in having a relatively higher body mass index, which is likely posing a dilemma for Indian interventional cardiologists in applying “East-Asian Paradox” evidence in clinical decision-making.

The survey also indicated that a “major bleeding event” was the most important consideration when switching from ticagrelor to prasugrel or clopidogrel. About one-third of respondents indicated that “ambiguity about dose requirements for lower body weight and elderly with prasugrel” was a major limitation. Twice daily dosing was considered a “fairly important” limitation with the use of ticagrelor. The consensus recommendations on switching between oral P2Y12 inhibitors have been represented in Figure 11.

Atorvastatin + clopidogrel is predominantly the most preferred combination of statin + SAPT for the management of CAD among the majority of surveyed Indian interventional cardiologists. Both atorvastatin and rosuvastatin were reported as the choice of statin for secondary prevention in our KAP study.

It is noteworthy that polypills containing the highest dose of atorvastatin (i.e., 80 mg) plus SAPT (aspirin or clopidogrel) are hardly available for Indian patients to allow aggressive statin dosing strategy during the initial duration of secondary prevention.

However, the findings of the secondary analysis of the LODESTAR trial, comparing rosuvastatin vs atorvastatin in patients with CAD, reported a higher risk of new-onset diabetes mellitus requiring anti-diabetic medication and the need for cataract surgery with rosvastatin treatment compared with atorvastatin treatment. Multicentric Indian studies have reported that treatment with atorvastatin 40 and 80 mg among Indian patients with ACS led to significant reductions in LDL-C and hs-CRP, with a well-accepted tolerance profile.

With regard to perception regarding international guidelines, a majority, about 166 (79.5%) of the respondents shared that current international guidelines on DAPT and SAPT “somewhat” cover the Indian perspective; a significant proportion of Indian interventional cardiologists believe India-specific guidelines on DAPT and SAPT may be needed, about 99 (47.4%) strongly believed that there is a need for India-specific guidelines on DAPT and SAPT and another half of respondents 98 (46.9%) also suggest that “it would be better” to have Indian-specific guidelines.

While selecting an antiplatelet strategy for those with established ACS, 140 (67%) of the respondents reported that following the latest CPGs is their biggest consideration while selecting an antiplatelet strategy in ACS. This consideration came ahead of the patient-centric approach, further indicating a need for the development of India-specific guidelines for DAPT and SAPT, which may likely be well-accepted to optimize treatment care outcomes.

The Indian subgroup of the EPICOR Asia study published by Sawhney et al. observed a gap between international recommendations and implementation for managing ACS in Indian patients. The mortality, along with composite events of death, MI, or ischemic stroke, was highest for patients with NSTEMI. The reported CV events were similar in STEMI and NSTEMI groups. Going forward, steps need to be taken to improve the identification, diagnosis, and management of patients with ACS to improve patient outcomes.

The development of Indian-specific guidelines may help address these India-
specific issues pertaining to ACS and help in effective management.

**Strengths of the Study**

A major strength of this study is the generalizability and diversity, as INDEPTH is a large, geographically diverse KAP survey. The study included interventional cardiologists across different regions of India, helping to cover the opinions of practicing interventionalists from heterogeneous geographical locations across the country. The present study revealed several key aspects of antiplatelet drug utilization and its applicability, in addition to improving our understanding of the myriad factors that require consideration in CAD medical management. The study also brought the need for Indian-specific guidelines regarding the use of DAPT and SAPT in CAD management.

**Limitations of the Study**

This study is limited by a descriptive survey, and the responses are from physician reports, which may not provide a true representation of patients’ responses and also limit data on patient outcomes. The choice of treatments given for CAD may have been influenced by the presence of different concomitant conditions, yet our questionnaire was unable to detect such potential interactions. Demographic details of the respondents were not captured in the questionnaire; such details are needed to understand and analyze the factors that impact the healthcare professionals’ choice of treatment. Other inevitable limitations associated with data collected from surveys that are relevant to the current study include recall bias, missing data, and overreporting of surveyed events.

**Conclusion**

The INDEPTH survey indicated that a majority of CAD patients received DAPT immediately after PCI, usually for 6–12 months or >12 months. In Indian real-world scenarios, bleeding risk evaluation still remains a clinical judgment in a large number of practice settings. Indian interventional cardiologists are prudent to consider the usual DAPT therapy duration of <12 months when needed.

Clopigrel was the most frequently prescribed antiplatelet agent in 50–75% of SAPT-eligible patients, as per the respondents of the survey. Atorvastatin + clopidogrel is predominantly the most preferred combination of statin + SAPT for the management of CAD. Secondary prevention polypills containing the highest dose of atorvastatin (i.e., 80 mg) plus SAPT (aspirin or clopidogrel) are hardly accessible in India.

Indian Perspective on De-escalation from Dual Antiplatelet Therapy to Single Antiplatelet Therapy (INDEPTH) study reemphasized that the choice of DAPT and SAPT is influenced by factors like balancing bleeding with ischemic risk, choice of stent, recurrent episodes/events, recommendations from the latest CPGs, and interindividual variability toward P2Y12 inhibitors.

International guidelines recommend 6 months of DAPT in high-bleeding risk (HBR) patients with ACS and 12 months of DAPT in non-HBR patients with ACS after PCI. In patients with non-ACS, 1–3 months of DAPT is recommended in HBR patients after PCI.

Lastly, this study brought out the need for Indian-specific guidelines regarding the use of DAPT and SAPT, which may be useful.

**Way Forward**

A de-escalation strategy of antiplatelet therapy represents a very practical and promising strategy for reducing bleeding, ischemic risk, and recurrent episodes/events in patients with CAD. Nevertheless, available evidence presents some limitations, such as the fact that many studies have been performed on Asian and European populations, limiting the generalization of their results to other ethnicities. To this extent, the implementation of Indian-specific guidelines may play an important role. The comparative advantage of P2Y12 inhibitors such as clopidogrel, ticagrelor, and prasugrel in real-world settings is yet to be established. It may be relevant to replicate findings of POPular-AGE and LODESTAR trials in the Indian patient population.

Secondary prevention polypills containing the highest dose of atorvastatin 80 plus clopidogrel may be an interesting opportunity to consider among stakeholders responsible for optimizing accessibility to these medications.

Such studies may further facilitate evidence-based decision-making regarding determining the choice of these critical pharmacological agents in the management of CAD, thereby further optimizing long-term treatment outcomes. The development of Indian-specific consensus or guidelines in this direction may also be useful.

**References**

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