ISSN : 0000-0000

CVRF Focus Journal

VOL. 1

CVRF
CardioVascular Research Foundation

CONTENTS

Establishing a Standard Long-Term Antithrombotic Therapy in Patients with Atrial Fibrillation and Coronary Artery Disease: The Clinical Benefit of Edoxaban Monotherapy in the EPIC-CAD Trial

Introduction

The EPIC-CAD trial evaluated the safety and efficacy of a long-term antithrombotic therapy in patients with atrial fibrillation (AF) and stable coronary artery disease (CAD). The study population requires both oral anticoagulants (to prevent stroke and systemic embolism due to AF) and antiplatelet therapy (to reduce ischemic events from CAD). Dual antithrombotic therapy (DAT), including both anticoagulants and antiplatelet agents, has been commonly used but carries a higher risk of bleeding. While current guidelines uniformly advocate for transitioning to oral anticoagulant monotherapy following an early phase of dual antithrombotic therapy, supporting evidence from randomized clinical trials for this approach is limited. Therefore, the EPIC-CAD trial was designed to evaluate the comparative efficacy and safety of edoxaban monotherapy versus DAT in long-term antithrombotic treatment.

Methods

The multicenter, open-label, adjudicator-masked randomized trial enrolled 1,040 patients across 18 sites in South Korea. Participants were randomized in a 1:1 ratio to receive either:

- Edoxaban monotherapy: Standard-dose oral anticoagulant (60 mg daily, adjusted to 30 mg for specific conditions).
- DAT: Edoxaban plus a single antiplatelet agent (aspirin or clopidogrel).

Eligibility criteria included age 18 years or older with prevalent or paroxysmal AF and concomitant stable CAD. Stable CAD was defined as previously treated CAD with either revascularization or medical therapy at least 6 months or 12 months prior to enrollment according to chronic or acute coronary syndrome. Exclusion criteria included a high risk of bleeding, a history of intracranial hemorrhage, prosthetic heart valves, and severe hepatic or renal dysfunction.

The primary outcome was net adverse clinical events (NACE), which was a composite of death, myocardial infarction, stroke, systemic embolism, unplanned revascularization, and major or clinically relevant nonmajor bleeding at 12 months after randomization. Secondary outcomes included individual components of the primary outcome and separate analyses of ischemic and bleeding events.

Results

Baseline characteristics were balanced between the two groups, with an average patient age of 72.1 years and a CHA_2DS_2-VASc score of 4.3. Approximately 65.7% of patients had previously undergone coronary revascularization. Key findings included:

1. Primary Outcome:

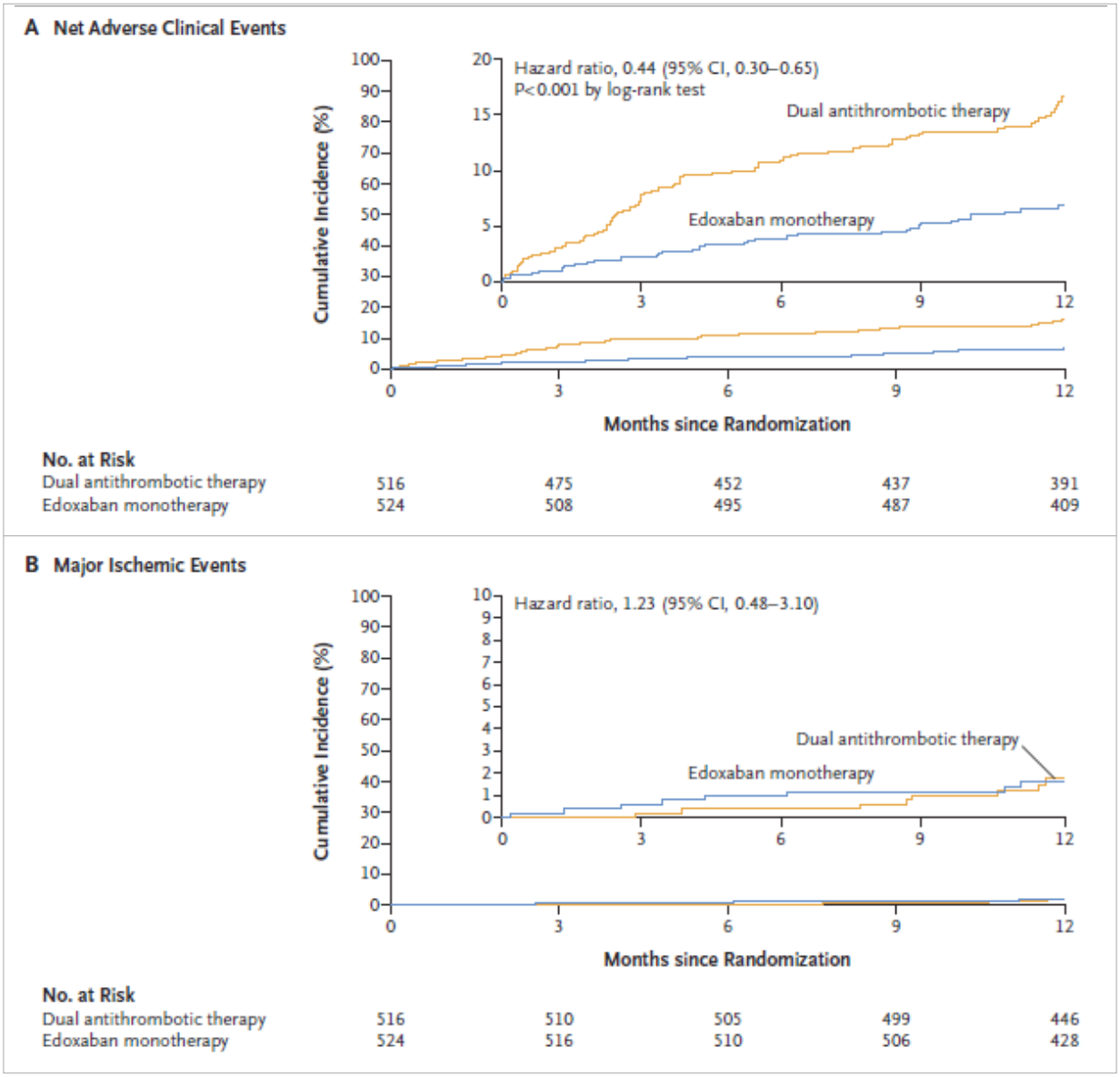
- The incidence was 6.8% in the edoxaban monotherapy group compared to 16.2% in the DAT group (hazard ratio [HR], 0.44; 95% confidence interval [CI], 0.30–0.65; P<0.001).

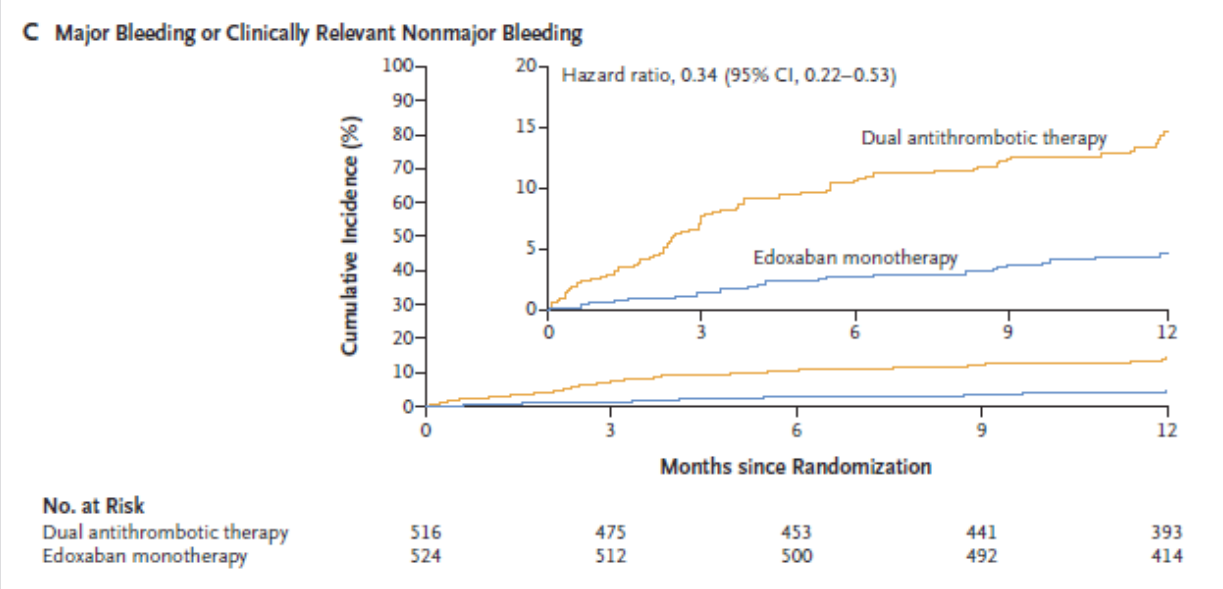
2. Secondary Outcomes:

- Major Ischemic Events: Rates of ischemic stroke, myocardial infarction, or systemic embolism were similar between groups, with cumulative ischemic event rates of 1.6% for edoxaban monotherapy and 1.8% for DAT.
- Bleeding Risk: Major or clinically relevant nonmajor bleeding occurred in 4.7% of patients receiving monotherapy versus 14.2% receiving DAT (HR, 0.34; 95% CI, 0.22–0.53).
- Mortality: No significant differences in all-cause or cardiovascular mortality were observed between groups.

3. Subgroup Analysis:

- Findings were consistent across prespecified subgroups, including those stratified by age, sex, creatinine clearance, and history of revascularization.





Discussion

The EPIC-CAD trial demonstrated that edoxaban monotherapy significantly reduced the net clinical adverse events at 12 months compared to DAT in patients with AF and stable CAD. This benefit was primarily driven by a reduction in bleeding events. Notably, the incidence of ischemic events was not significantly different between the two groups, highlighting the safety of edoxaban monotherapy while minimizing bleeding complications. These results align with prior studies (notably AFIRE and OAC-ALONE trials) and provided strong evidence through the use of a standardized edoxaban dosing protocol in patients with concomitant AF and CAD.

Limitations

1. Population Specificity: The focus on an East Asian population in the trial may limit applicability to broader demographics, especially in Western populations.
2. Open-Label Design: While independent adjudication of outcomes minimized bias, the open-label design might have introduced reporting bias.
3. Endpoint Composition: The primary composite outcome included a significant proportion of bleeding-related endpoints, which might have influenced the interpretation in favor of monotherapy.
4. Underrepresentation of Women: Only 22.9% of the participants were women, potentially affecting the applicability of findings to female patients.
5. Short Follow-Up: The 12-month follow-up period might not have captured long-term outcomes or dynamic changes in ischemic and bleeding risks over time.

Conclusions

In patients with AF and stable CAD, edoxaban monotherapy is superior to DAT in reducing net adverse clinical events, mainly due to a significant decrease in bleeding risk while maintaining ischemic protection, and these results support the adoption of simplified antithrombotic regimens for long-term management in this patient population. Further studies are needed to evaluate the generalizability of these results across diverse populations.

Funding and Acknowledgments

The trial was funded by the CardioVascular Research Foundation and supported by Daiichi Sankyo and Daewoong Pharmaceutical. The authors declared no conflicts of interest and ensured adherence to trial protocols and ethical standards.

Comment

The EPIC-CAD trial demonstrates the superiority of edoxaban monotherapy over dual antithrombotic therapy (DAT) in patients with atrial fibrillation and stable coronary artery disease. The study showed a significant reduction in net adverse clinical events (NACE) with monotherapy compared to DAT (6.8% vs 16.2%, HR 0.44), reinforcing current guidelines that recommend transitioning to oral anticoagulant monotherapy.

A distinctive feature of EPIC-CAD is its focus on East Asian populations, who have been historically underrepresented in cardiovascular trials. While this provides valuable data for this specific demographic, it also presents a limitation in generalizing the results to broader populations, particularly Western demographics.

Previous studies, including OAC-ALONE and AFIRE had limitations such as early termination leading to insufficient sample sizes or usage of non-standard dose of anticoagulant agent. EPIC-CAD overcame these limitations by using a standardized edoxaban dosing protocol and completing the planned enrollment, providing more reliable evidence for the efficacy of monotherapy.

However, it's important to note that the reduction in NACE was primarily driven by decreased bleeding events (4.7% vs 14.2%) rather than differences in ischemic outcomes (1.6% vs 1.8%). Given the low ischemic event rates observed in both groups, demonstrating any significant difference in efficacy between monotherapy and DAT would require an exceptionally large sample size, which would be challenging to achieve in practice.

In conclusion, EPIC-CAD provides valuable insights into long-term antithrombotic strategies, offering robust evidence supporting the safety and efficacy of oral anticoagulant monotherapy in this patient population while addressing previous studies' limitations.

Source

Cho, Min Soo, et al. "**Edoxaban Antithrombotic Therapy for Atrial Fibrillation and Stable Coronary Artery Disease**" *The New England Journal of Medicine*, vol. 391, no. 22, 2024, doi:10.1056/NEJMoa2407362

Edited by

Seongbong Wee, MD
Asan Medical Center, Korea (Republic of)

Do We Really Need Routine Stress Testing? New Evidence from High-Risk PCI Patients

Background

The POST-PCI trial was conducted to address the question of whether routine functional testing improves clinical outcomes in high-risk patients who have undergone percutaneous coronary intervention (PCI). Despite advances in stent technology and medical therapy, patients with obstructive coronary artery disease who undergo PCI are at risk of recurrent ischemia and cardiovascular events. Current guidelines recommend symptom-driven follow-up care, but routine stress testing is still performed in clinical practice, particularly for high-risk patients. However, there is limited evidence from randomized controlled trials to support this practice. The POST-PCI trial aimed to evaluate whether routine functional testing, conducted at 12 months after PCI, provides any additional benefit compared to standard care that includes stress testing only when clinically indicated.

Methods

This multicenter, randomized controlled trial was conducted in South Korea and included 1,706 patients with high-risk anatomical or clinical characteristics post-PCI. Patients were recruited from 11 hospitals and selected based on criteria such as left main coronary disease, bifurcation lesions, multivessel disease, diffuse long lesions, diabetes, or chronic renal failure.

Participants were randomized into two groups:

1. The **routine functional testing group**, which underwent stress testing (nuclear imaging, stress echocardiography, or exercise electrocardiography) 12 months after PCI.
2. The **standard care group**, which only received stress testing if symptoms or clinical indications arose.

The primary outcome was a composite of death from any cause, myocardial infarction (MI), or hospitalization for unstable angina over two years. Secondary outcomes included invasive coronary angiography, repeat revascularization, and hospitalization for any cause.

Data were analyzed on an intention-to-treat basis, and clinical events were adjudicated by a blinded committee.

Results

At the end of two years, the trial demonstrated no significant difference in the primary outcome between the two groups. In the routine functional testing group, 5.5% of patients experienced the composite endpoint of death, MI, or hospitalization for unstable angina, compared to 6.0% in the standard care group (Hazard Ratio [HR]: 0.90; 95% CI: 0.61–1.35; p=0.62).

For secondary outcomes, the routine testing group had slightly higher rates of invasive coronary angiography (12.3% vs. 9.3%) and repeat revascularization (8.1% vs. 5.8%). However, these increases did not result in a reduction in major adverse cardiovascular events or mortality. Hospitalization rates for any cause were similar between the two groups. Subgroup analyses showed consistent findings across different patient populations.

Table 1. Primary and Secondary Outcomes at 2 Years after Randomization.*

Outcome	Functional Testing (N=849)	Standard Care (N=857)	Difference in Event Rates (95% CI)	Hazard Ratio (95% CI)	P Value
	events (estimated percentage)		*percentage points*		
Primary composite outcome†	46 (5.5)	51 (6.0)	−0.53 (−2.76 to 1.70)	0.90 (0.61 to 1.35)	0.62
Death from any cause	23 (2.8)	28 (3.3)	−0.57 (−2.21 to 1.07)	0.82 (0.48 to 1.43)	
Myocardial infarction	4 (0.5)	10 (1.2)	−0.73 (−1.61 to 0.16)	0.40 (0.13 to 1.28)	
Hospitalization for unstable angina	19 (2.3)	14 (1.7)	0.63 (−0.72 to 1.98)	1.36 (0.68 to 2.72)	
Secondary outcomes					
Death or myocardial infarction	27 (3.2)	38 (4.5)	−1.28 (−3.12 to 0.56)	0.71 (0.43 to 1.17)	
Hospitalization					
Any reason	211 (25.5)	190 (22.8)	2.64 (−1.48 to 6.76)	1.12 (0.92 to 1.36)	
Cardiac reason	122 (14.8)	110 (13.3)	1.47 (−1.88 to 4.82)	1.10 (0.85 to 1.43)	
Noncardiac reason	89 (10.8)	80 (9.6)	1.16 (−1.75 to 4.07)	1.13 (0.83 to 1.52)	
Invasive coronary angiography	101 (12.3)	77 (9.3)	2.99 (−0.01 to 5.99)		
Showing restenosis or obstructive CAD	69 (68.3)	45 (58.4)			
Showing no restenosis or obstructive CAD	32 (31.7)	32 (41.6)			
Repeat revascularization	66 (8.1)	48 (5.8)	2.23 (−0.22 to 4.68)		
Target-lesion revascularization	34 (4.2)	26 (3.2)	1.00 (−0.81 to 2.81)		
Nontarget-lesion revascularization	32 (3.9)	22 (2.7)	1.24 (−0.48 to 2.96)		
PCI	64 (97.0)	45 (93.8)			
CABG	2 (3.0)	3 (6.3)			

* The number of events and estimated percentages were calculated with the use of a Kaplan–Meier survival analysis of data in the intention-to-treat population; therefore, the percentages may not reflect the ratio of the numerator and the denominator. Hazard ratios are for the routine functional-testing follow-up strategy as compared with the standard-care follow-up strategy. The 95% confidence intervals for secondary outcomes have not been adjusted for multiple comparisons, and therefore inferences drawn from these intervals may not be reproducible. CABG denotes coronary-artery bypass grafting, and CAD coronary artery disease.
† The primary composite outcome was death from any cause, myocardial infarction, or hospitalization for unstable angina.

The majority of patients in the routine testing group underwent functional testing as scheduled, while a small percentage of the standard care group received testing based on clinical need. Despite these differences, the study found no advantage to routine stress testing in terms of clinical outcomes.

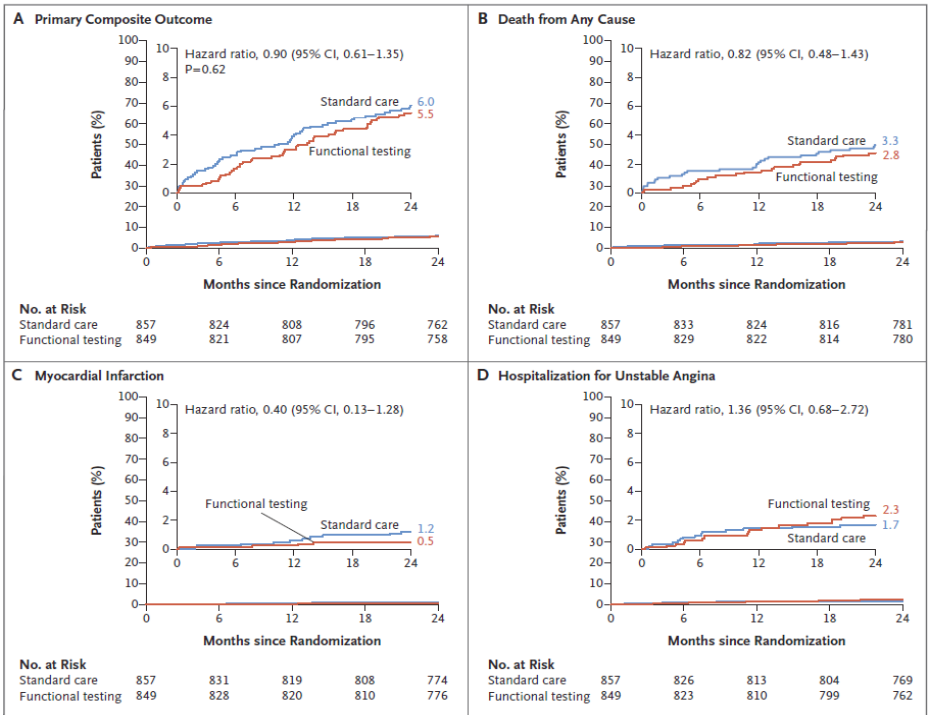


Figure 1. Time-to-Event Curves for the Primary Composite Outcome and the Components of the Primary Composite Outcome.
Shown is the cumulative incidence of the primary composite outcome of death from any cause, myocardial infarction, or hospitalization for unstable angina (Panel A), the cumulative incidence of death from any cause (Panel B), the cumulative incidence of myocardial infarction (Panel C), and the cumulative incidence of hospitalization for unstable angina (Panel D). The shown percentages are Kaplan–Meier estimates. The inset in each panel shows the same data on an enlarged y axis.

Discussion

The findings of the POST-PCI trial challenge the clinical utility of routine functional testing in high-risk PCI patients. While stress testing led to higher rates of invasive procedures, such as coronary angiography and revascularization, it did not translate into improved outcomes. This supports the growing evidence that symptom-driven follow-up care is sufficient for managing high-risk patients.

The results align with those of the ISCHEMIA trial, which demonstrated that aggressive initial invasive strategies did not yield better outcomes compared to conservative management in stable coronary artery disease patients. Together, these findings reinforce the "less is more" approach, suggesting that routine testing and invasive interventions should be reserved for patients with clear clinical indications.

The trial highlights the importance of focusing on guideline-directed medical therapy and individualized care rather than routinely performing stress tests. Advances in PCI techniques, stent technology, and adherence to secondary prevention strategies have already significantly improved patient outcomes, making routine testing less impactful.

Limitations

Several limitations should be considered when interpreting the results of this trial. First, the open-label design may have introduced bias, as patients and investigators were aware of the assigned follow-up strategy. Second, the study predominantly included male patients, limiting the generalizability of the findings to female populations. Third, the trial did not assess quality-of-life measures, cost-effectiveness, or the impact of radiation exposure from routine testing, which are important factors in evaluating the overall value of such strategies.

Although protocol adherence was high, some patients in the functional testing group did not complete stress testing due to medical reasons, reflecting real-world challenges in implementing routine testing. Lastly, the trial focused on short-term outcomes over two years, and longer-term implications of routine stress testing remain uncertain.

Conclusions

The POST-PCI trial provides robust evidence that routine functional testing at 12 months post-PCI does not improve clinical outcomes in high-risk patients compared to standard care. Symptom-driven follow-up, combined with intensive risk factor management and adherence to secondary prevention guidelines, is sufficient to optimize outcomes in this population. These findings suggest that routine stress testing can be safely omitted in stable high-risk PCI patients, reducing unnecessary procedures, costs, and patient burden.

This study supports a more conservative and personalized approach to post-PCI care, emphasizing the need to reserve interventions and diagnostic tests for clinically indicated cases. Future research should explore the long-term cost-effectiveness and quality-of-life impacts of different follow-up strategies, particularly in diverse patient populations.

Comment

The POST-PCI trial is a pivotal study that evaluates the necessity of routine functional testing in high-risk patients post-percutaneous coronary intervention (PCI). By targeting a population with complex anatomical or clinical risks, this trial fills a critical gap in evidence regarding optimal follow-up care. Its multicenter, randomized design and use of real-world data enhance the reliability and applicability of its findings.

The study's key takeaway is that routine functional testing does not improve clinical outcomes, such as reduced mortality or myocardial infarction, compared to symptom-driven standard care. This challenges the conventional reliance on routine testing and underscores the sufficiency of guideline-directed medical therapy and individualized care. These results align with the broader trend in cardiovascular medicine toward minimizing unnecessary interventions, reducing patient burden, and optimizing healthcare resources.

Notably, the trial emphasizes the importance of tailoring follow-up strategies to patient needs rather than applying uniform testing protocols. It also highlights the potential for cost savings and improved patient experiences by avoiding unnecessary stress testing. While robust in its design, the study opens doors for further research into long-term outcomes, subgroup-specific strategies, and greater inclusion of underrepresented populations, such as women.

In conclusion, the POST-PCI trial supports a shift toward symptom-driven care for high-risk PCI patients, reducing unnecessary procedures without compromising safety or efficacy. Its findings are likely to influence clinical guidelines and promote a more patient-centered, efficient approach to post-PCI care.

Source

Park, Duk-Woo, et al. "**Routine Functional Testing or Standard Care in High-Risk Patients after PCI**" *The New England Journal of Medicine*, vol. 387, no. 10, 2022, doi:10.1056/NEJMoa2208335

Edited by

Seunghan Lee, MD
Asan Medical Center, Korea (Republic of)

Preventive PCI for Vulnerable Plaques: Findings from the PREVENT Trial

Background

Acute coronary syndrome (ACS) and sudden cardiac death (SCD) are major causes of morbidity and mortality worldwide. These events often result from the rupture and thrombosis of lipid-rich atherosclerotic coronary plaques, commonly referred to as **vulnerable plaques (VPs)**. These plaques are typically non-flow-limiting, meaning they do not cause significant obstruction in the coronary arteries, making them difficult to detect using standard angiographic evaluation. Despite being inconspicuous, VPs are prone to rupture, leading to adverse cardiac events such as myocardial infarction (MI). Current guidelines recommend percutaneous coronary intervention (PCI) primarily for flow-limiting lesions or those causing ACS. The PREVENT trial was conducted to evaluate whether **preventive PCI**, targeting non-flow-limiting VPs, alongside optimal medical therapy (OMT), could reduce major adverse cardiac events (MACE) compared to OMT alone.

Methods

The PREVENT trial was a multicenter, open-label, randomized controlled trial conducted across 15 hospitals in South Korea, Japan, Taiwan, and New Zealand. Patients aged 18 or older with stable coronary artery disease or recent ACS undergoing cardiac catheterization were screened. Eligible patients had to have at least one non-flow-limiting VP, identified using advanced intracoronary imaging techniques, including intravascular ultrasound (IVUS) and optical coherence tomography (OCT). VPs were defined by features such as a small lumen area (<4.0 mm^2), high plaque burden (>70%), lipid-rich cores, or thin-cap fibroatheromas. A total of **1,606 patients** were randomly assigned to two groups:

1. **Preventive PCI + OMT Group (n=803):** PCI was performed on identified VPs, using bioresorbable vascular scaffolds or cobalt-chromium everolimus-eluting stents.
2. **OMT Group (n=803):** Patients received OMT alone, which included high-dose statins, antiplatelet therapy, and intensive management of risk factors.

The primary endpoint was a composite of cardiac death, target-vessel MI, ischemia-driven revascularization, or hospitalization for unstable angina at two years. Secondary endpoints included all-cause death, any MI, repeat revascularization, and patient-oriented composite outcomes. Patients were followed for a median of 4.3 years, with some followed for up to seven years.

Results

Preventive PCI significantly reduced adverse cardiac events compared to OMT alone. Over two years, the primary composite outcome occurred in **0.4%** of patients in the PCI group compared to **3.4%** in the OMT group, resulting in an absolute risk reduction of 3.0% (hazard ratio [HR]: 0.11; p=0.0003). This reduction was consistent across all components of the composite endpoint, including cardiac death, target-vessel MI, and ischemia-driven revascularization.

Long-term follow-up demonstrated sustained benefits, with fewer major adverse cardiac events in the PCI group even after seven years. Preventive PCI also reduced patient-oriented outcomes, such as all-cause death, MI, and revascularization. Patients treated with cobalt-chromium stents showed superior outcomes compared to those receiving bioresorbable vascular scaffolds. The procedure was safe, with procedural complications occurring in less than 1% of cases. Advanced imaging techniques such as IVUS and OCT, ensured precise identification and treatment of high-risk plaques, enhancing the efficacy and safety of the intervention.

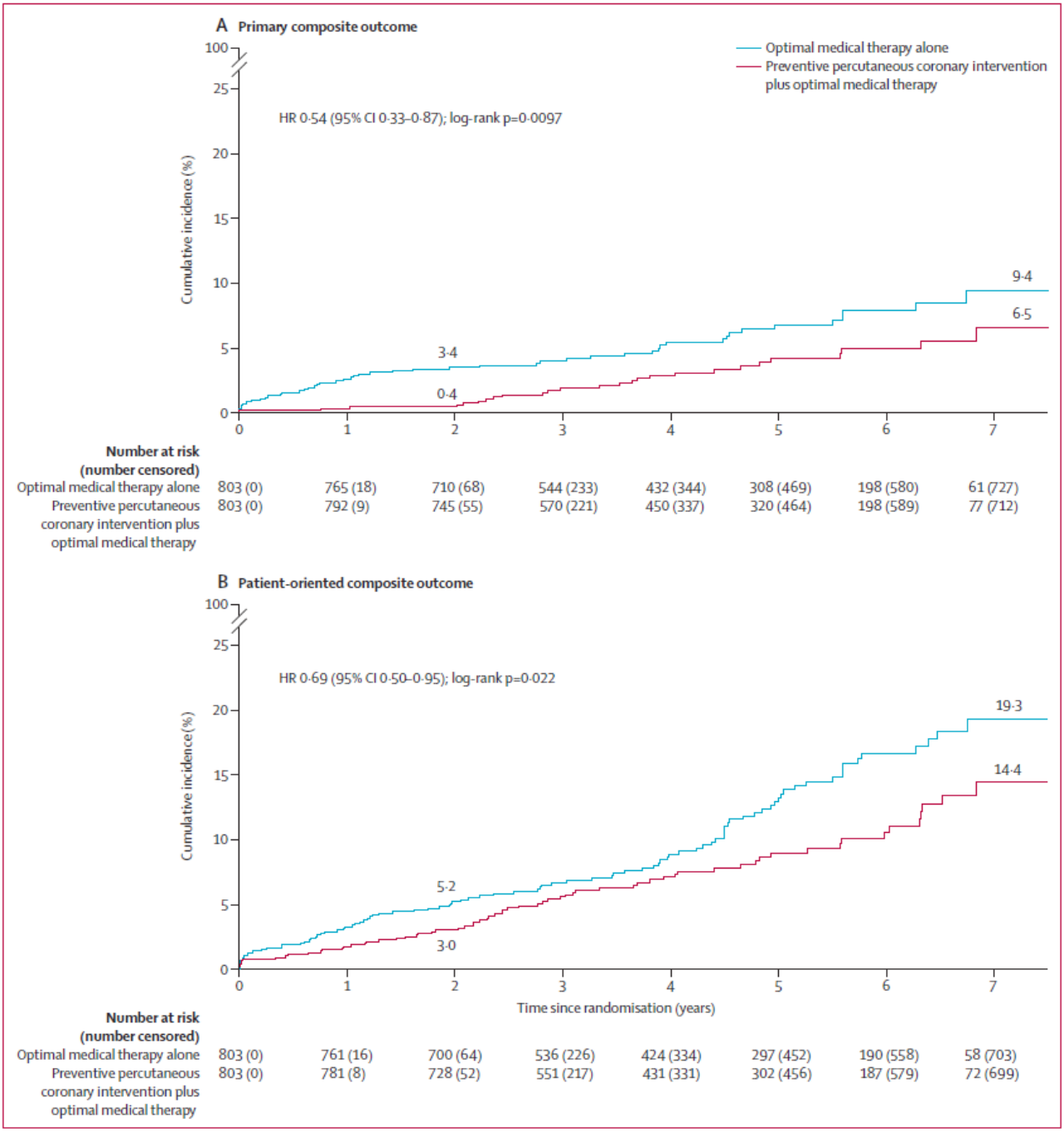


***Figure 1*: Time-to-event curves for the primary composite outcome and key secondary patient-oriented composite outcome**
(A) Cumulative incidence of the primary composite outcome of death from cardiac causes, target-vessel myocardial infarction, ischaemia-driven target-vessel revascularisation, or hospitalisation for unstable or progressive angina during the entire follow-up period. (B) Cumulative incidence of the secondary patient-oriented composite outcome of death from any cause, any myocardial infarction, or any repeat revascularisation. Event rates are noted at 2 years (the time of the primary endpoint) and at 7 years (maximum follow-up). HR=hazard ratio.

Discussion

The PREVENT trial underscores the transformative potential of preventive PCI for non-flow-limiting VPs. Current guidelines primarily address flow-limiting lesions, but the study reveals the substantial risk posed by seemingly mild plaques with high-risk features. Preventive PCI stabilizes these plaques by sealing lipid cores and thickening fibrous caps, reducing the risk of rupture and subsequent adverse events.

The findings advocate for revisiting treatment guidelines, as combined PCI with OMT delivered superior outcomes. Advanced imaging technologies played a crucial role in this strategy by allowing accurate identification of VPs that would otherwise go undetected.

Limitations

The study had several limitations. The geographic scope was limited to East Asia and New Zealand, with only 27% being women, which could restrict the generalizability of the findings. The open-label design introduced the possibility of bias, although adjudication of outcomes was blinded. Operator discretion in imaging modality selection could affect reproducibility. Additionally, the cost-effectiveness of widespread preventive PCI remain unexplored, warranting further research.

Conclusions

The PREVENT trial demonstrated that **preventive PCI**, combined with OMT, significantly reduces MACE in patients with non-flow-limiting VPs. This novel approach could lead to a paradigm shift in managing coronary artery disease by focusing on high-risk plaques identified through imaging, rather than solely on flow-limiting lesions. Future research should validate these findings in diverse populations, refine imaging criteria for plaque vulnerability, and assess the cost-effectiveness of this strategy.

Comment

The PREVENT trial marks a pivotal moment in interventional cardiology, challenging conventional guidelines by focusing on non-flow-limiting vulnerable plaques as targets for intervention. Traditionally, PCI has been reserved for flow-limiting lesions or those causing symptomatic ischemia. This study shifts the focus toward preventive strategies, demonstrating that early intervention on high-risk plaques can significantly reduce major adverse cardiac events (MACE) in both the short and long term.

A key strength of this trial lies in its use of advanced imaging modalities such as IVUS and OCT, enabling precise identification of high-risk plaques with features such as high plaque burden and small lumen area. This imaging-guided approach not only ensured procedural safety but also highlighted the importance of adopting innovative diagnostic tools in routine practice. The trial's results, with a 3% absolute risk reduction in MACE at two years and sustained benefits over seven years, underscore the potential of preventive PCI to redefine the management of coronary artery disease.

The findings also reinforce the value of combining preventive PCI with optimal medical therapy, suggesting that this dual strategy offers superior outcomes compared to medical therapy alone. Furthermore, the safety profile of PCI in this context, with minimal procedural complications, alleviates concerns about intervening on non-flow-limiting lesions.

Despite its strengths, the study's geographic focus and underrepresentation of women highlight the need for broader validation in diverse populations. Additionally, while the trial provides robust clinical evidence, further research is required to address cost-effectiveness and scalability, especially in resource-limited settings.

In conclusion, the PREVENT trial emphasizes the transformative potential of imaging-guided, preventive PCI in managing coronary artery disease. By expanding the scope of intervention to include non-flow-limiting vulnerable plaques, this study lays the groundwork for a more proactive and effective approach to cardiovascular risk reduction.

Source

Park, Seung-Jung, et al. "**Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial**" *The Lancet*, vol. 403, issue 10438, 2024, p. 1753, doi:10.1016/S0140-6736(24)00413-6

Edited by

Soo Yeon An, MD
Asan Medical Center, Korea (Republic of)

Rethinking Aspirin: Perioperative Strategies for Patients with Coronary Stents

Background

The ASSURE-DES trial was conducted to evaluate the perioperative management of antiplatelet therapy in patients with coronary drug-eluting stents (DES) undergoing low-to-intermediate risk noncardiac surgery. Patients in this category pose a significant challenge due to the dual risks of thrombotic events and bleeding. Current guidelines advocate for continuing aspirin perioperatively, but the supporting evidence is inconsistent and primarily based on observational studies or data from earlier-generation DES. The trial aimed to determine whether aspirin monotherapy or temporary cessation of all antiplatelet therapy provides superior outcomes in this clinical scenario.

Methods

This multicenter, randomized controlled trial was conducted across 30 centers in Korea, India, and Turkey. A total of 926 stable patients with a history of DES implantation at least one year prior were enrolled and randomized into two groups. The aspirin monotherapy group continued aspirin (100 mg daily) throughout the perioperative period, whereas the no antiplatelet therapy group stopped all antiplatelet agents five days before surgery and resumed therapy no later than 48 hours after surgery. The primary composite outcome was defined as the occurrence of death from any cause, myocardial infarction, stent thrombosis, or stroke within 30 days after surgery. Secondary outcomes included individual components of the primary outcome and bleeding events categorized as major or minor.

Patient characteristics were well-balanced between groups, with a mean age of approximately 68 years. Most surgeries were classified as intermediate or low risk for both cardiovascular and bleeding complications. The majority of participants had second-generation or newer DES.

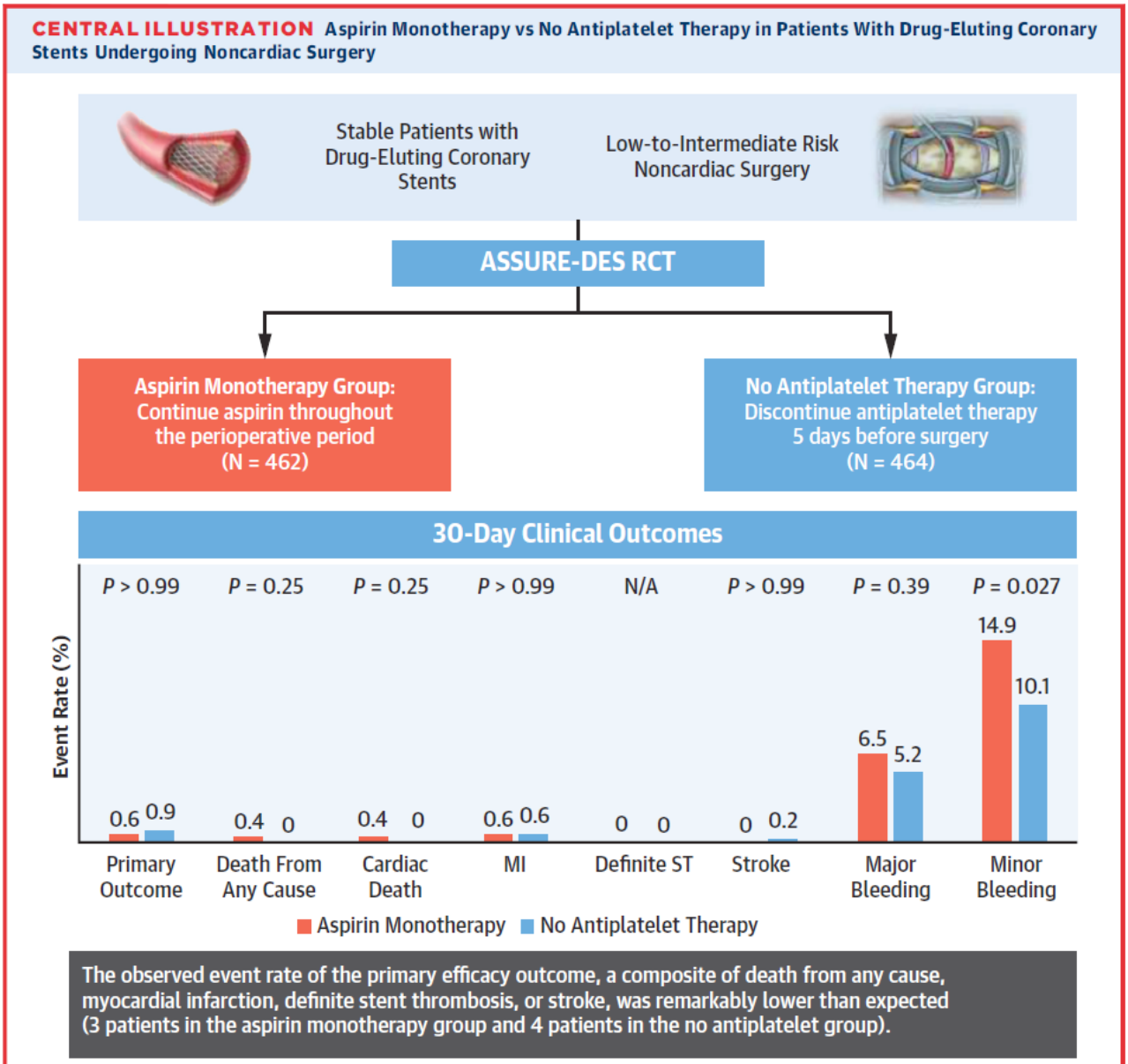
Results

The trial demonstrated no significant difference in the primary composite outcome between the aspirin monotherapy group and the no antiplatelet therapy group (0.6% vs. 0.9%; difference, -0.2 percentage points; 95% CI: -1.3 to 0.9; $P > 0.99$). Notably, there were no cases of stent thrombosis in either group.

The incidence of major bleeding was comparable between groups (6.5% vs 5.2%; $P = 0.39$). However, minor bleeding was significantly more frequent in the aspirin monotherapy group, affecting 14.9% of patients compared to 10.1% in the no antiplatelet therapy group ($P = 0.027$). As a result, the net adverse clinical event rate, encompassing both thrombotic and bleeding events, was higher in the aspirin group (21.9% vs. 16.2%; $P = 0.027$).

The trial also highlighted differences in postoperative antiplatelet management. Patients in the aspirin monotherapy group resumed antiplatelet therapy sooner and were more likely to restart dual antiplatelet therapy than those in the no antiplatelet group. These differences may have influenced postoperative outcomes, though their clinical significance remains uncertain.

CENTRAL ILLUSTRATION Aspirin Monotherapy vs No Antiplatelet Therapy in Patients With Drug-Eluting Coronary Stents Undergoing Noncardiac Surgery



Kang D-Y, et al. JACC. 2024;■(■):■-■.

ASSURE DES = Aspirin in Patients With Drug-Eluting Stents Undergoing Noncardiac Surgery; MI = myocardial infarction; RCT = randomized controlled trial; ST = stent thrombosis.

Discussion

The ASSURE-DES trial provides important insights into the evolving management of antiplatelet therapy in patients with DES undergoing noncardiac surgery. The findings challenge the traditional guideline recommendations that advocate for the continuation of aspirin during the perioperative period. In this study, temporarily holding antiplatelet therapy did not lead to an increase in ischemic events, including stent thrombosis, myocardial infarction, or stroke. This outcome is likely attributable to the improved safety profile of contemporary-generation DES, which have a lower thrombotic risk compared to earlier stents.

Despite these findings, the trial underscores the need for individualized decision-making in clinical practice. While most patients undergoing low-to-intermediate risk surgeries may safely discontinue antiplatelet therapy, certain high-risk subgroups may still benefit from continued aspirin use. Similarly, patients with elevated bleeding risk might derive greater safety from a strategy of temporary cessation.

The study's limitations should be considered when interpreting the results. The observed event rates were lower than expected, potentially limiting the statistical power to detect small differences between groups. Additionally, the study predominantly included East-Asian patients, who are known to have distinct bleeding and thrombotic risk profiles, limiting the generalizability of the findings to other populations. Furthermore, the study focused primarily on low-to-intermediate risk surgeries, leaving high-risk surgical scenarios underrepresented. The lack of systematic cardiac biomarker assessments in all patients may have also led to underestimation of subclinical myocardial infarction.

Conclusions

The ASSURE-DES trial suggests that for stable patients with DES undergoing low-to-intermediate risk noncardiac surgery, temporarily holding all antiplatelet therapy is a safe alternative to continuing aspirin monotherapy. While the continuation of aspirin did not significantly reduce ischemic events, it was associated with a modest increase in minor bleeding. These findings highlight the need for a flexible and patient-centered approach to perioperative antiplatelet management, considering individual risk factors and surgical profiles.

The trial's findings have important implications for clinical guidelines, supporting a more nuanced strategy for perioperative antiplatelet therapy in patients with DES. Future studies should aim to include more diverse populations and high-risk surgical scenarios to confirm and extend these results. Until then, clinicians should carefully weigh the risks and benefits of antiplatelet strategies to optimize patient outcomes in this complex clinical setting.

Comment

The ASSURE-DES study is a pivotal contribution to understanding perioperative antiplatelet management in patients with drug-eluting stents (DES). Its findings challenge conventional guidelines that recommend continuing aspirin during noncardiac surgeries, offering evidence that temporarily discontinuing antiplatelet therapy can be a safe alternative for low-to-intermediate risk procedures.

One of the key strengths of this study is its focus on contemporary-generation DES, which have significantly reduced thrombotic risks compared to earlier generations. By demonstrating no significant increase in ischemic events with temporary cessation of antiplatelet therapy, the study underscores the importance of reevaluating rigid perioperative practices in the context of modern stent technology. This finding allows for greater flexibility in managing patients, particularly those at high risk for bleeding.

The trial's emphasis on bleeding outcomes is another noteworthy aspect. While many studies have prioritized the prevention of thrombotic events, the ASSURE-DES trial highlights that continued aspirin use increases minor bleeding without providing substantial ischemic protection. This nuanced view is critical for optimizing perioperative care, especially for patients with elevated bleeding risks.

Despite its contributions, the study's limitations—such as low event rates and underrepresentation of high-risk surgeries—highlight the need for further research. Future studies should focus on higher-risk procedures and more diverse populations to enhance the applicability of these findings.

In conclusion, the ASSURE-DES study paves the way for a more individualized approach to perioperative antiplatelet management, aligning with advancements in stent technology and patient-specific risk profiles. Its findings hold the potential to improve patient outcomes and streamline clinical decision-making, fostering a more tailored and effective standard of care.

Source

Kang, Do-Yoon, et al. "**Aspirin Monotherapy vs No Antiplatelet Therapy in Stable Patients With Coronary Stents Undergoing Low-to-Intermediate Risk Noncardiac Surgery**" *JACC*, vol. 84, no. 24, 2024, p. 2380, doi:10.1016/j.jacc.2024.08.024

Edited by

Kyeongwon Seo, MD
Asan Medical Center, Korea (Republic of)

OCTIVUS Trial: Unveiling the Power of OCT and IVUS in Complex Coronary Interventions

Introduction

The OCTIVUS trial was conducted to investigate the comparative effectiveness and safety of optical coherence tomography (OCT) and intravascular ultrasound (IVUS) in guiding percutaneous coronary intervention (PCI) for complex coronary artery lesions. These lesions, such as bifurcations, left main disease, and diffuse long lesions, present unique challenges in clinical settings. The study aimed to directly compare these two imaging modalities, which are both well-regarded for their roles in optimizing PCI outcomes. Previous studies demonstrated the benefits of imaging-guided PCI over traditional angiography, but this trial sought to clarify which imaging technique offers superior advantages in challenging cases. The importance of resolving this question lies in the potential to refine clinical guidelines and enhance patient outcomes in scenarios where anatomical complexity complicates intervention strategies.

Methods

The trial enrolled 2,008 patients from nine South Korean centers between April 2018 and January 2022. Among these patients, 1,475 were classified as having complex coronary lesions. Participants were randomized into two groups: one underwent OCT-guided PCI, while the other received IVUS-guided PCI. By maintaining broad inclusion criteria and limiting exclusion factors, the study ensured a diverse population. The imaging protocols employed in both groups were designed to optimize stent implantation through precise measurement of lesion characteristics, stent sizing, and post-implantation assessment. Operators adhered to standardized algorithms to ensure consistency, while follow-ups were conducted at regular intervals over a five-year period.

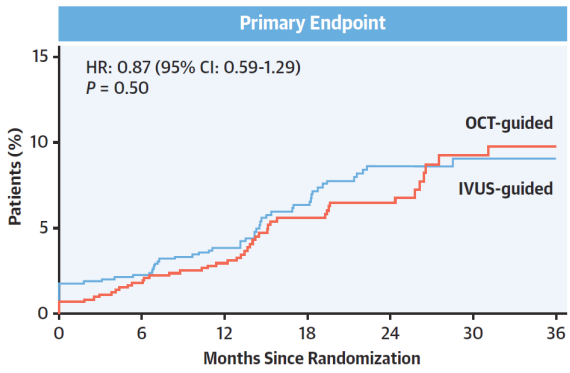
The primary endpoint was a composite of cardiac death, target vessel myocardial infarction (TVMI), and ischemia-driven target vessel revascularization (TVR). Secondary endpoints included individual components of the primary outcome, as well as procedural complications and imaging-based success rates. The design also accounted for subgroup analyses, providing insight into specific lesion types, such as in-stent restenosis and chronic total occlusions. Rigorous data collection protocols ensured that all clinical events were independently adjudicated by blinded committees to maintain objectivity.

Results

Results showed that baseline characteristics were generally similar between the two groups, with a slightly lower SYNTAX score observed in the OCT cohort. Notably, OCT-guided procedures required more contrast dye but were completed more quickly than IVUS-guided procedures. Over a median follow-up of two years, the primary endpoint occurred in 6.5% of the OCT group and 7.4% of the IVUS group, demonstrating comparable effectiveness (hazard ratio [HR]: 0.87; $p = 0.50$). However, OCT significantly reduced the incidence of TVMI, with rates of 0.8% compared to 2.4% in the IVUS group ($p = 0.03$). Procedural complications were also notably lower in the OCT group at 1.7% versus 3.4% in the IVUS group ($p = 0.03$).

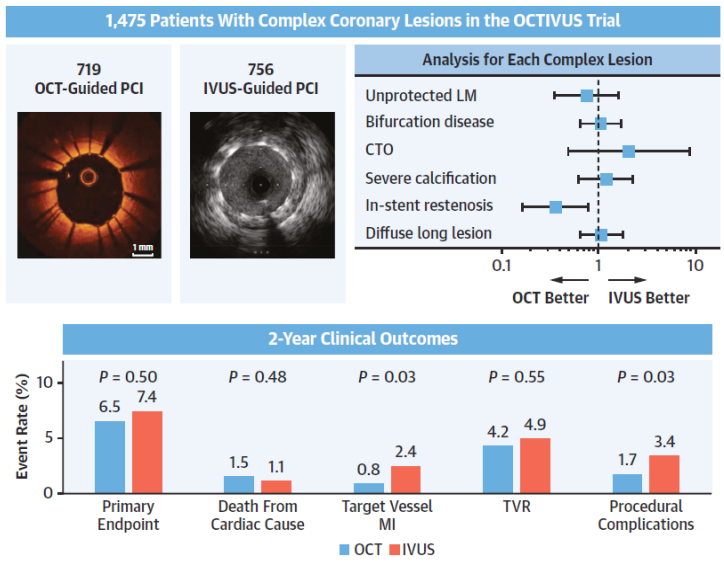
One of the standout findings was OCT's superiority in managing in-stent restenotic lesions. Its high-resolution imaging allows for detailed evaluation of neointimal hyperplasia and neoatherosclerosis, enabling more precise interventions. These capabilities make OCT particularly valuable for addressing stent failure mechanisms, a critical factor in recurrent coronary events. The imaging advantage was especially pronounced in complex bifurcation lesions, where accurate stent positioning is paramount. Despite these advantages, the trial noted that imaging optimization criteria were only met in approximately half of the patients, highlighting variability in real-world application. Further analysis of these trends suggests that operator experience and adherence to imaging protocols play significant roles in determining outcomes.

FIGURE 1 Time-to-Event Curves of the Primary Endpoint



The primary endpoint was a composite of death from cardiac causes, target vessel–related myocardial infarction, or ischemia-driven target vessel revascularization. HRs are presented for the OCT-guided PCI group, as compared with the IVUS-guided PCI group. Abbreviations as in Figure 1.

CENTRAL ILLUSTRATION Optical Coherence Tomography- vs Intravascular Ultrasound-Guided Percutaneous Coronary Intervention for Complex Coronary Artery Disease



Kang D-Y, et al. J Am Coll Cardiol. 2024;83(3):401–413.

In 2,008 randomized patients in the OCTIVUS (Optical Coherence Tomography versus Intravascular Ultrasound Guided Percutaneous Coronary Intervention) trial, 1,475 (73.5%) underwent imaging-guided percutaneous coronary intervention (PCI) for complex coronary artery lesions; 719 (48.7%) received optical coherence tomography (OCT)-guided and 756 (51.3%) received intravascular ultrasound (IVUS)-guided PCI. At a median follow-up of 2.0 years, the event rate of the primary endpoint, death from cardiac cause, target-vessel myocardial infarction (MI), ischemia-driven target-vessel revascularization (TVR) was comparable between 2 groups, whereas the incidence of target vessel MI and major procedural complications was lower in the OCT-guided group than in the IVUS-guided group. Overall results on primary endpoint appeared consistent across complex anatomical subgroups without a differential treatment effect between OCT and IVUS, except that OCT-guided PCI showed better outcomes than IVUS-guided PCI for treatment of in-stent restenotic lesions. CTO = chronic total occlusion; LM = left main.

Discussion

While OCT and IVUS offered similar overall outcomes, each modality displayed unique strengths. OCT's ability to reduce procedural complications and myocardial infarctions, combined with its exceptional resolution, underscores its utility in complex scenarios. The findings align with previous research showing that imaging-guided PCI improves outcomes compared to angiography alone. The nuanced capabilities of OCT, such as its ability to delineate plaque characteristics and assess stent expansion, make it a particularly valuable tool for high-risk and anatomically complex cases. However, the study also identified limitations, including lower-than-expected event rates, which reduced statistical power. Additionally, the unblinded design introduced potential bias, though rigorous randomization and adjudication minimized its impact. Geographic and ethnic differences further limit the generalizability of these findings, as vessel size and treatment regimens can vary across populations.

Limitations

The trial faced several limitations. The lower-than-expected event rates reduced statistical power, necessitating cautious interpretation of subgroup findings. The unblinded design introduced potential bias, although rigorous randomization helped mitigate its effects. Additionally, imaging optimization criteria were achieved in only about half of the patients, reflecting variability in operator adherence and interpretation. Geographic and ethnic considerations also limited the generalizability of the results, as differences in vessel size and treatment strategies can affect outcomes. Furthermore, the cost implications of widespread OCT adoption were not assessed, leaving an important gap in understanding the economic impact of this imaging strategy.

Conclusions

In conclusion, OCT-guided PCI proved to be as effective as IVUS-guided PCI while offering additional benefits such as fewer procedural complications and a lower risk of TVMI. These findings suggest that either modality can be chosen based on operator expertise and specific clinical scenarios, with OCT showing particular promise for treating in-stent restenosis. Future research should explore the cost-effectiveness of these techniques, identify patient subgroups that might benefit most, and investigate the potential for integrating advanced technologies like artificial intelligence to enhance imaging interpretation and decision-making. As the field evolves, the OCTIVUS trial reinforces the importance of tailoring imaging strategies to individual patients and their unique lesion characteristics. Additionally, the trial highlights the need for ongoing education and training to ensure that imaging optimization protocols are effectively implemented, maximizing the benefits of these advanced technologies in routine clinical practice.

Comment

The OCTIVUS trial stands out as a landmark study in the field of interventional cardiology, offering critical insights into the comparative roles of OCT and IVUS in managing complex coronary artery lesions. Unlike previous trials that predominantly compared imaging guidance with angiography, OCTIVUS provides a direct comparison between two advanced modalities, offering clinicians a clearer understanding of their respective advantages and limitations.

The trial's findings underscore the importance of high-resolution imaging in improving procedural safety and long-term outcomes. OCT's demonstrated ability to reduce target vessel myocardial infarctions and procedural complications positions it as a preferred modality in scenarios requiring meticulous stent placement and post-implantation assessment. Its superiority in managing in-stent restenosis represents a significant advancement in addressing recurrent coronary events.

Subgroup analyses provide valuable insights into OCT and IVUS performance across lesion types. The superior outcomes observed in OCT-guided treatment of bifurcation and in-stent restenosis reinforce its role in anatomically challenging cases. This level of granularity enables clinicians to tailor their imaging choice to specific patient needs.

Looking ahead, the implications of the OCTIVUS trial extend beyond the immediate findings. The study highlights opportunities for exploring cost-effectiveness, integrating artificial intelligence, and developing standardized imaging protocols. These advancements could further enhance the precision and efficiency of both modalities, reducing variability in outcomes and improving patient care. By emphasizing the need for operator training and protocol standardization, this study lays the groundwork for advancing imaging-guided PCI and shaping future clinical guidelines.

Source

Kang, Do-Yoon, et al. "**Guiding Intervention for Complex Coronary Lesions by Optical Coherence Tomography or Intravascular Ultrasound**" *JACC*, vol. 83, no. 3, 2024, p. 401, doi:10.1016/j.jacc.2023.10.017

Edited by

Hansu Park, MD
Asan Medical Center, Korea (Republic of)

CVRF Focus Journal

VOL.1

CVRF
CardioVascular Research Foundation

발 행 인 박 승 정

편 집 인 박 승 정

발 행 일 2025년 3월 25일 (통권 제1호)

발 행 소 재단법인 심장혈관연구재단
서울 송파구 올림픽로43길 88 (풍납동, 서울아산병원)

등 록 2024년 10월 10일 (송파,사00038, 연2회간)