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Revisiting Landmark Trials: How DCB Therapy and Plant-Based Diets Transform Chronic Coronary Syndrome Care

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Abstract

Landmark trials, from COURAGE to ISCHEMIA, have profoundly influenced clinical guidelines by emphasizing optimal medical therapy (OMT) as the primary management strategy for chronic coronary syndrome (CCS) due to limited incremental benefits demonstrated by invasive percutaneous coronary interventions (PCI) utilizing conventional stents. However, significant advancements in Drug-Coated Balloon (DCB) technology and Plant-Based Diet (PBD) strategies have demonstrated exceptional clinical outcomes, dramatically reshaping the therapeutic landscape. Clinical results, including exceedingly minor procedural complications, low rates of repeat revascularization, minimal restenosis (<2%), complete elimination of stent thrombosis, and markedly reduced bleeding risks associated with abbreviated or eliminated dual antiplatelet therapy (DAPT), are primarily attributed to meticulous lesion preparation protocols and diet-driven systemic improvements. This review comprehensively discusses these novel findings, exploring their implications for updating clinical guidelines. Real-world data from Bethsaida Hospital, chaired by Prof. Dasaad Mulijono, substantiates these outcomes, emphasizing the clinical superiority of integrating advanced DCB therapies and PBD, suggesting the need to revisit foundational conclusions drawn from previous landmark trials.

Keywords: Chronic coronary syndrome; Drug-Coated Balloon; ISCHEMIA trial; COURAGE trial; Optimal medical therapy; Restenosis; Stent thrombosis; Plant-based diets; Bethsaida Hospital; Prof. Dasaad Mulijono

Introduction

The management of CCS has been profoundly influenced by landmark clinical trials such as COURAGE, BARI 2D, FAME 2, ORBITA, and ISCHEMIA. Collectively, these trials established OMT as the primary recommended strategy, due to limited incremental benefits observed with invasive PCI involving conventional stenting. These studies consistently highlighted minimal reductions in primary cardiovascular outcomes, including mortality and myocardial infarction (MI), reinforcing the appropriateness of a conservative, medication-centered approach to CCS management [1-3].

However, the clinical landscape has undergone transformative changes driven by significant technological and lifestyle advancements. DCB therapy has emerged as a superior interventional strategy, addressing several critical limitations inherent in conventional stent technologies, such as restenosis, stent thrombosis, and bleeding complications associated with prolonged DAPT [4-51]. Concurrently, evidence supporting the systemic benefits

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of PBD has grown robustly, highlighting their role in significantly improving cardiovascular health outcomes by reducing inflammation, enhancing endothelial function, and decreasing thrombogenic risks [52-56].

Real-world clinical data from Bethsaida Hospital, under the leadership of Prof. Dasaad Mulijono, demonstrate groundbreaking outcomes that challenge established clinical paradigms. Over five years of follow-up involving nearly two thousand patients, integrated DCB and PBD strategies have consistently yielded exceptionally low complication rates: procedural complications remain minimal, repeat revascularization rates are less than 3%, restenosis rates have dropped below 2%, and stent thrombosis has been eliminated. Additionally, significantly reduced or eliminated reliance on prolonged DAPT has markedly decreased bleeding risks.

These compelling clinical achievements suggest that the foundational assumptions of the landmark trials, conducted primarily using older stent technologies, may no longer reflect the potential of modern therapeutic interventions. This review critically examines the implications of advanced DCB techniques combined with evidence-based nutritional interventions, proposing a necessary reappraisal of current clinical guidelines for CCS management. Such reassessment, supported by ongoing and future randomized controlled trials, is crucial for optimizing patient outcomes and defining the next era in cardiovascular care.

Optimal Medical Therapy vs. Intervention: Insights from Landmark Trials

Several pivotal trials have fundamentally reshaped clinical guidelines in managing CCS. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE, 2007) trial first demonstrated that adding PCI with conventional stenting to OMT did not significantly reduce mortality, MI, or major cardiovascular events in CCS patients, thus reinforcing the appropriateness of initial conservative management [57].

Further, the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D, 2009) trial confirmed similar outcomes in diabetic patients, indicating no substantial benefit in mortality or cardiovascular events with routine revascularization compared to intensive OMT alone [58].

The Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2 (FAME 2, 2012) trial demonstrated reduced urgent revascularization rates with FFR-guided PCI. Still, it failed to show significant reductions in mortality or MI rates, highlighting limited incremental benefits beyond symptom relief [59].

The Objective Randomized Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina (ORBITA) in 2017, a placebo-controlled trial, provided rigorous evidence showing a minimal symptomatic advantage of PCI over placebo, critically challenging established symptom-relief perceptions [60].

Finally, in 2019 the International Study of Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA) trial further solidified these findings, demonstrating that initial invasive strategies offered no significant advantage over OMT alone in reducing cardiovascular death or MI, thus firmly cementing OMT's role as the foundational management strategy in CCS guidelines [61].

Limitations of Landmark Trials with Advancements in DCB and PBD

Despite their critical influence, landmark trials from COURAGE to ISCHEMIA were conducted using conventional stent technologies, which were inherently limited by high rates of restenosis (10-20%), stent thrombosis (1-3%), and prolonged antiplatelet therapy-associated bleeding complications. Recent advancements, notably DCB therapy integrated with comprehensive lesion preparation and PBD, dramatically mitigate these limitations.

Over a five-year follow-up on almost two thousand patients, clinical evidence from Bethsaida Hospital highlights remarkable outcomes: no mortality reported, minor procedural complications, repeat revascularization rates below 3%, restenosis below 2%, complete elimination of stent thrombosis incidents, and negligible bleeding complications due to significantly shortened or eliminated DAPT. These outcomes indicate that advanced DCB therapies eliminate historical limitations and substantially enhance clinical efficacy and patient safety.

Role of Plant-Based Diets

Integration of plant-based dietary interventions significantly contributes to enhanced clinical outcomes through systemic improvements. PBD reduces inflammation, improves endothelial function, and lowers thrombogenicity, critically supporting lesion stabilization and vascular health post-DCB treatment [52-56]. These synergistic effects substantially mitigate the risk factors historically responsible for adverse cardiovascular outcomes post-intervention, including restenosis and thrombosis.

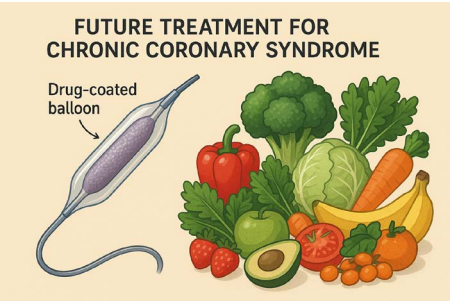

Figure 1: Experience at Our Cardiology Centre, Bethsaida Hospital, Indonesia.

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Implications for Clinical Practice and Guidelines

Given these substantial advancements, the foundational assumptions of landmark trials, particularly regarding the comparative efficacy and safety of invasive versus conservative strategies, require significant reconsideration. With advanced DCB interventions achieving unprecedentedly low complication rates and vastly superior outcomes, invasive strategies now potentially surpass the benefits of OMT alone, especially in complex or higher-risk patient populations previously deemed optimally managed conservatively. Larger randomized clinical trials are needed to confirm this view.

Conclusion

The integration of DCB therapy and PBD strategies represents a transformative evolution in the management of CCS. Advanced DCB interventions have overcome significant limitations previously associated with conventional stent technologies, drastically reducing restenosis, eliminating stent thrombosis, and minimizing bleeding risks related to DAPT. Furthermore, the systemic benefits of PBD substantially enhance vascular health and mitigate inflammation, augmenting the long-term effectiveness of invasive treatments. Under Prof. Dasaad Mulijono's leadership, real-world outcomes from Bethsaida Hospital underscore this integrative approach's clinical superiority and practical feasibility. Consequently, established guidelines, informed mainly by earlier landmark trials employing older technologies, require critical reassessment. Future randomized clinical trials are essential to validate these promising findings further and refine clinical practice, ultimately improving patient care and outcomes in contemporary cardiology.

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