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EDITORIAL COMMENT

Perforations in Complex PCI

Accepting the Risk, Minimizing the Harm With Intracoronary Imaging

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Coronary artery perforation (CAP) is a rare yet serious complication of percutaneous coronary intervention (PCI), occurring in approximately 1 in 250 cases. CAP incidence is increased in complex PCI, particularly in older patients, women, and those with calcified coronary anatomy.[1,2] Although recent meta-analyses, which included trials ILUMIEN IV (Optical Coherence Tomography-Guided versus Angiography-Guided PCI) and OCTOBER (OCT or angiography guidance for PCI in complex bifurcation lesions), demonstrate that intravascular imaging (intravascular ultrasound [IVUS]/optical coherence tomography)-guided PCI reduces major adverse cardiovascular events, data on the incidence of rarer complications like coronary perforation remain limited.[3] The 2024 European Society of Cardiology guidelines now strongly recommend imaging-guided PCI (Class 1A), emphasizing the importance of risk mitigation strategies as the global use of complex PCI grows.[4] However, the extent to which imaging mitigates the risk of CAP remains uncertain.

In this issue of *JACC: Asia*, the study of intravascular imaging use and coronary perforation by Sawayama et al[5] is a large observational study that looked at real-world data in a single large-volume center from January 2006 to October 2023. The main aim was to evaluate rates of CAP with intravascular imaging (IVI)-guided PCI. CAP occurred in 1.6% of patients (368 of 22,368), with higher short- and long-term mortality in those patients who developed CAP. This incidence is 4-fold higher than a recent large meta-analysis of all-comer PCI trials, likely reflecting the increased complexity of PCI performed in the present analysis.[1] In total, 63% of total cases used IVI, the majority of which were IVUS. The trends observed increasing PCI of moderately to severely calcified lesions. There was a temporal linear trend for IVI guided PCI; significantly more IVI-guided imaging procedures were performed with time, rising 30% in 2006 to 2010 to 97% in 2021 to 2023. This trend was associated with a reduction in the incidence of CAP from 2.1% to 1.18% ($P < 0.001$) over the same time.

Is this association or causation? Notably, the trend was observed regardless of coronary location and lesion type. IVI-guided PCI was associated with a lower risk of overall CAP incidence (adjusted OR: 0.78; 95% CI: 0.61-0.99; $P = 0.047$). This reduction was particularly driven by PCI for chronic total occlusion (CTO) (adjusted OR: 5.95; 95% CI: 4.72-7.50; $P < 0.001$) and moderate to severe calcification (adjusted OR: 1.92; 95% CI: 1.49-2.47; $P < 0.001$), both of which were robustly associated with an increased risk of CAP. The evaluation of vessel and plaque characteristics using imaging is crucial, but the imaging catheter alone does not change outcomes. Instead, the operator's interpretation of the findings, particularly, vessel size, plaque morphology and calcium can help guide the lesion modification strategy and appropriate balloon and stent selection. This ultimately, may reduce the risk of CAP. Prevention is better than cure.

Sawayama et al[5] highlight the ongoing mortality risk up to 5 years post-CAP, emphasizing the need for standardized CAP management protocols to reduce these significant mortality rates. A recent meta-analysis examining CAP incidence and temporal trends found that only one-half of the included studies reported on CAP management, with treatment data likely confounded by the heterogeneous strategies used across studies.[1] This underscores the

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importance of algorithmic management to optimize outcomes. Future research evaluating the effectiveness of contemporary thin-strut covered stents such as the Papyrus stent (Biotronik) when deployed and sealed under imaging guidance would provide valuable insights.

LIMITATIONS AND CLINICAL CONTEXT

As a nonrandomized retrospective observational study, it was subject to selection bias and other confounders, including the collective experience of the department over time, which may have contributed to the observed reduction in coronary perforation. Additionally, the treatment strategy for CAP was not standardized, and most cases used IVUS rather than optical coherence tomography, limiting the generalizability of the findings to other intravascular imaging modalities.

A wealth of accumulating data has led to the recent European Society of Cardiology Class 1A guideline recommendation in support of IVI imaging-guided PCI. The earliest of these was the ULTIMATE trial (Intravascular ultrasound versus angiography-guided drug-eluting stent implantation: the ULTIMATE Trial),[6] which was the first paper of its kind to directly compare IVI-guided to angiography-guided PCI. RENOVATE-COMPLEX PCI (Intravascular imaging-guided or angiography-guided complex PCI),[7] OCTOBER,[8] and ILUMIEN IV[9] expanded upon ULTIMATE, and collectively demonstrated that IVI use resulted in an overall reduction in death from a cardiac cause, definite/probable stent thrombosis, and target-vessel related acute coronary syndrome, when compared with angiography guidance over a 2-year period. This outcome was observed in anatomically complex bifurcation, long, and CTO lesions, as well as in clinically complex patients with high-risk comorbidities or an acute coronary syndrome presentation. OCTIVUS (Optical coherence tomography-guided or intravascular ultrasound-guided percutaneous coronary intervention: the OCTIVUS Randomized Clinical Trial)[10] and GNOCCI (Glasgow Natural History Study of Covered Stent Coronary Interventions)[2] are robust studies that complement the conclusions drawn by Sawayama et al.[5] They observed that IVI did not result in procedural-related complications, nor was its use associated with an increased rate of higher severity Ellis grade CAP, respectively. Imaging catheter use following perforation can guide stent optimization, potentially reducing risk of adverse outcomes following implantation of covered stents which have significantly higher rates of target lesion failure and related poor longer-term patient outcomes.[2]

However, conflicting literature on this topic persists, likely caused by confounding factors inherent to nonrandomized trials. For example, a large-scale Thai registry demonstrated a higher incidence of CAP among patients undergoing IVI-guided PCI compared with angiographic-guided PCI.[11] This was found regardless of whether or not IVI was clinically indicated per the guidelines, although this association was only statistically significant in the nonclinically indicated group. Similarly, in a large retrospective analysis of nearly 40,000 patients, IVI was independently associated with an almost 3-fold increased risk of CAP; however, the authors concede that this finding may reflect lesion complexity rather than a direct effect of IVI itself.[12]

FUTURE DIRECTIONS AND VISION FOR RESEARCH

Given these conflicting observational findings, it is imperative that data from randomized trials be used to clarify the relationship between IVI use and CAP. Observational data, no matter how carefully adjusted, cannot fully account for unmeasured confounders. Furthermore, a meta-analysis of the rare event of CAP would be an ideal approach to aggregate data from multiple randomized controlled trials (RCTs). Meta-analyses, often overused, are perfectly suited to study these rare complications by pooling data across randomized controlled trials and providing a more definitive understanding of the association between IVI use and CAP.

In summary, Sawayama et al[5] demonstrate that the increased use of IVI-guided PCI was associated with a reduced incidence of CAP, particularly in complex cases such as CTO PCI and those involving moderate to severe calcification. These findings underscore the benefit of routine IVI use in preventing PCI-related complications, although further randomized trials and meta-analyses are essential to validate this association and guide future clinical practice.

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