IJC Heart & Vasculature 52 (2024) 101400

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

Editorial

Optical coherence tomography to optimize results of coronary interventions. Evidence-based?

1. Introduction

Coronary angiography (ANG) provides important information on the extent and severity of coronary artery disease (CAD) allowing to inform revascularization decisions in the clinical setting. However, this time-honored technique has well-established limitations [1–3]. ANG only visualizes the coronary lumen silhouette depicted in a 2-dimensional format in multiple projections. Nevertheless, CAD is a disease of the vessel wall that, by definition, cannot be visualized by ANG [1–3]. Alternatively, intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are tomographic intracoronary imaging techniques (ICI) that provide unique insights into the presence and characteristics of atheroma at the vessel wall [1–3]. Over decades, IVUS has accumulated robust evidence supporting its value to complement ANG to assess coronary anatomy and guide stent optimization [2,3]. IVUS depicts the entire vessel wall and remains unrivaled to visualize the external elastic lamina which is needed to determine remodeling phenomena and CAD progression/regression. Conversely, OCT provides a 10-fold superior spatial resolution (~15 μm) compared to IVUS and is unsurpassed to disclose subtle yet important details of complicated plaques (cap thickness, cap ruptures, erosion, calcified nodules, thrombi) [1–3]. OCT has a limited penetration and may fail to delineate the external elastic lamina at segments with large plaque burden, but it is usually able to visualize the entire vessel wall at the angiographically normal segments selected as reference for stent sizing. OCT provides more accurate measurement of lumen area than IVUS that, due to its lower resolution, overestimates lumen area. After stenting OCT is also superior to IVUS in detecting stent underexpansion, malaposition, tissue protrusion and edge-dissections. Finally, at follow-up, OCT is superior to IVUS to characterize the tissue causing in-stent restenosis [1–3]. All the above would suggest that OCT may be superior not only to ANG but also to IVUS to guide stent optimization.

Recently, ILUMIEN IV, the largest randomized clinical trial (RCT) comparing OCT with ANG, met its primary anatomic endpoint (minimal stent area [MSA] superior with OCT) but failed to meet the co-primary clinical endpoint (target vessel failure [TLF] at 2 years similar with the 2 strategies) [4]. Conversely, in the OCTOBER RCT, OCT guidance in lesions at bifurcation reduced major adverse cardiac events (MACE) at 2 years [5]. This generated controversy and uncertainty in the scientific community. In this scenario, rigorous, well-performed *meta*-analysis offer the most effective approach to address this conundrum [6–13].

1.1. Present study

In this issue of the Journal, Ahmed et al. [14] present a timely *meta*-analysis comparing OCT-guided with ANG-guided PCI including 11 RCT with 5,139 patients. The search ended in September 2023 when 2 major RCT (ILUMIEN IV and OCTOBER) were presented as late-breaking clinical trials at the European Society of Cardiology congress. OCT-guidance resulted in a larger MSA (mean difference 0.35 mm^2) (primary endpoint) and reduced cardiovascular mortality (RR 0.56, 95 %CI 0.32–0.99) (co-primary endpoint) and also stent thrombosis, stent malapposition and major edge-dissection. However, no differences were observed regarding all-cause mortality, myocardial infarction (MI) or MACE, although all point estimates favoured OCT guidance. Target lesion revascularization (TLR) (RR 0.94, 95 %CI 0.69–1,28) was similar in both groups. Meta-regression excluded an effect of the publication year on the primary endpoint. Although many outcome measures were analyzed, not all of them were reported in each individual RCT. Considering the potential clinical implications of this study some issues should be considered [14].

First, the study is of clear value because most previous *meta*-analyses compared ICI to ANG included only a small number of OCT studies [6–13]. The present study focused on OCT to provide more homogeneous and comprehensive information on the potential value of this high-resolution technique compared with ANG. In addition, the current study included more RCT, providing a larger sample size and more robust evidence.

Second, importantly, this study demonstrates that OCT-guidance was associated with a significant reduction in cardiovascular mortality and with a strong trend ($p = 0.06$) for a reduction in all-cause mortality. Authors suggested that the larger MSA achieved by OCT-guidance may reduce the rates of stent thrombosis, that is associated with large spontaneous MI and adverse clinical outcomes.

Third, the study clearly demonstrates that OCT is superior to ANG regarding final MSA. This is important from a mechanistic standpoint and complements data from previous *meta*-analyses. In the *meta*-analysis of Siddiqi et al. [8] OCT-guidance was associated with a numerically larger MSA, but the difference was not statistically significant. A larger MSA has been associated in multiple studies to improved clinical outcomes mainly driven by a reduction in TLR [2,3]. Surprisingly, in this study, a larger final MSA was not associated with a significant reduction in either TLR or MI. Although authors claim that a lack of power might explain the anatomical-clinical disconnection, this issue remains of concern and deserves additional investigation. Likewise, the reduction in stent thrombosis rates without a concomitant reduction in the rates of MI is also difficult to understand. One might speculate that MI resulting from ST are larger than those unrelated to stent thrombosis, thus explaining the differences in cardiovascular mortality. Nevertheless, data on stent thrombosis and MI were only reported in some of the trials

https://doi.org/10.1016/j.ijcha.2024.101400
Received 27 March 2024; Accepted 28 March 2024
Available online 14 May 2024
2352-9067/© 2024 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC license (http://creativecommons.org/licenses/by-nc/4.0/).

studied and this factor could also explain the lack of correlation.

Fourth, in this study OCT, as compared with ANG-guidance, reduced the number of stents showing malapposition and major edge dissection. These findings have not been analyzed in previous *meta*-analyses yet are important from a mechanistic standpoint as they might be related to improved clinical outcomes [14].

1.2. Previous Meta-Analyses on OCT vs ANG guidance

Overall, in previous *meta*-analyses the benefit of ICI guidance has been well-established including surrogate anatomic endpoints and clinical outcomes [6–13]. However, in most of these studies, few RCT analyzed the efficacy of OCT guidance [6–13]. "Network" *meta*-analyses (allowing direct and indirect comparisons) are of unique value in this regard. A recent network *meta*-analysis by Stone et al. [11], comparing ICI vs ANG guidance, included 22 RCTs with 15,964 patients. ICI-guidance reduced the risk of TLF (RR 0.71, 95 %CI 0.63–0.80), cardiac death (0.55 95 %CI 0.41–0.75), TLR (0.72, 95 %CI 0.60–0.86), MI, stent thrombosis and all-cause death (0.75, 95 %CI 0.6–0.93). Results were similar using frequentist or Bayesian methodology. In addition, all treatment effect estimates were similar for IVUS and OCT guidance [11]. Another recent network *meta*-analysis by Giacoppo et al. [12] (comparing ICI vs ANG but also IVUS vs OCT), included 24 RCTs with 15,489 patients. IVUS was associated with reduced TLR rates compared with ANG (OR 0.69, 95 %CI 0.54–0.87), but no significant differences were found between OCT and ANG (OR 0.83, 95 %CI 0.63–1.09]) or between OCT and IVUS (OR 1.21, 95 %CI 0.92–1.58). In pairwise comparisons, ICI-guidance reduced TLR, cardiac death, and stent thrombosis without differences in MI. The results from frequentist analyses were replicated in Bayesian models. Authors concluded that ICI was associated with a reduction in ischemia-driven TLR compared with ANG with the benefit most evident for IVUS [12].

2. Final remarks

Should OCT be systematically used in all interventions to ensure an optimal stent implantation? Before addressing this burning question, it is important to keep in mind that in these RCT OCT guidance was only tested in clinical and anatomical settings where imaging was considered technically feasible (i.e., hemodynamically unstable patients, calcified or tortuous vessels or distal lesions, were mostly excluded). Consequently, the generalizability of current results to an unselected (all comers) population remains unsettled. In addition, the "optimal" criteria for OCT guidance, still remain unclear. Furthermore, in all these RCT only a visual analysis was performed in the ANG arm. Notably, a recent RCT suggested that the ANG arm could provide similar clinical outcomes to ICI if "quantitative" coronary angiography is systematically used [13]. Of note, this technique is not expensive, does not require special expertise and it is readily available in all cardiac catheterization laboratories.

The present study by Ahmed et al. [14] provides compelling evidence of the value of OCT to optimize stent implantation that, eventually, translates into improved clinical outcomes, including cardiovascular mortality. Due to its superior spatial resolution, OCT might be currently considered as the most attractive imaging modality to guide stent optimization. However, none of the discussed *meta*-analyses had access to "individual patient-level data" and, therefore, the clinical and anatomic subsets that might particularly benefit from OCT guidance remain unsettled. Further studies are required to identify the patient and lesion subtypes benefiting most from OCT guidance. In any case, additional efforts are warranted to overcome impediments to facilitate a higher use of ICI guidance in routine clinical practice.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] F. Alfonso, R. Virmani, New morphological insights on coronary plaque rupture: bridging the gap from anatomy to clinical presentation? JACC Cardiovasc. Interv. 4 (2011) 83–86.
[2] L. Räber, G.S. Mintz, K.C. Koskinas, et al., Clinical use of intracoronary imaging. Part 1: guidance and optimization of coronary interventions. An expert consensus document of the European Association of Percutaneous Cardiovascular Interventions, EuroIntervention. 14 (2018) 656–677.
[3] F. Alfonso, F. Prati, Optical coherence tomography or intravascular ultrasound to optimize coronary stent implantation, Eur Heart J. 38 (2017) 3148–3151.
[4] Z.A. Ali, U. Landmesser, A. Maehara, et al., Optical coherence tomography-guided versus angiography-guided PCI, N Engl J Med. 389 (16) (2023) 1466–1476.
[5] N.R. Holm, L.N. Andreasen, O. Neghabat, et al., OCT or angiography guidance for PCI in complex bifurcation lesions, N Engl J Med. 389 (16) (2023) 1477–1487.
[6] D.H. Shin, S.J. Hong, G.S. Mintz, et al., Effects of intravascular ultrasound-guided versus angiography-guided new-generation drug-eluting stent implantation. meta-analysis with individual patient-level data from 2,345 randomized patients, J Am Coll Cardiol Intv 9 (2016) 2232–2239.
[7] S. Buccheri, G. Gabriele Franchina, S. Sara Romano, et al., Clinical outcomes following intravascular imaging-guided versus coronary angiography-guided percutaneous coronary intervention with stent implantation. A systematic review and bayesian network meta-analysis of 31 studies and 17,882 patients, J Am Coll Cardiol Intv 10 (2017) 2488–2498.
[8] T.J. Siddiqi, M.S. Khan, K.K. Galougahi, et al., Optical coherence tomography versus angiography and intravascular ultrasound to guide coronary stent implantation: a systematic review and meta-analysis, Catheter Cardiovasc Interv. 100 (2022) S44–S56.
[9] T. Kuno, Y. Kiyohara, A. Maehara, et al., Comparison of intravascular imaging, functional, or angiographically guided coronary intervention, J Am Coll Cardiol. 82 (23) (2023) 2167–2176.
[10] A. Attar, A. Hosseinpour, P. Azami, E. Kohansal, R. Javaheri, Clinical outcomes of optical coherence tomography versus conventional angiography guided percutaneous coronary intervention: a meta-analysis, Curr Probl Cardiol. 49 (2) (2023) 102224.
[11] G.W. Stone, E.H. Christiansen, Z.A. Ali, et al., Intravascular imaging-guided coronary drug-eluting stent implantation: an updated network meta-analysis, Lancet 403 (2024) 824–837.
[12] D. Giacoppo, C. Laudani, G. Occhipinti, et al., Coronary angiography, intravascular ultrasound, and optical coherence tomography in the guidance of percutaneous coronary intervention: a systematic review and network meta-analysis, Circulation (2024), https://doi.org/10.1161/CIRCULATIONAHA.123.067583. Online ahead of print.
[13] P.H. Lee, S.J. Hong, H.-S. Kim, et al., Quantitative coronary angiography vs intravascular ultrasonography to guide drug-eluting stent implantation: a randomized clinical trial, JAMA Cardiol. (2024) e240059, https://doi.org/10.1001/jamacardio.2024.0059. Online ahead of print.
[14] M. Ahmed, H. Javaid, M. Talha Maniya et al., Optical coherence-guided versus angiography-guided percutaneous coronary intervention. A meta-analysis of randomized controlled trials. IJC Heart and Vasculature, 2024 (in press) (Cross reference).

Fernando Alfonso*, Alexander Marschall, David Del Val
Department of Cardiology. Hospital, Universitario de La Princesa, Madrid, Spain

* Corresponding author at: Department of Cardiology. Hospital, Universitario de La Princesa, Universidad Autónoma de Madrid, Instituto de Investigación Sanitaria Princesa, IIS-IP, CIBERCV, Diego de León 62, Madrid 28006, Spain.
E-mail address: falf@hotmail.com (F. Alfonso).