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Is triple antithrombotic therapy, or rather its duration and composition, the true culprit for the excess of bleeding events observed in patients with atrial fibrillation undergoing coronary intervention?

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This commentary refers to 'Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials' by H.B. Golwala *et al.*, 2018;39:1726–1735.

Golwala *et al.*[1] claimed that dual (DAT) and triple antithrombotic therapy (TAT) are equally effective in preventing cardiovascular events with DAT being safer by approximately halving bleeding risk.[1] We do not concur with the conclusive statement that these 'findings support the concept that DAT may be a better option than TAT in many patients with atrial fibrillation (AF) following percutaneous coronary intervention (PCI)'. Triple antithrombotic therapy duration amongst the included studies exceeded 6-months in a relevant proportion of patients. In the WOEST and PIONEER-AF PCI, 66% and 25% of patients received TAT for 12-months, respectively (*Figure 1*). In the RE-DUAL PCI, in which TAT was assigned for a maximum of 3-months, almost one-third of patients continued TAT, reaching up to 12-months in 14% of cases. The ISAR-TRIPLE, in which TAT was discontinued in all patients at 6-months, found no bleeding excess vs.

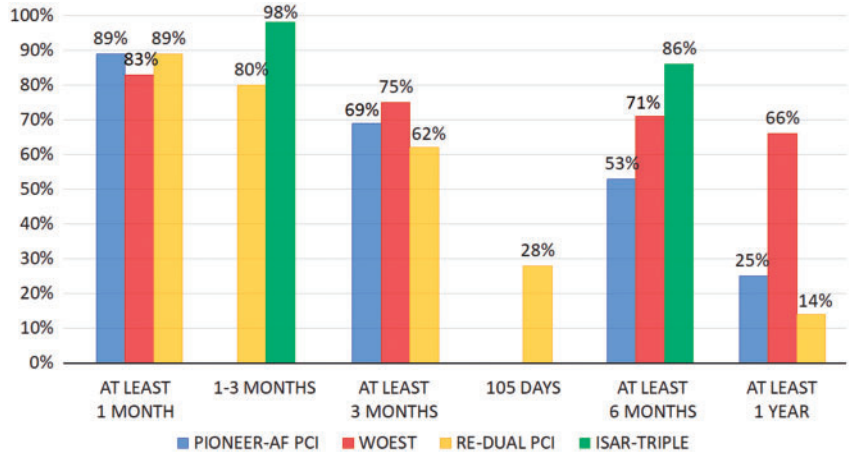

Figure 1 Percentage of patients on actual triple antithrombotic therapy in four randomized trials.

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1-month therapy. By inspecting the upper boundary of the 95% confidence interval, DAT can double myocardial infarction risks compared to TAT. This raises concerns given the trade-off of ischaemic vs. bleeding events on the actual net clinical benefit[2] and should be openly discussed with patients. Finally, TAT composition [vitamin K antagonists (VKAs) vs. direct oral anticoagulant (DOAC)] varied significantly amongst study groups, limiting definite conclusions. The 2017 ESC focused update on dual antiplatelet therapy[3] recommended not to routinely skip TAT, rather keep it short and preferentially use DOAC. The safety and efficacy of 1-month vs. a more prolonged TAT duration, while allowing DOAC to be used in both study groups, is being investigated in the MASTER DAPT (NCT03023020). We thus believe that further studies are needed to clarify whether TAT *per se*, or rather its duration and/or composition, should be blamed for the excess of bleeding complications observed across the few available studies.

Conflict of interest: none declared.

References

1. Golwala HB, Cannon CP, Steg PG, Doros G, Qamar A, Ellis SG, Oldgren J, Ten Berg JM, Kimura T, Hohnloser SH, Lip GYH, Bhatt DL. Safety and efficacy of dual vs. triple antithrombotic therapy in patients with atrial fibrillation following percutaneous coronary intervention: a systematic review and meta-analysis of randomized clinical trials. *Eur Heart J* 2018;**39**:1726–1735a.
2. Valgimigli M, Costa F, Lokhnygina Y, Clare RM, Wallentin L, Moliterno DJ, Armstrong PW, White HD, Held C, Aylward PE, Van de Werf F, Harrington RA, Mahaffey KW, Tricoci P. Trade-off of myocardial infarction vs. bleeding types on mortality after acute coronary syndrome: lessons from the Thrombin Receptor Antagonist for Clinical Event Reduction in Acute Coronary Syndrome (TRACER) randomized trial. *Eur Heart J* 2017;**38**:804–810.
3. Valgimigli M, Bueno H, Byrne RA, Collet J-P, Costa F, Jeppsson A, Jüni P, Kastrati A, Kolh P, Mauri L, Montalescot G, Neumann F-J, Petricevic M, Roffi M, Steg PG, Windecker S, Zamorano JL, Levine GN, Badimon L, Vranckx P, Agewall S, Andreotti F, Antman E, Barbato E, Bassand J-P, Bugiardini R, Cikirikcioglu M, Cuisset T, De Bonis M, Delgado V, Fitzsimons D, Gaemperli O, Galiè N, Gilard M, Hamm CW, Ibanez B, Iung B, James S, Knuuti J, Landmesser U, Leclercq C, Lettino M, Lip G, Piepoli MF, Pierard L, Schwerzmann M, Sechtem U, Simpson IA, Uva MS, Stabile E, Storey RF, Tendera M, Van de Werf F, Verheugt F, Aboyans V, Windecker S, Aboyans V, Agewall S, Barbato E, Bueno H, Coca A, Collet J-P, Coman IM, Dean V, Delgado V, Fitzsimons D, Gaemperli O, Hindricks G, Iung B, Jüni P, Katus HA, Knuuti J, Lancellotti P, Leclercq C, McDonagh T, Piepoli MF, Ponikowski P, Richter DJ, Roffi M, Shlyakhto E, Simpson IA, Zamorano JL, Windecker S, Aboyans V, Agewall S, Barbato E, Bueno H, Coca A, Collet J-P, Coman IM, Dean V, Delgado V, Fitzsimons D, Gaemperli O, Hindricks G, Iung B, Jüni P, Katus HA, Knuuti J, Lancellotti P, Leclercq C, McDonagh T, Piepoli MF, Ponikowski P, Richter DJ, Roffi M, Shlyakhto E, Simpson IA, Zamorano JL, Roithinger FX, Aliyev F, Stelmashok V, Desmet W, Postadzhiyan A, Georghiou GP, Motovska Z, Grove EL, Marandi T, Kiviniemi T, Kedev S, Gilard M, Massberg S, Alexopoulos D, Kiss RG, Gudmundsdottir IJ, McFadden EP, Lev E, De Luca L, Sugraliyev A, Haliti E, Mirrakhimov E, Latkovskis G, Petrauskiene B, Huijnen S, Magri CJ, Cherradi R, Ten Berg JM, Eritsland J, Budaj A, Aguiar CT, Duplyakov D, Zavatta M, Antonijevic NM, Motovska Z, Fras Z, Montoliu AT, Varenhorst C, Tsakiris D, Addad F, Aydogdu S, Parkhomenko A, Kinnaird T. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018;**39**:213–260.