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## **Clinical Outcomes of Prolonged Dual Antiplatelet Therapy after Coronary Drug-Eluting Stent Implantation in Dialysis Patients: a population-based study**

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**Objectives:** End-stage renal disease (ESRD) is susceptible to both ischemic and bleeding events. Optimal duration of dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) implantation is not established in dialysis patients who are usually excluded from randomized studies. Since recent studies reported benefits of prolonged DAPT over 12 months in chronic kidney disease, we investigated the effectiveness and safety of prolonged DAPT specifically in ESRD with higher cardiovascular risks.

**Methods:** In this population-based retrospective study using healthcare claims data, dialysis patients who underwent DES implantation from 2008 to 2015 were initially enrolled. Landmark analyses including free-of-event participants at 12 (n=2,246), 15 (n=1,925), and 18 (n=1,692) months after DES implantation were performed to compare the effects of continued versus discontinued DAPT on clinical outcomes. The primary outcome was major adverse cardiovascular events (MACE), a composite of mortality, non-fatal myocardial infarction, coronary revascularization, and stroke. Major bleeding was analyzed as a safety outcome. Inverse probability weighted (IPTW) Cox regressions were performed to address selection biases.

**Results:** Mean follow-up periods were 278.3 to 292.4 days depending on landmarks. Incidences were lower for MACE and higher for major bleeding in continued DAPT groups. Incidences of major bleeding were far lower than those of MACE.

In IPTW Cox analyses, continued DAPT reduced the hazards of MACE at 12- (HR, 0.74; 95% CI, 0.61-0.90;  $P=0.003$ ), 15- (HR, 0.78; 95% CI, 0.64-0.96;  $P=0.02$ ), and 18-month (HR, 0.79; 95% CI, 0.63-0.99;  $P=0.04$ ) landmarks, but without significant increase in major bleeding at 12- (HR, 1.39; 95% CI, 0.90-2.16;  $P=0.1$ ), 15- (HR, 1.13; 95% CI, 0.75-1.70;  $P=0.6$ ), and 18-month (HR, 1.27; 95% CI, 0.83-1.95;  $P=0.3$ ) landmarks.

**Conclusions:** Prolonged DAPT over 12 months after DES implantation can reduce MACE without significant increase in major bleeding in dialysis patients. Dialysis might be a risk factor for ischemic complications rather than bleeding in deciding on DAPT duration.

Table. Association of DAPT with clinical outcomes in Cox analyses

**Table.** Associations of the dual antiplatelet therapy maintenance with clinical outcomes in Cox regressions with different adjustment methods.<sup>a</sup>

|                                | 12 months <sup>a</sup>              |                    | 15 months <sup>a</sup>              |                   | 18 months <sup>a</sup>              |                   |
|--------------------------------|-------------------------------------|--------------------|-------------------------------------|-------------------|-------------------------------------|-------------------|
|                                | Hazard ratios (95% CI) <sup>a</sup> | P <sup>a</sup>     | Hazard ratios (95% CI) <sup>a</sup> | P <sup>a</sup>    | Hazard ratios (95% CI) <sup>a</sup> | P <sup>a</sup>    |
| <b>MACE<sup>a</sup></b>        |                                     |                    |                                     |                   |                                     |                   |
| Overall <sup>a</sup>           |                                     |                    |                                     |                   |                                     |                   |
| Unadjusted <sup>a</sup>        | 0.72 (0.59-0.87) <sup>a</sup>       | 0.001 <sup>a</sup> | 0.77 (0.63-0.95) <sup>a</sup>       | 0.01 <sup>a</sup> | 0.79 (0.63-0.99) <sup>a</sup>       | 0.04 <sup>a</sup> |
| MV-adjusted <sup>a</sup>       | 0.73 (0.60-0.89) <sup>a</sup>       | 0.002 <sup>a</sup> | 0.78 (0.63-0.96) <sup>a</sup>       | 0.02 <sup>a</sup> | 0.78 (0.62-0.98) <sup>a</sup>       | 0.03 <sup>a</sup> |
| IPTW <sup>a</sup>              | 0.74 (0.61-0.90) <sup>a</sup>       | 0.003 <sup>a</sup> | 0.78 (0.64-0.96) <sup>a</sup>       | 0.02 <sup>a</sup> | 0.79 (0.63-0.99) <sup>a</sup>       | 0.04 <sup>a</sup> |
| Mortality <sup>a</sup>         |                                     |                    |                                     |                   |                                     |                   |
| Unadjusted <sup>a</sup>        | 0.57 (0.41-0.80) <sup>a</sup>       | 0.001 <sup>a</sup> | 0.77 (0.55-1.09) <sup>a</sup>       | 0.1 <sup>a</sup>  | 0.64 (0.45-0.92) <sup>a</sup>       | 0.02 <sup>a</sup> |
| MV-adjusted <sup>a</sup>       | 0.59 (0.42-0.82) <sup>a</sup>       | 0.002 <sup>a</sup> | 0.78 (0.55-1.10) <sup>a</sup>       | 0.2 <sup>a</sup>  | 0.65 (0.45-0.93) <sup>a</sup>       | 0.02 <sup>a</sup> |
| IPTW <sup>a</sup>              | 0.58 (0.42-0.81) <sup>a</sup>       | 0.001 <sup>a</sup> | 0.81 (0.57-1.14) <sup>a</sup>       | 0.2 <sup>a</sup>  | 0.67 (0.47-0.96) <sup>a</sup>       | 0.03 <sup>a</sup> |
| Non-fatal MI <sup>a</sup>      |                                     |                    |                                     |                   |                                     |                   |
| Unadjusted <sup>a</sup>        | 1.01 (0.64-1.61) <sup>a</sup>       | 0.9 <sup>a</sup>   | 0.87 (0.54-1.41) <sup>a</sup>       | 0.6 <sup>a</sup>  | 0.88 (0.52-1.48) <sup>a</sup>       | 0.6 <sup>a</sup>  |
| MV-adjusted <sup>a</sup>       | 1.03 (0.64-1.65) <sup>a</sup>       | 0.9 <sup>a</sup>   | 0.90 (0.54-1.49) <sup>a</sup>       | 0.7 <sup>a</sup>  | 0.88 (0.51-1.50) <sup>a</sup>       | 0.6 <sup>a</sup>  |
| IPTW <sup>a</sup>              | 1.01 (0.64-1.61) <sup>a</sup>       | 0.9 <sup>a</sup>   | 0.87 (0.54-1.39) <sup>a</sup>       | 0.6 <sup>a</sup>  | 0.93 (0.55-1.56) <sup>a</sup>       | 0.8 <sup>a</sup>  |
| Revascularization <sup>a</sup> |                                     |                    |                                     |                   |                                     |                   |
| Unadjusted <sup>a</sup>        | 0.95 (0.69-1.31) <sup>a</sup>       | 0.8 <sup>a</sup>   | 0.94 (0.66-1.34) <sup>a</sup>       | 0.7 <sup>a</sup>  | 1.20 (0.81-1.76) <sup>a</sup>       | 0.4 <sup>a</sup>  |
| MV-adjusted <sup>a</sup>       | 0.94 (0.69-1.29) <sup>a</sup>       | 0.7 <sup>a</sup>   | 0.96 (0.67-1.37) <sup>a</sup>       | 0.8 <sup>a</sup>  | 1.15 (0.78-1.70) <sup>a</sup>       | 0.5 <sup>a</sup>  |
| IPTW <sup>a</sup>              | 0.96 (0.70-1.33) <sup>a</sup>       | 0.8 <sup>a</sup>   | 0.93 (0.65-1.32) <sup>a</sup>       | 0.7 <sup>a</sup>  | 1.14 (0.78-1.68) <sup>a</sup>       | 0.5 <sup>a</sup>  |
| Stroke <sup>a</sup>            |                                     |                    |                                     |                   |                                     |                   |
| Unadjusted <sup>a</sup>        | 0.68 (0.44-1.05) <sup>a</sup>       | 0.08 <sup>a</sup>  | 0.59 (0.38-0.94) <sup>a</sup>       | 0.03 <sup>a</sup> | 0.59 (0.34-1.03) <sup>a</sup>       | 0.06 <sup>a</sup> |
| MV-adjusted <sup>a</sup>       | 0.72 (0.46-1.11) <sup>a</sup>       | 0.1 <sup>a</sup>   | 0.59 (0.38-0.93) <sup>a</sup>       | 0.02 <sup>a</sup> | 0.57 (0.33-0.98) <sup>a</sup>       | 0.04 <sup>a</sup> |
| IPTW <sup>a</sup>              | 0.73 (0.47-1.15) <sup>a</sup>       | 0.2 <sup>a</sup>   | 0.60 (0.37-0.95) <sup>a</sup>       | 0.03 <sup>a</sup> | 0.55 (0.31-0.97) <sup>a</sup>       | 0.04 <sup>a</sup> |
| Major bleeding <sup>a</sup>    |                                     |                    |                                     |                   |                                     |                   |
| Unadjusted <sup>a</sup>        | 1.46 (0.93-2.28) <sup>a</sup>       | 0.1 <sup>a</sup>   | 1.20 (0.79-1.81) <sup>a</sup>       | 0.4 <sup>a</sup>  | 1.30 (0.85-2.00) <sup>a</sup>       | 0.2 <sup>a</sup>  |
| MV-adjusted <sup>a</sup>       | 1.45 (0.92-2.28) <sup>a</sup>       | 0.1 <sup>a</sup>   | 1.18 (0.78-1.80) <sup>a</sup>       | 0.5 <sup>a</sup>  | 1.28 (0.83-1.98) <sup>a</sup>       | 0.3 <sup>a</sup>  |
| IPTW <sup>a</sup>              | 1.39 (0.90-2.16) <sup>a</sup>       | 0.1 <sup>a</sup>   | 1.13 (0.75-1.70) <sup>a</sup>       | 0.6 <sup>a</sup>  | 1.27 (0.83-1.95) <sup>a</sup>       | 0.3 <sup>a</sup>  |

Abbreviations: CI, Confidence Interval; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; MV, Multivariable; IPTW, Inverse Probability of Treatment Weighting.<sup>a</sup>

Figure. Cumulative probabilities of MACE and major bleeding according to DAPT status

