ANNEXES TO CHAPTER 3

Clinical Question IXa. In which situations is it necessary to indicate antithrombotic prophylaxis after creating/repairing the arteriovenous fistula?

Three publications by the same research group address this issue, presenting data from a systematic review with meta-analysis that analyses the effect of anticoagulant therapy in patients with chronic kidney failure (Palmer 2012, 2013a, 2013b). The reviews analyse the effects of antiplatelet therapy in all patients studied, but do not differentiate specific situations that arise after repair of vascular access, distinguishing the analyses only according to vascular access by fistula or by graft. However, the available information serves to help us decide whether to recommend antithrombotic prophylaxis in general after repair of vascular access in patients in whom prophylaxis is not contraindicated for other reasons.

General effects of antithrombotic prophylaxis in patients with chronic kidney failure

The Cochrane systematic review of Palmer 2013 included 50 studies that recruited 27,139 participants; 44 of these studies (21,460 participants) compared one antiplatelet agent with placebo or no treatment, while the other six (5,679 participants) directly compared one antiplatelet agent to another. It should be noted that the evidence collected also includes patients who have not yet developed end-stage renal disease and who underwent haemodialysis. Compared with placebo or no treatment, antiplatelet agents reduce the **risk of myocardial infarction** (17 studies, 14,451 participants; RR 0.87, 95% CI: 0.76-0.99), but not **all-cause mortality** (30 studies, 16,152 participants; RR 0.93, 95% CI: 0.81-1.06), **cardiovascular mortality** (19 studies, 9,337 participants; RR 0.89, 95% CI: 0.70 to 1.12) or the risk of **cerebrovascular accident** (11 studies, 9,544 participants; RR 1.00, 95% CI: 0.58-1.72). On the other hand, antiplatelet agents increased **the risk of major bleeding** (26 studies, 15,992 participants; RR 1.33, 95% CI: 1.10-1.65) and **minor bleeding** (18 studies 13,106 participants; RR 1.49, 95% CI: 1.12-1.97). The meta-regression analysis found no difference in relative benefit or treatment injury (risk of all-cause mortality, myocardial infarction or severe bleeding) by type of antiplatelet agent or by stage of disease. The data were insufficient to make direct comparisons between different antiplatelet drugs, treatment in patients with kidney transplant, primary prevention or risk of end-stage renal disease. The authors concluded that antiplatelet agents **reduce the risk of myocardial infarction, but increase the risk of major bleeding**. The risks may outweigh the benefits among people with a low annual risk of cardiovascular events, including those with early stages of chronic kidney failure who do not have clinically evident occlusive cardiovascular disease.	**Moderate quality**

Antithrombotic prophylaxis after vascular access

The publication of Palmer 2103b, taken from the Cochrane review of Palmer 2013a, is a systematic review analysing the effect of antiplatelet treatments in adults on long-term haemodialysis treatment. It included 21 ACE (angiotensin-converting enzyme) inhibitors (4,826 participants), comparing antiplatelet therapy with placebo or no treatment and assessing outcomes of vascular access for haemodialysis. It included 12 trials (3,118 participants) that analysed the effect of antiplatelet therapy after vascular access creation	

surgery for dialysis, which continued to be administered for approximately 6 months. The authors highlighted the following limitations of the evidence: risk of high or unclear bias in most of the trials included, and data from very few patients that were insufficient for analysing certain effects, in particular antiplatelet effects on graft function and vascular access adequacy for dialysis.	
The data of different meta-analyses of that study are presented below. **- Fistula failure (due to thrombosis or loss of permeability)** The antiplatelet treatment reduced thrombosis or loss of permeability by half (6 trials, 188 events, 1,242 participants; RR 0.49, 95% CI: 0.30 to 0.81; I2 = 29%). In absolute terms, the treatment of 100 individuals with antiplatelet agents for 1-6 months (aspirin, ticlopidine or clopidogrel) would prevent fistula failure in 6-21 individuals, assuming a baseline risk of 30% of one or more events. **- Graft failure (due to thrombosis or loss of permeability)** Antiplatelet treatment had little or no effect on graft thrombosis or loss of permeability (3 trials, 374 events, 956 participants; RR 0.94, 95% CI: 0.80-1.10). **- Early failure of vascular access in fistulas** Five (5) studies (1,105 participants) assessed the results before 8 weeks after surgery. In this subgroup of trials, antiplatelet drugs significantly reduced early thrombosis or fistula failure due to loss of permeability by 57% compared with placebo or no treatment (177 events; RR 0.43, 95% CI: 0.26-0.73, I2 = 25%). The review did not provide relevant data on patients with grafts. **- Failure to achieve adequate vascular access for dialysis** **In fistulas**: non-statistically significant differences (2 trials, 470 events, 794 participants; RR 0.57, 95% CI: 0.13-2.51). **In grafts:** Non-statistically significant differences (1 trial, 12 events, 649 participants; RR 0.51, 95% CI: 0.16-1.68). **- Need for intervention to achieve permeability or to facilitate maturation of vascular access** **In fistulas**: non-statistically significant differences (1 study, 17 events, 866 participants; RR 0.69, 95% CI: 0.26-1.83). **In grafts:** non-statistically significant differences (1 study, 196 events, 649 participants; RR 0.89, 95% CI: 0.64 to 1.25). **- Severe bleeding:** non-statistically significant differences (10 studies, 3,930 participants; RR 0.93, 95% CI: 0.58 to 1.49). **- Minor bleeding:** non-statistically significant differences (4 studies, 237 participants; RR 1.22, 95% CI: 0.51-2.91). **- Discontinuation of antiplatelet treatment** There was no difference among the treatment groups for this outcome (8 studies, 1,973 participants; RR 1.01, 95% CI: 0.84-1.20)	**Moderate quality**
Antithrombotic prophylaxis after repair of vascular access	
No studies have been found that analyse the effects of antithrombotic prophylaxis after repair of vascular access.	

Summary of evidence	
In patients with fistulas, antithrombotic prophylaxis after surgery and for a 6-month period reduces the risk of fistula failure (due to thrombosis or loss of permeability) and is not accompanied by negative effects in other outcomes analysed.	**Moderate quality**
In patients with grafts, antithrombotic prophylaxis shows no positive effect in any of the outcomes of interest.	**Moderate quality**
Patient values and preferences *No relevant studies on this aspect have been found.*	
Use of resources and costs *No relevant studies on this aspect have been found.*	
Recommendations [Proposal]	
Weak	In patients with fistulas, the use of antithrombotic prophylaxis is recommended for 6 months after vascular access creation surgery to reduce the risk of access failure due to thrombosis or loss of permeability.
Weak	In patients with grafts, the use of antithrombotic prophylaxis is not recommended after vascular access creation surgery.

References

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