CHAPTER 3.2 Prophylactic antithrombotic management in kidney transplantation

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Background

With a reported incidence of 0–13%, arterial or venous thrombosis of kidney allografts is a major cause of allograft loss, mostly within the first week after paediatric kidney transplantation (KTx) [1–3].

Body of evidence

Antithrombotic prophylaxis with heparin (anticoagulation) or acetylsalicylic acid (ASA) (platelet aggregation inhibition) appears to be beneficial in preventing arterial and venous kidney graft thrombosis (Figure 1) [4].

The following evidence-based and pathophysiological considerations may be helpful in the decision-making process:

- The risk of thrombosis is higher in paediatric than in adult KTx [5].
- Antithrombotic prophylaxis should be considered in patients with a positive history of thromboembolic events [6, 7].
- Congenital and acquired prothrombotic risk factors due to chronic kidney disease should be considered [3, 6, 7].
- The risk of kidney transplant thrombosis is highest in the first week after KTx [8]. Therefore, it seems reasonable to initiate antithrombotic prophylaxis pre- or intraoperatively and to discontinue it within a few weeks (< 4–6 weeks) after KTx [9, 10].
- Platelet aggregation plays a crucial role in the early phase of coagulation activation [11, 12]. The administration of ASA immediately before or during

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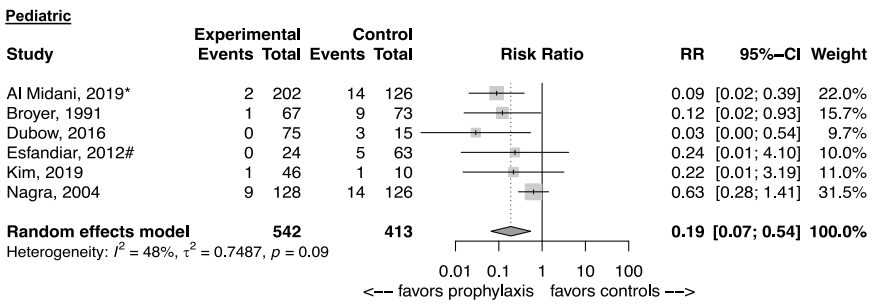
Figure 1 Results of a systematic review and meta-analysis of antithrombotic strategies to prevent allograft thrombosis in paediatric and adult kidney transplantation: heparin monoprophylaxis unless otherwise stated (*acetylsalicylic acid [ASA] monoprophylaxis, #ASA/heparin dual prophylaxis). However, the poor quality of the available data and inconsistent management protocols do not allow an unrestricted recommendation of antithrombotic prophylaxis for paediatric KTx. In addition, the uncertain evidence does not allow reliable conclusions to be drawn on several clinical issues: Choice of drug class or agent, mono- or combination therapy, dosage, timing and duration of prophylaxis, route of administration, dosing according to thrombosis risk, drug monitoring and adverse effects.



KTx is avoided due to the lack of antidotes and the limited therapeutic drug monitoring compared to heparin. Nevertheless, the perioperative bleeding risk of ASA can be classified as low to moderate [12–15].

- The most commonly used drugs are (in decreasing order):
  - Unfractionated heparin (UFH) intravenously + low molecular weight heparin (LMWH) subcutaneously
  - LMWH subcutaneously + ASA per os
  - UFH intravenously
  - LMWH subcutaneously
  - ASA per os
  - UFH intravenously + ASA per os

  (if 2 drugs are specified: sequential use) [16].
- In the presence of impaired graft function, altered pharmacokinetics with an increased risk of accumulation (LMWH) and risk of bleeding should be considered [17, 18].

The data on antithrombotic agents and doses in paediatric kidney transplantation from a systematic review and an international survey are summarised in the following table [4, 16]:

Results of the systematic review

Active ingredient (group) + mode of application	Dose	Timing	Duration	Study
ASA p.o.	1 mg/kg, max. 75 mg OD	d 0	≥ 4 weeks	[19]
LMWH s.c.	Start: 0.5 mg/kg initial dose Continuation: 0.4 mg/kg BD	d −1 d +1	21 d	[20]
UFH i.v. continuously **UFH i.v. bolus** (in case of concerns for increased risk of thrombosis)	10 IU/kg/h 10 IU/kg	d 0 d 0 (intraoperatively)	5–7 d	[21]
UFH s.c.	<15 kg: 1000 IU TD 15–20 kg: 1500 IU TD 20–40 kg: 2500 IU TD	d 0	Until mobilisation	[22]
Low thrombosis risk:				[23]*
UFH i.v. continuously **ASA p.o.**	10 IU/kg/h 3–5 mg/kg/d 3 x/week	Postoperatively Subsequently	7 d 1 year	
High thrombosis risk:				
UFH i.v. continuously **LMWH (Enoxaparin) s.c.** **ASA p.o.**	10 IU/kg/h 1 mg/kg OD 3–5 mg/kg OD 3 x/week	Postoperatively Subsequently Subsequently	7 d 8 weeks 1 year	

* Study publication after completion of the systematic review, therefore not included in the latter and presented separately. Abbreviations: ASA, acetylsalicylic acid; BD, twice a day; d, day; h, hour; IU, international units; i.v., intravenously; kg, kilograms (body weight); LMWH, low molecular weight heparin; mg, milligrams; OD, once a day; p.o., per os; s.c., subcutaneously; TD, thrice a day; UFH, unfractionated heparin; 0 = day of transplantation

International survey results compared with general dosing recommendations [16, 24]

Active ingredient (group) + mode of application	Dosage	
	Survey results	Dosing recommendations from a paediatric formulary
ASA p.o.	1–5 mg/kg OD	1 month–18 years: 3–5 mg/kg OD, max. 80 mg/d [11, 25]
UFH i.v. bolus intraoperatively	5000 IU once 20–40 IU/kg once	–
UFH i.v. continuously	100–400 IU/kg/d	(perioperative thrombosis prophylaxis) 1 month–18 years: 10 IU/kg/h [24]
LMWH s.c. (Enoxaparin)	0.5–1 mg/kg OD or divided in BD	(Indication: prophylaxis) 2 months–18 years: 0.5 mg/kg BD (= 100 IU/kg/d) [26]

Abbreviations: ASA, acetylsalicylic acid; BD, twice a day; d, day; h, hour; IU, international units; i.v., intravenously; kg, kilograms (body weight); LMWH, low molecular weight heparin; mg, milligrams; OD, once a day; p.o., per os; s.c., subcutaneously; UFH, unfractionated heparin; 0 = day of transplantation

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