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Antithrombin substitution practice in pediatric cardiac surgery: A European survey

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Data statement:

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/pan.14633](https://doi.org/10.1111/pan.14633)

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The antithrombin concentration of neonates is approximately half that of adults. Low preoperative antithrombin concentration in this population have been associated with increased transfusion requirements.¹ Similarly, low antithrombin concentration result in poor response to unfractionated heparin and inability to establish adequate anticoagulation during extracorporeal circulation (e.g., cardiopulmonary bypass, CPB), placing patients at risk for thrombosis.² Despite obvious mode of action, there are no well-described clinical benefits of antithrombin usage in clinical practice.

The aim of this survey was to identify the practice of antithrombin usage in pediatric cardiac surgery across Europe. The authors developed a 55-item electronic questionnaire to evaluate the following areas: the local practice of antithrombin management and substitution, including antithrombin monitoring and target levels, antithrombin administration techniques, and monitoring of anticoagulation. The survey was endorsed by the European Association of Cardiothoracic Anesthesiology and Intensive Care (EACTAIC) and distributed among its members. Respondents had to identify themselves as pediatric cardiac anesthesiologists before they were allowed to enter the questionnaire.

A total of 118 responses were received. The half of respondents confirmed that they were currently working as pediatric cardiac anesthesiologists and were allowed to participate in the survey.

Sixty-eight percent of participants (39/57) regularly measure antithrombin concentration and 79% (31/39) regularly substitute antithrombin in different pathophysiological scenarios in pediatric congenital heart surgery (Table). Thirty-two percent (12/37) substitute antithrombin in all cardiac surgery cases with low antithrombin concentration. In the setting of CPB, 41% (15/37) substitute antithrombin. In patients < 6 months of age scheduled for cardiac surgery, half of the respondents (54%, 20/37) not routinely substitute antithrombin. In pediatric patients with low antithrombin concentration on veno-arterial extracorporeal membrane oxygenation (ECMO), 78% (29/37) replace antithrombin. In all cardiac patients (with or without cardiac surgery), more than 65% (21/32) of respondents measure antithrombin concentration only when specifically indicated, 28% (9/32) before administration, and 25% (8/32) preoperatively (in case of cardiac surgery). In patients on veno-arterial ECMO, 50% (16/32) measure antithrombin once daily, 31% (10/32) before administration, 28% (9/32) only on specific indication, 25% (8/32) after administration or before ECMO implantation, respectively. The primary strategy for antithrombin concentration below target was immediate substitution in 54% (14/26) of respondents. Twenty-seven (7/26) percent opted for repeated measurements to make a final decision. In a situation with low antithrombin concentration and known heparin resistance, 100% (31/31) of responders substitute antithrombin. In a situation with known heparin resistance and unmeasured antithrombin concentration, half of the participants (52%, 16/31)

not substitute antithrombin. In unclear clinical situations with suspected low antithrombin concentration (e.g., disseminated intravascular coagulation), 77% (24/31) not substitute antithrombin without a previous level measurement. Antithrombin substitution occurred in 66% (18/27) using calculations as provided by the manufacturer, in 22% (6/27) using a standard dose (e.g., 500 U antithrombin concentrate), and in 11% (3/27) using a calculation based on a custom formula.

In this European survey examining the use of antithrombin in pediatric cardiac patients, we found widespread use of antithrombin measurement and substitution strategies. The most important areas for antithrombin monitoring and substitution were ECMO, in patients with inadequate elevation of activated clotting time during cardiac surgery with CPB, and in patients with known heparin resistance in combination with low antithrombin concentration.

The most common consensus in the literature regarding antithrombin administration is inadequate response to heparin.^{3,4} In our survey, antithrombin was substituted in all cases when a low antithrombin concentration was present in combination with detected heparin resistance. Regarding the use of antithrombin in different procedures without surgery, this study confirms large differences between institutions. One possible explanation is the lack of evidence in the literature for the use of antithrombin in specific cardiac lesions including specific cardiac surgery populations as for example cyanotic patients with high hematocrit. This survey underlines again the need for further, adequately powered studies regarding antithrombin monitoring and substitution in the pediatric cardiac patients undergoing surgery or interventions.

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Table: Antithrombin substitution practice in different pathophysiological and clinical conditions

Condition	Antithrombin substitution	Antithrombin substitution	Antithrombin substitution
	- YES -	- NO -	- no answer -
Sano shunt / mBT or central shunt	45.95 (17/37)	51.35 (19/37)	2.70 (1/37)
Glenn operation (PCPC)	45.95 (17/37)	51.35 (19/37)	2.70 (1/37)
Fontan operation (TCPC)	45.95 (17/37)	51.35 (19/37)	2.70 (1/37)
Cyanotic patients	40.54 (15/37)	59.46 (22/37)	---
Low cardiac output state	32.43 (12/37)	67.57 (25/37)	---
Redo surgery	45.95 (17/37)	54.05 (20/37)	---
Routinely in patients on UFH	47.22 (17/36)	52.78 (19/36)	---
Routinely in patients on LMWH	30.56 (11/36)	69.44 (25/36)	---
Routinely in patients with the need for high heparin doses to reach institutional ACT target	80.56 (29/36)	19.44 (7/36)	---
On occasion (e.g., no adequate ACT increase during cardiac surgery)	77.78 (28/36)	22.22 (8/36)	---

Legend: mBT, modified Blalock-Taussig shunt; PCPC, partial cavo-pulmonary connection; TCPC, total cavo-pulmonary connection; UFH, unfractionated heparin; LMWH, low molecular weight heparin; ACT, activated clotting time. Numbers are percentages (number of positive or negative responses for each question / total number of responses per question).