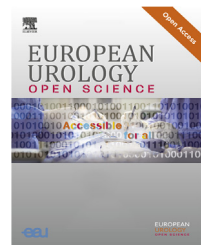




European Association of Urology



## Pediatric Urology

# Managing Preoperative Anxiety and Thromboprophylaxis in Children Undergoing Urological Procedures: An Update of the European Association of Urology/European Society for Paediatric Urology Guidelines on Paediatric Urology

Michele Gnech<sup>a,†,\*</sup>, Lisette 't Hoen<sup>b,†</sup>, Martin Skott<sup>c</sup>, Guy Bogaert<sup>d</sup>, Marco Castagnetti<sup>e</sup>, Fardod O'Kelly<sup>f,g</sup>, Josine Quaedackers<sup>h</sup>, Yazan F. Rawashdeh<sup>c</sup>, Uchenna Kennedy<sup>i</sup>, Allon van Uitert<sup>j</sup>, Yuhong Yuan<sup>k,l</sup>, Marco Capecci<sup>m,n</sup>, Andrea Artoni<sup>n</sup>, Gülhan Karaöz-Bulut<sup>o</sup>, Niklas Pakkasjärvi<sup>p,q</sup>, Berk Burgu<sup>r</sup>, Anna Bujons<sup>s</sup>, Mesrur Selcuk Silay<sup>t</sup>, Christian Radmayr<sup>u</sup>

<sup>a</sup> Department of Paediatric Urology, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; <sup>b</sup> Department of Pediatric Urology, Erasmus Medical Center, Rotterdam, The Netherlands; <sup>c</sup> Department of Urology, Section of Pediatric Urology, Aarhus University Hospital, Aarhus, Denmark; <sup>d</sup> Department of Urology, University of Leuven, Leuven, Belgium; <sup>e</sup> Department of Surgical, Oncological and Gastroenterological Sciences, University of Padova, Padova, Italy; <sup>f</sup> Division of Paediatric Urology, Beacon Hospital Dublin, Dublin, Ireland; <sup>g</sup> University College Dublin, Dublin, Ireland; <sup>h</sup> Department of Urology, University Medical Center Groningen, Groningen, The Netherlands; <sup>i</sup> Department of Pediatric Urology, University Children's Hospital Zurich, Zurich, Switzerland; <sup>j</sup> Department of Urology, Radboud University Medical Centre, Nijmegen, The Netherlands; <sup>k</sup> Department of Medicine, London Health Science Centre, London, Ontario, Canada; <sup>l</sup> Department of Medicine, McMaster University, Hamilton, Ontario, Canada; <sup>m</sup> Division of Hematology, Gruppo Ospedaliero Moncucco, Lugano, Switzerland; <sup>n</sup> Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; <sup>o</sup> Department of Pediatric Anesthesiology, Erasmus Medical Center, Rotterdam, The Netherlands; <sup>p</sup> Department of Pediatric Surgery, New Children's Hospital, Helsinki University Hospital, Helsinki, Finland; <sup>q</sup> Department of Pediatric Surgery, Section of Urology, University Children's Hospital, Uppsala, Sweden; <sup>r</sup> Department of Pediatric Urology, Ankara University School of Medicine, Ankara, Turkey; <sup>s</sup> Division of Pediatric Urology, Urology Department, Fundació Puigvert, Universitat Autònoma Barcelona, Barcelona, Spain; <sup>t</sup> Division of Pediatric Urology, Department of Urology, Biruni University, Istanbul, Turkey; <sup>u</sup> Department of Urology, Medical University of Innsbruck, Innsbruck, Austria

## Article info

### Article history:

Accepted February 23, 2025

### Associate Editor:

Véronique Phé

### Keywords:

Premedication  
Midazolam  
Clonidine  
Analgesia  
Anaesthesia

## Abstract

**Context:** The literature on preventative measures against anxiety and antithrombotic management in children undergoing urological procedures is still limited, resulting in a generally low level of evidence. These guidelines aim to provide a practical approach based on a consensus from the European Association of Urology (EAU)/European Society for Paediatric Urology (ESPU) Paediatric Urology Guidelines Panel.

**Objective:** The authors aim to provide the 2024 EAU/ESPU Paediatric Urology Guidelines Panel update of the chapter on perioperative management of urological procedures in children.

**Evidence acquisition:** A structured literature review was performed for all relevant publications published from the last update until April 03, 2023.

<sup>†</sup> Michele Gnech and Lisette 't Hoen share co-first authorship.

\* Corresponding author. Department of Paediatric Urology, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy. Tel. +39 339 7044959, +41 79 468 9877.

E-mail address: [michele.gnech@policlinico.mi.it](mailto:michele.gnech@policlinico.mi.it) (M. Gnech).



Antithrombotic prophylaxis  
Thromboembolism  
Catheter-associated thrombosis

**Evidence synthesis:** The most important updates include the following: anxiety and distress should be prevented or relieved by combining measures such as premedication, distraction techniques, and presence of parents or caregivers. Clinicians should select the appropriate premedication depending on the patient's age, underlying conditions, and psychological status. A particular focus must be placed on paediatric patients with "special needs", including children with psychophysical disorders that impact their relational and cognitive abilities. This unique population requires carefully tailored perioperative management. The incidence of perioperative thromboembolic events in the paediatric population is generally low. Controversies still exist on whether to perform a preoperative coagulation panel test on a routine basis. Neonates and adolescents are at a higher risk of perioperative thromboembolic events than the other children. Standard perioperative antithrombotic prophylaxis is not recommended due to a lack of high-quality evidence-based data.

**Conclusions:** This paper is a summary of evidence on preventative measures against anxiety and antithrombotic management in children undergoing urological procedures.

**Patient summary:** In this summary and update of the European Association of Urology/European Society for Paediatric Urology guidelines on paediatric urology, we provide practical considerations for preventative measures against anxiety and antithrombotic management in children undergoing urological procedures.

© 2025 The Author(s). Published by Elsevier B.V. on behalf of European Association of Urology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

These guidelines aim to provide a practical approach for the perioperative management of children undergoing urological surgery based on a thorough literature review and risk analysis.

This publication summarises the 2024 update of the chapter on perioperative management of children undergoing urological surgery of the European Association of Urology (EAU) and European Society for Paediatric Urology (ESPU) guidelines. We specifically highlight the available evidence for preventative measures around diagnostic and surgical procedures and antithrombotic prophylaxis in this specific age group.

In paediatric urology, surgical procedures may not only induce anxiety, but also use more invasive diagnostic procedures, including the placement of a catheter. Recently, more evidence about anxiety around diagnostic and surgical procedures and their management has become available. As part of the EAU/ESPU Paediatric Urology Guidelines Panel, we consider this a topic of particular importance and want to highlight the preventative management options in this statement paper.

To our knowledge, there are no such publications on this topic summarising the different aspects that need to be considered for adequate preventative measures for a child undergoing urological procedures as well as antithrombotic prophylactic measures.

Unfortunately, the available evidence is still scarce, and the lack of robust prospective randomised controlled trials limits the strength of the established guidelines since the majority of studies are retrospective, include heterogeneous groups, and have poor-quality stratification.

## 2. Methods

The various chapters of the EAU/ESPU paediatric urology guidelines are updated at regular intervals. For the update of this particular chapter, a structured literature search was performed by a research information specialist and reviewed by at least two panel members for all relevant publications published since the previous update from June 2019 until April 2023, followed by a critical appraisal of the full texts (Supplementary material). After discussion with the guideline panel in a face-to-face meeting, it was decided that inclusion of all relevant literature would be too much for the guidelines itself. However, a statement paper on these topics was considered relevant. The literature search was performed using the following databases: MEDLINE, Embase, Cochrane CENTRAL, and Cochrane CDSR (via Ovid). Keywords related to preoperative management and urological surgeries were searched using Boolean operators. Variations of root words were searched. Conference abstracts were excluded. Only publications in English were eligible for inclusion. The search strategy is provided in the Supplementary material of the Guidelines chapter [1].

## 3. Evidence synthesis

### 3.1. Preventative measures against anxiety

A significant group of children undergoing invasive diagnostic procedures, anaesthesia, and surgery develop anxiety that could lead to adverse reactions. Many factors may influence preoperative anxiety such as age, environment, American Society of Anesthesiologists (ASA) status, previous hospitalisation/anaesthesia/surgery, preoperative pain, and parental/caregiver stress [2]. Anxiety and distress

should be prevented or relieved by combining various measures such as distraction techniques, presence of parents or caregivers, and premedication [3]. Studies have shown that children with increased anxiety before surgery are more prone to develop adverse clinical outcomes, such as emergence delirium and increased analgesic requirements. In addition, negative postoperative behavioural changes, such as sleep disturbances, separation anxiety, eating problems, new-onset enuresis, and aggression, are seen more often [4]. Children react to the surgery and anaesthesia in an age-dependent manner. Infants usually accept parental surrogates and experience less anxiety on separation from parents than older children. A reduction in fasting times to a minimum will usually result in a calmer infant. Patients aged 1–3 yr are less vulnerable to separation anxiety than older ones. Children older than 3 yr should be prepared for surgical and anaesthetic procedures with child-friendly and age-appropriate explanations, which are usually effective in reducing anxiety.

#### 3.1.1. Nonmedical preventative measures

Nonpharmacological methods (distraction techniques), such as play therapy, toys, storybooks, videos, tablets, mobile phones, clowns, immersive virtual reality, and hypnosis, as well as the presence of parents during the procedure or induction can be effective techniques for and considered an indispensable part of procedural sedation and/or analgesia in children, although these are often underestimated. These measures can be an alternative to pharmacological sedation, reducing possible adverse reactions and contributing to a much quicker recovery. Elevated stress and anxiety can affect healing negatively. Additionally, there is an improvement in satisfaction of the children and their families, which is essential for their emotional well-being and can facilitate their collaboration with the entire professional paediatric team. Before the procedure, it is important to provide information directed at the child and parents, adjusted to their level of understanding, as well as additional sensory information (what the child can expect to feel, see, hear, and smell) to make the event more predictable for the child [5,6].

Studies have shown that the introduction of clowns into children's medical care can significantly reduce anxiety, pain during the preoperative period, recovery time, and also care costs [7,8].

Immersive virtual reality has also proved to be effective in providing distraction and information about procedures interactively, potentially being more effective than usual medication in reducing pain or anxiety. It is recommended for short procedures where stress and immobilisation can negatively impact the children's experience. The content must be ensured to be suitable for children's age and cognitive development [9–11].

Although more studies are required, hypnosis has shown promising results compared with pharmacological sedation, indicating its potential as a useful tool in reducing preoperative anxiety. Other strategies that could be included are games and music. These techniques should also be adapted according to the child's age and individual preferences to increase their effectiveness and efficiency [6].

The presence of parents can have both positive and negative effects on the child's anxiety level. Anxious parents can have a negative effect on the stress levels of an otherwise calm child. There are indications that the presence of parents who have specifically been prepared and trained to provide their child with adequate support during the induction leads to less distress and postoperative pain in the child [12].

All these strategies represent measures for more patient-centred care, focusing not only on their physical aspects, but also on their emotional and psychological well-being.

#### 3.1.2. Premedication

The main purpose of premedication is to reduce anxiety, which can facilitate separation from the parents/caregivers and make the induction of anaesthesia easier. During the anaesthetic visit, it is fundamental to establish with the parents/caregivers the right methods of administration of pre-anaesthetic drugs, type of administration, dosage of administration, route of administration, and time of administration, in order to prevent physiological stress and amnesia, reduce the demand for anaesthetics drugs, decrease antiemetic effects, and reduce secretions and analgesia [13].

Evaluation of anxiety is the first step in prevention and treatment. Numerous scales, such as the modified Yale Preoperative Anxiety Scale, Children's Fear Scale, Spielberger short version State-Trait Anxiety Inventory, and Wong-Baker FACES, can be used for the evaluation.

Preanaesthetic sedatives in children, such as midazolam, clonidine, ketamine, and dexmedetomidine, are used as premedication, but no consensus has been reached on the best choice to prevent preoperative anxiety (Table 1). Clinicians should select the appropriate premedication depending on the patient's age, and disease and psychological status [4]. In noncollaborating children, premedication should be administered 45/60 min before transfer to the operating room, and it is advisable to combine sugar with the oral sedative or dilute the drug with a patient's favourite beverage in a teaspoon (clear liquids).

**3.1.2.1. Midazolam.** Midazolam is the most commonly used premedication in children, usually administered approximately 20 min prior to induction. The benefits include a rapid and reliable onset and antegrade amnesia with minimal respiratory depression. It is usually administered orally (water soluble) at a dose of 0.3–0.75 mg/kg, up to a maximum of 20 mg, after which sedation and anxiolysis are usually achieved within 20 min. Midazolam, administered orally, has a bitter taste even if various agents are used to increase palatability. Oral midazolam may fail to reduce anxiety in 20% of patients, and a small number of patients can even have paradoxical reactions. Postoperative prolonged sedation could be a side effect if the surgical procedure is short. Side effects are postoperative behavioural changes, paradoxical reactions, and respiratory depression. It can also be administered intranasally (0.3 mg/kg), rectally (0.5 mg/kg), or via a sublingual (0.3 mg/kg) route. For these alternative routes of administration, peak plasma levels may be reached faster than for the oral route. However, discomfort has been associated

**Table 1 – Summary of evidence and recommendations for the premedication management**

Summary of evidence
Many factors may influence preoperative anxiety such as age, environment, ASA status, previous hospitalisation/anaesthesia/surgery, preoperative pain, and parental/caregiver stress.
Anxiety and distress should be prevented or relieved by combining premedication, distraction techniques, and parental or caregivers' presence.
Children with increased anxiety before surgery are more prone to develop adverse clinical outcomes.
Preanaesthetic sedatives in children, such as midazolam, clonidine, ketamine, and dexmedetomidine, are used as premedication, but no consensus has been reached on the best choice against preoperative anxiety.
Clinicians should select the appropriate premedication depending on the patient's age, disease, and psychological status.
Particular attention must be given to the paediatric patients with "special needs". Perioperative management of this particular population must be planned carefully.
ASA = American Society of Anesthesiologists.

with secondary local irritations at the administration site. Midazolam can also be administered intravenously (i.v.), if the i.v. line is in situ (0.05–0.2 mg/kg), just before wheeling the child into the operating room [4].

**3.1.2.2. Clonidine.** Clonidine is another common drug used preoperatively to reduce anxiety in uncooperative children. Clonidine (3–4 µg/kg) administered by the oral route is absorbed rapidly, achieving a peak plasma concentration within 1–1.5 h after administration and with a relatively long onset time (approximately 45 min). It reduces the need for rescue analgesia and decreases agitation, post-operative nausea, and vomiting. The most frequent side effects are hypotension and bradycardia. Unlike midazolam, intranasal clonidine (2–4 µg/kg) is not associated with local discomfort, but it does not achieve rapid peak plasma concentration faster than midazolam. Clonidine is superior to midazolam in terms of inducing sedation, reducing postoperative pain and agitation, as well as decreasing postoperative nausea and vomiting [4,13].

**3.1.2.3. Dexmedetomidine.** Dexmedetomidine has anxiolytic and analgesic effects; it reduces opioid requirements without causing respiratory depression. Dexmedetomidine has a shorter terminal half-life (approximately 2 h in children), and compared with midazolam, it produces more satisfactory sedation upon parent separation and mask acceptance. Its oral administration (2.5–4 µg/kg) is associated with poor bioavailability. Intranasal dexmedetomidine has been used successfully at a dose of 1 µg/kg administered 45–60 min prior to induction. The limitations to its use include long onset times (30 min), bradycardia, and hypotension similar to clonidine [13,14].

**3.1.2.4. Ketamine.** Ketamine benefits include analgesic properties and the ability to cause sedation without respiratory depression. The most common side effects include increased salivation and bronchial secretions, emergence delirium, and prolongation of recovery. Owing to the availability of premedication agents with fewer side effects, ketamine is replaced with other drugs described earlier or is often reserved for older patients. It can be administered via the oral (5–8 mg/kg), intramuscular (4–6 mg/kg), or i.v. (1–2 mg/kg) routes [4,15].

**3.1.2.5. Melatonin.** Some authors report melatonin to have a protective effect against delirium, has sedative effects, and decreases sedative consumption. It can be used

as a sedative agent administered by the oral route (0.5 mg/kg) 30 min before surgery.

**3.1.2.6. Topical analgesia.** Topical anaesthesia should be used to reduce or eliminate the pain of intravenous access placement when intravenous induction is required. The most used local aesthetic creams require 20–60 min for maximal effect, but these can cause vasoconstriction, which could make it even more difficult to identify a proper vein for cannulation [2].

**3.1.2.7. Children with "special needs".** Particular attention must be given to the paediatric patients with "special needs" such as children suffering from psychophysical disorders with related relational and cognitive problems. Perioperative management for this particular population must be planned carefully, in order to make the entire hospitalisation process as comfortable as possible and least traumatic. First-line medications include midazolam, clonidine, and dexmedetomidine; ketamine is a second-line drug. All these should always be administered under supervision, and devices for supplemental oxygen administration and support for ventilation and resuscitation should always be available. The oral route should be considered the first choice, followed by the intramuscular route. Distraction techniques and parental/caregivers' presence can be very helpful in "special needs" children [13].

### 3.2. Antithrombotic prophylaxis

Antithrombotic prophylaxis involves preventive measures to reduce the risk of blood clot formation. Unlike in adults, this is not routinely indicated perioperatively in children. However, in specific situations with underlying medical conditions carrying an increased risk of thrombotic events, such as malignancies or congenital heart diseases, antithrombotic prophylaxis may be considered. Owing to the lack of clinical trials on the use of anticoagulants in the paediatric population, very limited and low-quality data on their efficacy and safety are available (Table 2).

The incidence of venous thromboembolism (VTE) in children is low; however, it has increased over time as a consequence of the intensified use of central venous catheters (CVCs), improved awareness among clinicians, and the use of high-resolution imaging modalities, which has led to detection improvement [16,17]. An incidence of five to eight cases of symptomatic VTE per 10 000 hospital admissions (0.05–0.08%) has been reported, but these figures may rep-



**Table 2 – Summary of evidence and recommendations for the management of antithrombotic prophylaxis management**

Summary of evidence
The incidence of perioperative thromboembolic events in the paediatric population is generally very low.
Ultrasound or magnetic resonance represents the imaging technique of choice in case of a suspicion of VTE.
Controversies still exist on the opportunity to routinely perform a coagulation panel test before surgery.
Neonates and adolescents are at a higher risk of perioperative thromboembolic events.
A CVC placed in the internal jugular vein is associated with the lowest risk of thrombosis.
The standard perioperative antithrombotic prophylaxis is not recommended due to a lack of high-quality RCTs and accepted guidelines.
CVC = central venous catheter; RCT = randomised controlled trial; VTE = venous thromboembolism.

resent an underestimation considering that in the majority of cases, VTE is clinically silent in the paediatric age group with an incidence rate that rises to around 15% [17]. A bimodal distribution has been described, with a first incidence peak under 2 yr of age and the second appearing during adolescence [18].

The most relevant risk factors for VTE in infants are represented by sepsis, congenital haematological disorders, malignancies, nephrotic syndrome, and total parenteral nutrition, while in adolescence, additional risk factors typical of what are seen in adulthood may materialise [17]. These factors include smoking, obesity, pregnancy, and use of oestrogen-containing oral contraceptives. Oral contraceptive use is responsible for the higher prevalence of VTE in females, with a male to female ratio of 1:2 [19].

Aside from the aforementioned age-specific risk factors, the majority (40–46%) of paediatric events are surgery related, with CVCs being the most significant [19]. VTE after urological surgery has been shown to have an incidence of 0.12%, which increases to 0.2% in case the surgery is prolonged [20,21].

Overall, before adolescence, the risk of VTE after major surgery, trauma, or immobilisation is low, even in the presence of thrombophilia abnormalities, compared with adolescents (>13 yr), especially in the presence of one or more risk factors for thrombosis [18,22].

### 3.2.1. Diagnostic evaluation

A VTE diagnosis in the paediatric population represents a real challenge for clinicians, since most cases are asymptomatic. In children, the absolute necessity of identifying asymptomatic VTE is also debated. Whereas asymptomatic events in adults have the same risk of morbidity and mortality as overt events and necessitate prompt identification and adequate management, the condition in children lacks any strong treatment recommendations, given the very limited epidemiological and outcome data in the literature.

Paediatric signs and symptoms of deep vein thrombosis are similar to presentations in adult patients and depend on the site of the vein involved. Pain, oedema of the involved area, and development of collateral vessel circulation are typical of limb venous thrombosis; dyspnoea, thoracic pain, and haemoptysis are features of pulmonary embolism and headache; and generalised neurological deficits and seizures are typical of cerebral vein thrombosis (CVT). Neonates, especially in the first 2 wk of life, may present with a peculiar and dramatic clinical picture characterised by systemic coagulopathy and necrotic cutaneous ulcers; this condition is known as neonatal purpura fulminans, and is caused by a deficit of the natural anticoagulant

protein C and less frequently of its cofactor protein S. This condition should promptly be recognised and treated to prevent its progress towards multiorgan failure.

When a deep venous thrombosis is suspected, the first-line imaging technique depends on the thrombosis site. Ultrasound is recommended for the initial evaluation of thrombosis in lower and upper limbs. In case of absence of documented thrombosis in the ultrasound image of the lower limbs but in the presence of a high clinical suspicion of thrombosis, another ultrasound should be repeated within a week in order not to miss proximal progression of an initial thrombus in a calf vein. In case of absence of documented thrombosis in an ultrasound image of the upper limbs, with a high clinical suspicion of thrombosis of the proximal/intrathoracic veins, a magnetic resonance (MR) venography or, in selected cases, a venography should be performed. The gold standard for the diagnosis of suspected CVT is represented by contrast-enhanced computed tomography (CT) venography or the preferred MR venography, due to the absence of the need of contrast administration and the absence of ionising radiation. In neonates, the first choice is represented by transfontanelar Doppler ultrasound, which is a widely available and noninvasive technique, although highly operator dependent. In case CVT is suspected, the diagnostic imaging should also evaluate the petrous temporal bones and sinuses to exclude the presence of a sinusitis and/or mastoiditis, which represents the most common risk factor for CVT in children and adolescents [23].

In case a pulmonary embolism is suspected, contrast-enhanced CT angiography or ventilation/perfusion lung scintigraphy represents the gold standard for diagnosis, similar to that in adults.

When facing a nonfunctioning CVC, causes other than thrombosis, such as catheter kink or mispositioned tip, should be excluded by performing a chest x-ray. If catheter thrombosis is suspected, ultrasound or venography (to evaluate proximal/intrathoracic veins) should be considered. Serial imaging to identify asymptomatic CVC thrombosis is not recommended in children [18].

### 3.2.2. Laboratory evaluation before surgery

The currently available international guidelines of the ASA and the British Committee for Standards in Hematology recommend against performing preoperative coagulation testing (prothrombin time [PT] and activated partial thromboplastin time [aPTT]) in healthy patients without a personal history of abnormal bleeding [24,25]. Indeed, these tests have low sensitivity and negative predictive value, showing poor performance as routine presurgery screening

tests. Furthermore, in addition to being ineffective, indiscriminate testing may cause unnecessary delays in surgery.

Despite the aforementioned guidelines, controversies still exist regarding the routine performance of a coagulation panel test before surgery. The largest retrospective cohort study published to date, involving over 600 000 patients undergoing routine surgery, found an association between the test results and perioperative bleeding risk [26].

Abiding by the current guideline recommendations of not to perform a preoperative coagulation screening mandates quick availability of such tests in cases of intraoperative bleeding, in order to exclude haemostatic abnormalities that may require rapid intervention.

Given these controversies in adult patients, evidence available for the paediatric population is even sparse. In such patients, personal bleeding history may not be sufficient to guide the choice between testing or not, due to a shorter exposure time to potential haemorrhagic triggers. Considering the current lack of evidence, we suggest performing in paediatric patients undergoing surgery a complete blood test to evaluate the platelet count and a basic coagulation panel test including PT, aPTT, and fibrinogen. We also recommend careful evaluation of the family bleeding history and, if clearly positive, consideration of additional blood testing such as von Willebrand factor panel testing even in the presence of a normal bleeding screening.

### 3.2.3. Perioperative antithrombotic prophylaxis

**3.2.3.1. Physical interventions.** Physical treatments for antithrombotic prophylaxis are the same as the ones used in adult patients: graduated compression stockings (GCSs), intermittent pneumatic compression (IPC) devices, and venous foot pumps. No paediatric sizes of GCSs or IPC devices are available so far, so these are applicable only in older patients, usually over 40 kg in weight or older than 13 yr. IPC devices have been used for intraoperative use in children aged 13 yr and older with a weight of >40 kg and those who are expected to have prolonged (>60 min) surgery [18].

The evidence for using these devices is significantly lower than for pharmacological treatment, and limited data are available regarding their use in children and adolescents [27].

General preventive measures are fundamental to prevent VTE and should include adequate peri- and postoperative hydration, in addition to encouraging early mobilisation after surgery in patients of all ages. Moreover, rapid removal of CVCs that are no longer required should be considered. In female patients of child-bearing age who are on combined oral contraceptives, withdrawal of CVCs 4 wk before surgery should be considered based on the presence of known thrombophilia abnormalities or a strong family history of thrombosis [18].

**3.2.3.2. Pharmacological methods.** Evidence on the use of anticoagulant agents to prevent VTE in children is very scarce. None of the currently available preparations are licensed for use in the paediatric population. Owing to the more predictable pharmacokinetics of low-molecular-

weight heparin (LMWH) than that of unfractionated heparin, LMWH has become the anticoagulant of choice in this setting, for both prophylaxis and treatment. Notably, LMWH does not need monitoring with anti-Xa activity except in selected cases and is associated with a lower incidence of major bleeding events, which is particularly low for prophylactic doses, in comparison with unfractionated heparin [28]. Children younger than 8 wk of age and/or with a weight of <5 kg require higher doses of LMWH due to a larger volume of distribution and reduced antithrombin levels secondary to decreased production and higher renal clearance. The most commonly used drugs are enoxaparin and dalteparin, which should be used at a dose of 100 IU/kg once daily or at an increased dose of 150 IU/kg once daily in the aforementioned situations. Vitamin K antagonists may be used in children and considered in selected cases for antithrombotic prophylaxis even though management in this setting is cumbersome and not standardised. Direct oral anticoagulants are not licensed for primary antithrombotic prophylaxis in the paediatric population, with rivaroxaban being the only one approved exclusively for VTE treatment and secondary prophylaxis.

**3.2.3.3. Identification of patients with indication for pharmacological antithrombotic prophylaxis.** Considering that there are no clear guidelines on the use of perioperative antithrombotic prophylaxis in paediatric patients, the decision should be made on an individual basis, balancing the risk/benefit ratio in terms of thrombotic and bleeding risk.

Neonates and adolescents are at a higher risk in paediatric age, and the most common risk factors include the presence of a CVC, immobility, trauma, sepsis, cancer, and congenital heart disease.

The presence of a CVC is the most significant risk factor for VTE in children [18]. Therefore, especially in patients at an increased risk of VTE for other causes, a CVC should be placed in the right internal jugular vein, which represents the site that seem to be associated with the lowest risk, while the femoral vein should be avoided as it is associated with the highest risk of thrombosis [29]. The risk of catheter-associated thrombosis is even higher in specific settings such as in children with acute lymphoblastic leukaemia receiving L-asparaginase, in whom not only the CVC location, but also the insertion technique (cut down vs percutaneous approach) exerts an important role [29]. Therefore, a CVC should be avoided in this specific setting. Primary antithrombotic prophylaxis in patients with a CVC is not recommended and should be reserved to patients with concomitant risk factors for thrombosis.

Another setting in which primary antithrombotic prophylaxis should be considered involves adolescents older than 13 yr with multiple risk factors for thrombosis, especially in those undergoing major surgery, in whom immobilisation for >48 h is expected [28].

All patients with a previous episode of venous thrombosis should undergo postoperative antithrombotic prophylaxis.

In all the other situations, the decision regarding when to institute primary antithrombotic prophylaxis is more challenging and should take into account the personal history,

with the aim to evaluate the exposure to previous risk factors for thrombosis and the consequent outcome and the family thrombotic history. In case of clear positivity of the family history for thrombosis, a thrombophilia screening may be considered to identify possible thrombophilia abnormalities that may help decide instituting antithrombotic prophylaxis.

#### 4. Conclusions

Numerous factors can impact preoperative anxiety, including age, environment, ASA status, prior hospitalisations, anaesthesia, surgery, preoperative pain, and parental or caregiver stress. It is crucial to prevent or alleviate anxiety and distress through a combination of premedication, distraction techniques, and the presence of parents or caregivers. Children exhibiting heightened anxiety before surgery are more susceptible to experiencing adverse clinical outcomes. Various preanaesthetic sedatives, such as midazolam, clonidine, ketamine, and dexmedetomidine, are used for premedication in children. However, consensus regarding the optimal choice for managing preoperative anxiety is lacking. Clinicians should select appropriate premedication carefully based on the patient's age, medical condition, and psychological state. Special attention should be directed towards paediatric patients with "special needs", necessitating meticulous planning for their perioperative care.

The incidence of perioperative thromboembolic events among the paediatric population is typically low. Despite on-going controversies regarding the necessity of routine coagulation panel assessments prior to surgery, we recommend conducting a complete blood count test to assess platelet levels and a basic coagulation panel assessment encompassing PT, aPTT, and fibrinogen levels, alongside a comprehensive family bleeding history evaluation. Neonates and adolescents face a higher risk of perioperative thromboembolic complications. Opting for CVCs inserted into the internal jugular vein minimises the risk of thrombosis. Standard antithrombotic prophylaxis during the perioperative phase is not advised due to insufficient high-quality randomised controlled trials and established guidelines. It may be prudent to consider antithrombotic prophylaxis with LMWH for adolescents displaying additional risk factors. Primary antithrombotic prophylaxis for patients with a CVC is not recommended.

**Author contributions:** Michele Gnech had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Gnech, 't Hoen, Skott, Bogaert, Castagnetti, O'Kelly, Quaedackers, Rawashdeh, Kennedy, van Uitert, Yuan, Capecchi, Artoni, Karaöz-Bulut, Pakkasjärvi, Burgu, Bujons, Silay, Radmayr.

**Acquisition of data:** Gnech, 't Hoen, Skott, Bogaert, Castagnetti, O'Kelly, Quaedackers, Rawashdeh, Kennedy, van Uitert, Yuan, Capecchi, Artoni, Karaöz-Bulut, Pakkasjärvi, Burgu, Bujons, Silay, Radmayr.

**Analysis and interpretation of data:** Gnech, 't Hoen, Skott, Bogaert, Castagnetti, O'Kelly, Quaedackers, Rawashdeh, Kennedy, van Uitert, Yuan,

Capecchi, Artoni, Karaöz-Bulut, Pakkasjärvi, Burgu, Bujons, Silay, Radmayr.

**Drafting of the manuscript:** Gnech, 't Hoen, Capecchi, Karaöz-Bulut, Radmayr.

**Critical revision of the manuscript for important intellectual content:** Gnech, 't Hoen, Skott, Bogaert, Castagnetti, O'Kelly, Quaedackers, Rawashdeh, Kennedy, van Uitert, Yuan, Capecchi, Artoni, Karaöz-Bulut, Pakkasjärvi, Burgu, Bujons, Silay, Radmayr.

**Statistical analysis:** None.

**Obtaining funding:** None.

**Administrative, technical, or material support:** Gnech.

**Supervision:** Radmayr.

**Other:** None.

**Financial disclosures:** Michele Gnech certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

**Funding/Support and role of the sponsor:** This work was supported by the European Association of Urology. The sponsor played a role in the collection and management of the data and preparation and review of the manuscript.

#### Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.euro.2025.02.006>.

#### References

- [1] EAU Guidelines Office. Development handbook. Version March 2022.
- [2] Getahun AB, Endalew NS, Mersha AT, Admass BA. Magnitude and factors associated with preoperative anxiety among pediatric patients: cross-sectional study. *Pediatric Health Med Ther* 2020;11:485–94.
- [3] Kain ZN, Mayes LC, Caldwell-Andrews AA, Karas DE, McClain BC. Preoperative anxiety, postoperative pain, and behavioral recovery in young children undergoing surgery. *Pediatrics* 2006;118:651–8.
- [4] Dave NM. Premedication and induction of anaesthesia in paediatric patients. *Indian J Anaesth* 2019;63:713–20.
- [5] Kühlmann AYR, van Rosmalen J, Staals LM, et al. Music interventions in pediatric surgery (the music under surgery in children study): a randomized clinical trial. *Anesth Analg* 2020;130:991–1001.
- [6] Wang R, Huang X, Wang Y, Akbari M. Non-pharmacologic approaches in preoperative anxiety, a comprehensive review. *Front Public Health* 2022;10:854673.
- [7] Fusetti V, Re L, Pigni A, et al. Clown therapy for procedural pain in children: a systematic review and meta-analysis. *Eur J Pediatr* 2022;181:2215–25.
- [8] Raisin G, Cohen R, Galant O, et al. Medical clowns versus sedation for paediatric urinary catheter insertion—a randomised pilot study. *Acta Paediatr* 2023;112:1319–23.
- [9] Wong CL, Choi KC. Effects of an immersive virtual reality intervention on pain and anxiety among pediatric patients undergoing venipuncture: a randomized clinical trial. *JAMA Netw Open* 2023;6:e230001.
- [10] Gold JL, SooHoo M, Laikin AM, Lane AS, Klein MJ. Effect of an immersive virtual reality intervention on pain and anxiety associated with peripheral intravenous catheter placement in the pediatric setting: a randomized clinical trial. *JAMA Netw Open* 2021;4:e2122569.

- 
- [11] Eijlers R, Utens E, Staals LM, et al. Systematic review and meta-analysis of virtual reality in pediatrics: effects on pain and anxiety. *Anesth Analg* 2019;129:1344–53.
- [12] Jain S, Patel S, Arora KK, Sharma A. A comparative study on effectiveness of parental presence versus sedative premedication for reducing anxiety in children undergoing general anesthesia. *Int J Appl Basic Med Res* 2023;13:101–5.
- [13] Ciccozzi A, Pizzi B, Vittori A, et al. The perioperative anesthetic management of the pediatric patient with special needs: an overview of literature. *Children (Basel)* 2022;9:1438.
- [14] Peng K, Wu SR, Ji FH, Li J. Premedication with dexmedetomidine in pediatric patients: a systematic review and meta-analysis. *Clinics (Sao Paulo)* 2014;69:777–86.
- [15] Yang CQ, Yu KH, Huang RR, Qu SS, Zhang JM, Li YL. Comparison of different sedatives in children before general anaesthesia for selective surgery: a network meta-analysis. *J Clin Pharm Ther* 2022;47:1495–505.
- [16] Klaassen ILM, Sol JJ, Suijker MH, Fijnvandraat K, van de Wetering MD, Heleen van Ommen C. Are low-molecular-weight heparins safe and effective in children? A systematic review. *Blood Rev* 2019;33:33–42.
- [17] Karande GY, Hedgire SS, Sanchez Y, et al. Advanced imaging in acute and chronic deep vein thrombosis. *Cardiovasc Diagn Ther* 2016;6:493–507.
- [18] Morgan J, Checketts M, Arana A, et al. Prevention of perioperative venous thromboembolism in pediatric patients: guidelines from the Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI). *Paediatr Anaesth* 2018;28:382–91.
- [19] Nguyen LT, Laberge JM, Guttman FM, Albert D. Spontaneous deep vein thrombosis in childhood and adolescence. *J Pediatr Surg* 1986;21:640–3.
- [20] Takemoto CM, Sohi S, Desai K, et al. Hospital-associated venous thromboembolism in children: incidence and clinical characteristics. *J Pediatr* 2014;164:332–8.
- [21] Ahn JJ, Merguerian PA, Shnorhavorian M. Incidence and risk factors associated with 30-day post-operative venous thromboembolism: a NSQIP-pediatric analysis. *J Pediatr Urol* 2018;14, 335.e1–6.
- [22] Journeycake JM, Manco-Johnson MJ. Thrombosis during infancy and childhood: what we know and what we do not know. *Hematol Oncol Clin North Am* 2004;18:1315–38, viii–ix.
- [23] Capecchi M, Abbattista M, Martinelli I. Cerebral venous sinus thrombosis. *J Thromb Haemost* 2018;16:1918–31.
- [24] American Society of Anesthesiologists Task Force on Perioperative Blood Management. Practice guidelines for perioperative blood management: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management. *Anesthesiology* 2015;122:241–75.
- [25] Chee YL, Crawford JC, Watson HG, Greaves M. Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British Committee for Standards in Haematology. *Br J Haematol* 2008;140:496–504.
- [26] Lim K, Satkunasivam R, Nipper C, et al. Association between isolated abnormal coagulation profile on transfusion following major surgery: a NSQIP analysis of individuals without bleeding disorders. *Transfusion* 2022;62:2223–34.
- [27] Sharma M, Carpenter SL. Thromboprophylaxis in a pediatric hospital. *Curr Probl Pediatr Adolesc Health Care* 2013;43:178–83.
- [28] Pągowska-Klimek I. Perioperative thromboembolism prophylaxis in children—is it necessary? *Anaesthesiol Intensive Ther* 2020;52:316–22.
- [29] Male C, Julian JA, Massicotte P, Gent M, Mitchell L. Significant association with location of central venous line placement and risk of venous thrombosis in children. *Thromb Haemost* 2005;94:516–21.