

## Anesthesia recommendations for **TAR Syndrome**

**Disease name:** TAR Syndrome (Thrombocytopenia with Absent Radius)

**ICD 10:** Q87.2

**ICD 11:** LD2F.1y *Other specified syndromes with multiple structural anomalies, not of environmental origin*

**ORPHAcode:** 3320

**Synonyms:**

Thrombocytopenia-Absent Radius (TAR) Syndrome [1]

Thrombocytopenia with Absent Radii Syndrome [2]

Congenital Hypomegakaryocytic Thrombocytopenia with Radial Aplasia [3,4]

Congenital Thrombocytopenia with Bilateral Absence of the Radius [5]

Thrombocytopenia with Bilateral Radial Aplasia [1]

Chromosome 1q21.1 deletion syndrome, 200Kb [6]

**Disease summary:** Thrombocytopenia-Absent Radius (TAR) Syndrome is a rare congenital disorder defined by bilateral absence or hypoplasia of the radii with preservation of the thumbs, and neonatal thrombocytopenia due to reduced megakaryocyte production [7,8,9,10].

The estimated prevalence is 1:100,000 live births, with a slight female predominance [2,11].

TAR Syndrome does not conform to a classic autosomal dominant or -recessive model [6], rather it follows a compound-inheritance pattern [12,13] involving a microdeletion at chromosome 1q21.1 encompassing RBM8A, and a hypomorphic non-coding variant in the second RBM8A allele. The resulting deficiency of the Y14 protein impairs RNA splicing and megakaryopoiesis, leading to thrombocytopenia which is most pronounced in infancy [9,12,13,14].

This represents a quantitative platelet defect rather than a functional qualitative abnormality. Bleeding severity varies and is usually greatest in the first year of life, when intracranial or gastrointestinal hemorrhage may occur. Platelet counts often improve with age, potentially reaching near-normal levels by late childhood [2,7,8,10].

Skeletal malformations primarily affect the upper limbs but may extend to the lower limbs, hips, and knees [5]. Additional anomalies can include cardiac septal defects (15-30 %), renal malformations (20-30 %), and cow's-milk protein intolerance (~50 %) [2,3,8]. Scoliosis and sensorineural hearing loss have also been reported. Craniofacial features such as micrognathia or retrognathia are reported in up to one half of patients [3,8].

Most patients now survive to adulthood with multidisciplinary care and improved transfusion support. Prognosis depends on the severity of neonatal bleeding and associated organ anomalies [3,8,9].

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Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this guideline Perhaps new knowledge.



Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

Translations may not always reflect the most recent updates of the English version.



**Find more information on the disease, its centers of reference and patient organizations on Orphanet: [www.orpha.net](http://www.orpha.net)**

## Emergency information

<b>A</b>	<b>AIRWAY / ANESTHETIC TECHNIQUE</b>	<p>Micrognathia or retrognathia: potentially difficult facemask ventilation or laryngoscopy.</p> <p>Cleft or high-arched palate (rare): risk of airway leak and aspiration.</p> <p>Thrombocytopenia: increased risk of mucosal bleeding with traumatic or nasal intubation (avoid).</p> <p>General anesthesia (GA) preferred due to airway protection and rapid hemodynamic control.</p> <p>Regional / neuraxial anesthesia (RA) carries bleeding risk – avoid if platelet count is low or unknown.</p>
<b>B</b>	<b>BLOOD PRODUCTS (COAGULATION)</b>	<p>Severe thrombocytopenia: High risk of bleeding.</p> <p>Use HLA-selected apheresis platelets if prior transfusions or alloimmunization.</p> <p>Tranexamic acid (TXA) or Desmopressin (DDAVP) may be used under hematology guidance.</p> <p>TEG / ROTEM may assist transfusion decisions in major hemorrhage.</p>
<b>C</b>	<b>CIRCULATION</b>	<p>Congenital heart disease: ASD, VSD, outflow tract anomalies (conotruncal defects) common.</p> <p>Avoid air bubbles in IV lines due to paradoxical embolism risk.</p> <p>Arterial line recommended for major surgery or expected blood loss.</p>
<b>D</b>	<b>DRUGS</b>	<p>Avoid NSAIDs, aspirin, and ketorolac (platelet inhibition).</p> <p>Adjust renally excreted agents (e.g., TXA) if renal anomalies present.</p> <p>No TAR-specific drug sensitivities or risk of malignant hyperthermia (MH).</p>
<b>E</b>	<b>EQUIPMENT</b>	<p>Prepare difficult-airway equipment (video/fiberoptic scope, SGA, surgical airway).</p> <p>Ultrasound guidance recommended for vascular access.</p> <p>Padding and limb protection essential – prevent traction or pressure injury on deformed or reconstructed limbs.</p> <p>Ensure blood products immediately available; postoperative HDU/ICU observation advised.</p>

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## Typical surgery and procedures

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Patients with TAR Syndrome most often undergo orthopedic reconstruction of upper- and lower-limb deformities, followed by orthotic or prosthetic fitting. Hand and limb correction procedures, including distraction and centralization techniques, are typically performed in early childhood [1,5].

Other reported interventions include cardiac surgery for congenital defects, maxillofacial or dental reconstruction, and various plastic or soft-tissue repairs. Obstetric procedures (particularly cesarean section) [15] have also been safely managed under general anesthesia (GA) [3,8,9].

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## Type of anesthesia

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GA is preferred for most TAR patients, providing airway protection, hemodynamic control, and secure ventilation when thrombocytopenia, congenital heart disease, or craniofacial anomalies are present. Published case reports – including orthopedic and obstetric procedures – show consistently favorable outcomes under GA. Main intraoperative risks are airway or surgical bleeding and hemodynamic fluctuation which are best managed with atraumatic technique and immediate platelet availability.

Regional and neuraxial anesthesia may be contraindicated when platelet counts are low or uncertain. No TAR-specific threshold exists; neuraxial techniques should be used only when platelet counts and coagulation are clearly normal following a multidisciplinary discussion with hematology. Modern obstetric guidance allows lower platelet thresholds in selected parturients [16] but this should not be extrapolated directly to TAR.

Peripheral nerve blocks can be performed for analgesia or limb surgery once hemostasis is stable. Always use ultrasound guidance to avoid vascular puncture. Fisher et al. reported nine successful axillary blocks in four TAR patients, supporting the feasibility of regional anesthesia in carefully selected, well-prepared cases [17].

In summary, GA remains the safest and most widely reported technique for both elective and emergency procedures, while regional techniques should be reserved for cases with stable hemostasis, experienced operators, and multidisciplinary oversight.

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## Necessary additional pre-operative testing (beside standard care)

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Echocardiography is recommended when a murmur, cardiac history, or symptoms are present, or before major surgery, as septal and occasional outflow-tract anomalies have been reported in TAR syndrome [5,9,18].

Renal ultrasound should be performed when there is a history or examination finding suggestive of renal abnormality or recurrent urinary tract infection as vesicoureteral reflux and hydronephrosis have been described.

Viscoelastic hemostasis testing (TEG/ROTEM) may be used as an adjunct in high bleeding-risk procedures to guide transfusion decisions, though it has not been validated specifically in TAR syndrome [19].

Genetic or differential diagnostic testing (e.g., *RBM8A* analysis or chromosomal breakage studies) is indicated only when the phenotype is atypical – for example, absent thumbs or cytopenias beyond thrombocytopenia – to exclude Fanconi anemia or other mimics. Once the diagnosis of TAR syndrome is confirmed, further genetic testing does not influence anesthetic management [2,9,10].

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### **Particular preparation for airway management**

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Craniofacial features such as micrognathia, retrognathia, high-arched or cleft palate, and mid-face hypoplasia may make mask ventilation or laryngoscopy more difficult. Since a truly difficult airway cannot always be predicted, each case should be approached with careful anticipation and planning [3, 10]. Where feasible, the availability of an ENT surgeon should be considered in advance.

Before induction, an experienced anesthetist should lead a detailed plan that includes equipment for advanced airway management – video-laryngoscope, fiberoptic bronchoscope, supraglottic devices, and a surgical airway kit. Smaller, well-lubricated endotracheal tubes and a gentle technique reduce mucosal trauma, an important consideration in thrombocytopenic patients. Nasal instrumentation should be avoided unless the platelet count is normal [7,19]. When thrombocytopenia is severe, platelet optimization and availability of transfusion products are essential before airway manipulation [8, 20].

Induction should be controlled and atraumatic. Video- or fiberoptic-assisted intubation is preferred when difficulty is anticipated [8], and spontaneous ventilation may be maintained until the airway is secured. Multiple attempts increase mucosal bleeding and should be avoided [19]. Suction must be immediately available.

Extubation should occur only when the patient is fully awake, hemodynamically stable, and able to maintain their airway; deep extubation is therefore not recommended. Having a fiberoptic scope or airway-exchange catheter ready for re-intubation is prudent, and topical vasoconstrictors may be used if minor bleeding is evident.

After surgery, close observation in a high-dependency or intensive-care setting is advisable for patients with significant thrombocytopenia, airway or facial surgery, or major orthopedic or obstetric procedures, to allow early recognition of bleeding or airway obstruction [8,19]. Any abnormal bleeding should prompt reassessment, including repeat platelet counts and early hematology input. Postoperative care should include humidified oxygen, gentle suctioning, and avoidance of nasal instrumentation.

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### **Particular preparation for transfusion or administration of blood products**

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Ongoing coordination between hematology and the blood bank is essential to ensure product availability and timely management for all TAR patients.

Platelet transfusion remains the cornerstone of perioperative management in TAR Syndrome [7,10,19]. Decisions should be guided by clinical bleeding risk rather than platelet count alone and made in conjunction with hematology and the hospital blood bank.

Leukocyte-reduced, ABO-matched, single-donor or HLA-selected apheresis platelets are preferred to minimize alloimmunization and transfusion refractoriness, which may occur after

repeated exposure [3,10,20]. Cross-match or reservation of platelets and red cells should be arranged pre-operatively for any procedure with expected blood loss.

Thrombopoietin-receptor agonists (e.g., eltrombopag, romiplostim) have been used to raise platelet counts in refractory cases but are not established for perioperative use and should only be considered in consultation with a specialist center [8]. Recombinant activated factor VII (rFVIIa) has been reported as rescue therapy in isolated cases [8] of uncontrolled surgical bleeding, however these cases were not TAR patients [21].

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### **Particular preparation for anticoagulation**

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Close coordination with hematology and the surgical team is essential to balance thrombosis and bleeding risk in each case.

Clinically significant thrombosis is uncommon in TAR Syndrome, and anticoagulation is rarely indicated during infancy, when thrombocytopenia is most pronounced [9,10]. As platelet counts typically improve with age, anticoagulation considerations arise mainly in adolescent or adult patients with concurrent risk factors such as pregnancy, immobility, or venous thromboembolism [8].

If anticoagulation is required, therapy should be individualized to platelet count and bleeding history [20]. Prophylactic low-molecular-weight heparin can usually be given safely when platelet counts exceed  $50 \times 10^9/L$ , and cautiously at  $30-50 \times 10^9/L$  in the absence of bleeding. Therapeutic anticoagulation should be reserved for patients with stable counts  $\geq 50 \times 10^9/L$  and managed under hematology supervision.

Mechanical thromboprophylaxis (stockings or pneumatic compression) remains first-line where platelet counts are  $< 50 \times 10^9/L$  or bleeding risk is high.

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### **Particular precautions for positioning, transportation and mobilization**

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Skeletal abnormalities in TAR Syndrome, which always involve absent or hypoplastic radii and occasionally involve the ulna, humerus, or lower limbs [1,2,5,10] predispose patients to joint instability, fractures, and pressure injury during positioning or transfer. In those with previous orthopedic reconstruction or external fixation, limbs may be fragile or immobile at fixed angles. Careful review of recent imaging or surgical notes is advised before theatre positioning.

Padding should protect prominent bony points and limb stumps, and tourniquets used only when essential and for the shortest possible duration. During transportation, the upper limbs should be supported in neutral alignment to avoid traction on hypoplastic bones or surgical grafts.

Venous and arterial access can be challenging due to small caliber vessels and limited limb extension; ultrasound guidance is strongly recommended [7,10,22]. Avoid venipuncture or blood-pressure cuffs on limbs with recent grafts, hardware, or vascular anomalies.

Postoperatively, early physiotherapy and assisted mobilization should be planned collaboratively with orthopedic and rehabilitation teams to prevent joint contracture and maintain function, weighed against the risk of bleeding or fracture.

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## Interactions of chronic disease and anesthesia medications

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There are no known TAR-specific pharmacological interactions with standard anesthetic agents. The syndrome does not alter hepatic or enzymatic drug metabolism. Anesthetic implications arise primarily from thrombocytopenia, skeletal abnormalities, and associated organ malformations, rather than intrinsic pharmacodynamic changes [9,10].

The most relevant interaction concern is with platelet-inhibiting drugs such as NSAIDs and aspirin, which can markedly increase bleeding risk and should be avoided unless absolutely indicated [20].

Renal anomalies, present in a subset of patients, may require dose adjustment of renally excreted agents (e.g., tranexamic acid, morphine metabolites) and avoidance of nephrotoxic medications. Congenital cardiac defects may influence hemodynamic responses to anesthetic drugs and determine perioperative anticoagulation requirements [18].

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## Anesthetic procedure

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Pre-operative assessment and case allocation: Patients with TAR Syndrome are considered high anesthetic risk due to thrombocytopenia, potential airway anomalies, congenital heart disease, and difficult vascular access [7,8,9,10,19,22,23]. They should be evaluated in a pre-operative clinic, with early hematology involvement and allocation to an experienced anesthetic team. Detailed perioperative planning is essential, as outlined in previous sections.

Vascular access and monitoring: IV and arterial access may be technically challenging because of prior cannulations and skeletal deformities. Ultrasound guidance is recommended for all peripheral or central cannulation. Invasive monitoring should be individualized to surgical bleeding risk and cardiac status; the benefit of central venous or arterial access must be weighed against bleeding risk when platelet counts are low.

Airway management: As detailed under *Airway preparation*, micrognathia, retrognathia, and cleft palate can complicate ventilation or intubation. A difficult-airway plan with video- or fiberoptic options and supraglottic devices should be ready. Avoid traumatic or nasal instrumentation unless hemostasis is secure.

Hemostasis during anesthesia: Maintain atraumatic technique, avoid platelet-inhibiting drugs (NSAIDs, aspirin), and ensure platelet products are available when bleeding risk exists. Tranexamic acid may be used as an adjunct if renal function permits, with desmopressin considered under hematology guidance if required. TEG/ROTEM can assist decision-making in complex cases, though not validated specifically for TAR.

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## Particular or additional monitoring

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Non-invasive blood pressure measurement may be limited by limb deformities or prior orthopedic reconstruction. If reliable readings are unobtainable, use invasive arterial monitoring. Femoral access is preferred when distal sites are unsuitable; brachial cannulation is acceptable with careful hemostasis and post-removal observation.

For long or transfusion-heavy procedures, or when frequent sampling is required, insert a central or peripherally inserted central line [7,10]. Tunneled lines are appropriate if multiple surgeries or prolonged therapy are expected.

## Possible complications

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Intra-operative complications in TAR Syndrome relate mainly to thrombocytopenia, airway anomalies, and associated congenital malformations [7,8,9,10,19,23].

Hemorrhage: This is the most frequent and serious complication. Bleeding may arise from the surgical field, airway instrumentation, vascular puncture, or neuraxial procedures. Even minor trauma can cause significant blood loss; platelet products must be immediately available [7,8,10,22,23].

Airway trauma or obstruction: Micrognathia, cleft palate, and mucosal fragility increase the risk of bleeding and postoperative edema. Gentle, atraumatic technique and careful postoperative observation are essential.

Hemodynamic instability: This may result from blood loss or congenital cardiac defects, which also predispose to paradoxical embolism [18].

Infection and alloimmunization: Repeated transfusions and indwelling lines increase risk of transfusion reactions, alloimmunization, and blood-borne infection; use leukoreduced, HLA-selected components whenever possible.

Positioning injury: Limb deformities, contractures, or orthopedic implants predispose to nerve compression and soft-tissue injury; meticulous padding and joint protection are required.

## Postoperative care

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Postoperative management in TAR Syndrome should include close observation for bleeding, airway compromise, and hemodynamic instability. High-dependency (HDU) or intensive-care (ICU) observation is advisable when thrombocytopenia is significant, surgery is major, or airway involvement is expected.

Inspect the surgical site, airway, and vascular access points regularly for bleeding or hematoma formation, and repeat platelet counts as indicated. Coordinate platelet and blood-product management with hematology and the blood bank to ensure appropriate support [10,20].

Provide appropriate non-NSAID analgesia and avoid agents that impair platelet function. Resume mechanical or pharmacologic thromboprophylaxis only when platelet counts and clinical status permit [20].

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## Disease-related acute problems and effect on anesthesia and recovery

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Acute problems in TAR syndrome mainly arise from thrombocytopenia, leading to perioperative bleeding and hemodynamic instability. Airway bleeding or obstruction may occur after instrumentation due to mucosal fragility.

Episodes of acute thrombocytopenia can be triggered by infection, stress, or cow's milk exposure in infants, prolonging recovery and transfusion needs.

Recovery may also be delayed by anemia, transfusion reactions, or cardiac dysfunction in those with congenital lesions.

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## Ambulatory anesthesia

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Ambulatory anesthesia is generally not recommended for patients with TAR Syndrome due to the risk of perioperative bleeding, airway complications, and unpredictable platelet fluctuations.

If day-case surgery is considered, it should be minor, non-invasive, and performed only when recent platelet counts are stable and within a safe range, with hematology consultation and the ability to admit postoperatively if complications arise.

All procedures must be done in centers equipped for immediate transfusion support and advanced airway management [10].

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## Obstetrical anesthesia

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Pregnant patients with TAR syndrome require early multidisciplinary planning involving obstetrics, anesthesia, hematology, and neonatology. Although platelet counts often normalize by adulthood, some women experience recurrent or worsening thrombocytopenia during pregnancy, which can influence the anesthetic plan [15,24]. Platelet counts in TAR Syndrome can fluctuate markedly over short periods; therefore, obstetric and anesthetic management decisions should always be based on the most current laboratory values.

Neuraxial anesthesia: No TAR-specific platelet threshold exists. Decision-making should be individualized with hematology input [16]. Current obstetric consensus (SOAP 2021) supports neuraxial techniques at lower platelet counts in selected parturients after multidisciplinary review, although many institutions still target  $\geq 70-80 \times 10^9/L$  for epidural or spinal placement and removal. If neuraxial anesthesia is considered, single-shot spinal techniques may be preferred over epidural catheter techniques where clinically appropriate, to minimize the risks associated with an indwelling catheter. When neuraxial techniques are contraindicated or platelet counts unstable, remifentanyl PCA for labor and multimodal or intravenous opioid analgesia after cesarean are suitable alternatives.

General anesthesia: GA is appropriate when platelet counts are low or uncertain, neuraxial block is unsafe, or urgent delivery is required. Anticipate difficult airway and mucosal bleeding due to micrognathia or cleft palate; use gentle, atraumatic techniques and ensure immediate platelet and blood-product availability. Viscoelastic testing (TEG/ROTEM) may assist transfusion decisions during major hemorrhage, though it is not validated specifically for TAR.

Peripartum care: Maintain ready access to blood products, avoid NSAIDs and aspirin, and resume mechanical or pharmacologic thromboprophylaxis only once platelet counts are sufficient and hemostasis secure.

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*This recommendation was prepared in 2015 by:*

**Authors**

**Conan McCaul**, Anesthesiologist, The Rotunda Hospital, Dublin, Ireland  
[cmccaul@rotunda.ie](mailto:cmccaul@rotunda.ie)

**Co-Author**

**G. Valchev**, Anesthesiologist, The Rotunda Hospital, Dublin, Ireland  
[valchevil@gmail.com](mailto:valchevil@gmail.com)

**Disclosure:** The authors have no financial or other competing interest to disclose. This recommendation was unfunded.

*This recommendation was reviewed by:*

**Reviewer(s)**

**Helga Toriello**, Department of Clinical Genetics, Spectrum Health Hospitals, Grand Rapids, Michigan, USA  
[Helga.Toriello@hc.msu.edu](mailto:Helga.Toriello@hc.msu.edu)

**Harald Schulze**, Department of Hemostaseology, University Hospital Wuerzburg, Germany  
[harald.schulze@uni-wuerzburg.de](mailto:harald.schulze@uni-wuerzburg.de)

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*Please note that this guideline has not been reviewed by an anesthesiologist but by two disease experts instead.*

**Update and revision (2026)**

**Conan McCaul**, Anesthesiologist, The Rotunda Hospital, Dublin, Ireland

**Gareth Stephan Stott**, Anesthesiologist, The Mater Misericordiae University Hospital, Dublin, Ireland  
[garethstott@mater.ie](mailto:garethstott@mater.ie)

**Reviewer**

Jean-Philippe Salaün, Specialist in pediatric anesthesia and intensive care medicine, Assistant Professor, CHU Caen Normandie, France

**Editorial Review**

**Christine Gaik**, Anesthesiologist, Department of Anesthesiology and Intensive Care Medicine, University Hospital Giessen and Marburg, Campus Marburg and Philipps University of Marburg, Germany  
[gaikc@med.uni-marburg.de](mailto:gaikc@med.uni-marburg.de)

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