orphanaesthesia

Anesthesia recommendations for

Achondroplasia

Disease name: Achondroplasia

ICD 10: Q77.4

ORPHAcode: 15

Synonyms: Chondrodysplasia, chondrodystrophia fetalis

Disease summary: Achondroplasia is the most frequent of more than 100 described types of skeletal dysplasia which lead to dwarfism. The incidence is approx. 0.5-1.5 in 10,000 newborns [1]. Spontaneous mutations cause up to 80% of the diseases. Hereditary propagation takes place in terms of autosomal-dominant transmission. Females and males are equally affected. Genetically speaking, this is the mutation of the fibroblast growth factor receptor 3 gene (FGFR3) [2,3]. This mutation results in an inhibition of cartilage proliferation and a disorder of enchondral ossification. As a consequence, premature ossification of epiphyseal cartilage is observed. Clinically speaking, the following symptoms are characteristic: disproportionate dwarfism, a relatively large head, midfacial hypoplasia, deformations of the spine, leg axis deviation, „trident hand“. As a primary or secondary consequence, other organ systems can be affected [1,4]. As a result, specific anesthetic particularities have to be observed.

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

A	**AIRWAY / ANESTHETIC TECHNIQUE**	Both general (GA) and regional anesthesia (RA) may be challenging, increasing in older patients. Individualized approach is needed. GA: Difficult bag-mask ventilation (small mouth opening, large tongue, narrow nostrils, midface hypoplasia, large adenoids, short neck, tracheobronchomalacia). Difficult intubation: Minimize neck/head movement (risk of spinal cord compression at the level of the cranio-cervical junction, narrow foramen magnum); relatively small tube diameter (choose size according to weight rather than age); significant risk of bronchial intubation (short trachea) Tracheostomy can be extremely difficult. Restrictive/obstructive lung disease. (Central/obstructive) sleep apnea. Difficult IV access. RA: Neuraxial RA can be difficult (lumbar hyperlordosis, scoliosis; narrow lumbar canal, less CSF volume, obesity); epidural anesthesia or a low-dose CSE should be preferred (possibility of titration); spinal anesthesia with reduced height-adjusted dose; increased risk of neurological sequelae; Peripheral RA: feasible.
B	**BLOOD PRODUCTS (COAGULATION)**	Not reported.
C	**CIRCULATION**	Increased cardiovascular risk (restrictive lung diseases, pulmonary hypertension, cor pulmonale).
D	**DRUGS**	Avoid negative inotropic medication.
E	**EQUIPMENT**	Difficult airway equipment, different sizes of blood pressure cuffs, ultrasound (IV access, RA) should be available.

Typical surgery and procedures

Otorhinolaryngology: tonsillectomy, adenotomy, grommet (tympanostomy tube); oral and maxillofacial surgery: dysgnathia (tightly aligned teeth); neurosurgery: ventricular shunt, craniectomy (foramen magnum stenosis); spinal surgery: spinal canal stenosis, kyphoscoliosis, (pediatric-)orthopedics: malposition of the extremities, lengthening; bariatric surgery.

Type of anesthesia

A general recommendation regarding the ideal anesthetic regime cannot be given, as both general and regional anesthesia present potential problems [2,4,5]. Therefore, individual decisions are necessary.

General anesthesia: typical described problems are:

Excessive anxiety [2,3,6,7] difficult intravenous access (10-50%) [2,8]; difficult mask ventilation, difficult intubation [2,5,9-13]; risk for cervicomedullary compression or rather spinal cord ischemia (reported sudden death events, above all in children < 4 years) [14-16]; eight-fold higher obesity rate potentiating the effects of the existing problems [1,4]; increased incidence of sleep apnea (obstructive and/or central) – rarely secondary pulmonary hypertension, restrictive lung diseases already at an early age [1,17-21]; chronic respiratory infections [1,20]; ten-fold increased cardiovascular risk – with a maximum between 25 and 35 years of age [20,22], tendency toward hypersalivation. In early childhood, a nasopharyngeal muscular hypotonia can become a problem [17,23], as well as gastroesophageal reflux [24].

There are descriptions of unproblematic general anesthesia [3,8].

Despite the altered respiratory system, general anesthesia is often regarded as the method of choice [1,10]. Due to the anatomical changes in the spine and the craniocervical junction as well as due to an increased incidence of hydrocephalus, neuraxial anesthetics might be contraindicated in some cases.

Neuraxial regional anesthesia: this type of regional procedure is considered to be technically difficult (narrow spinal canal/stenoses, reduced epidural space, kyphoscoliosis, vertebral body deformities [10]. The conus medullaris often is positioned lower than usual. In some cases, epidural anesthesia was carried out successfully [5,13,25,26]. There are reports about accidental dural punctures, difficulties in advancing the catheter [1], increased risk of venous puncture [5], irregular or unpredictable (unpredictably high) spread of anesthesia [5,13]. Epidural anesthesia should be preferred because of the possibility of titration [27].

In most cases, injection of local anesthetic into the caudal canal is easier in the case of pediatric patients.

Also spinal anesthesia has been applied successfully [28,29]. Inadequate quality of neuraxial analgesia [28], punctio sicca and the risk of high spinal anesthesia are conceivable [4]. Regarding both procedures, the use of opiates has been described [4,30], however, clear dosage recommendations are lacking. A reduced spinal dose of 5 to 7.5 mg of hyperbaric bupivacaine in adults or a dosage based on height (0.06 mg/cm height of 0.5% hyperbaric bupivacaine) appears to have a sufficient blocking effect [31].

Furthermore, successful CSE with low spinal dose with the possibility to increase the height of the block using the epidural catheter is described. Ultrasound guidance can be very helpful to identify vertebral interspaces and to determine the distance to the ligamentum flavum [31-33].

Patients with (symptomatic) spinal stenosis are at greater risk of neurological complications following neuraxial anesthesia [31,32].

Peripheral regional anesthesia: possible. Needle placement can be complicated.

Conscious sedation / awake anesthesia: There are no reports about severe occurrences. Caution is advised in the case of pre-existing sleep apnea syndrome [20].

Necessary additional preoperative testing (beside standard care)

The preoperative diagnostic assessment depends on the respective symptoms of the patient and is arranged on the basis of a detailed anamnesis and physical examination. Particular attention has to be paid to signs indicating a difficult intubation (small mouth opening, big tongue, limited cervical vertebrae extension, tonsillar hyperplasia, instability of the cervical spine) [9,34].

Besides the usual preoperative care, the following pathognomonic clinical symptoms would indicate that a refined diagnostic assessment would make sense [1,17,20,34]:

- Chronic/current infections (otitis media): otorhinolaryngology consultation
- Severe scoliosis/Rib cage deformities: lung function, echocardiography, blood gas analysis, thoracic radiography

Annotation: conventional pulmonary function tests are indexed to height and are unreliable. An equation to estimate vital capacity and long volumes of patients with achondroplasia exists [35].

- Neurological symptoms (hydrocephalus, cervicomedullary compression, spinal canal stenoses): neurology consultation, CT, MRI
- Sleep apnea: otorhinolaryngology consultation, sleep laboratory, blood gas analysis
- Cardiopulmonary problems (restrictive lung diseases, pulmonary hypertension, cor pulmonale, heart diseases): lung function, electrocardiography, echocardiography, blood gas analysis, thoracic radiography, if necessary further examinations.

Annotation: Cardiac output is based on body surface area formulas that rely on height which lead to a lower predicted value of the cardiac output requirements. Probably, the Boyd formula provides the most realistic cardiac index [36].

Particularly before a planned regional anesthesia procedure, pre-existing neurological abnormalities have to be documented [5]. Frequently, achondroplasia patients show neurological abnormalities [15]. In infancy and childhood, but above all in adulthood, they often suffer from chronic pain due to skeletal changes [14,15].

Particular preparation for airway management

Inadequate preparation for difficult airway management contributes significantly to potentially catastrophic outcomes in achondroplasia.

For anatomical reasons, problems may occur when face mask ventilation or intubation are performed [2,5,9-13,37]. The big tongue and pronounced adenoid vegetations may lead to complications. However, a frequent reason for intubation difficulties is also a limited flexibility of the atlanto-occipital joint [10,11,19]. On the other hand, due to the risk of a foramen magnum stenosis and cervical instability (risk of medullary compression), hyperextension of the cervical spine during intubation should strictly be avoided [3,5,8,10,11,16]. This is emphasized by a case report about a non-traumatic cervical spinal cord infarction which led to quadriplegia in a child – even without preceding manipulation of the cervical spine [38].

In case of a clinically expected difficult intubation ensure that the standard difficult-airway devices used in your institution are prepared and ready for use.

Awake fiberoptic intubation (N.B. mid-facial hypoplasia) is considered the preferred method but often not feasible by the pronounced anxiety in these patients [2,3,6,39]. A video laryngoscope is not an option for an awake intubation. Using this device is not always possible due to macroglossia and the probably limited mouth opening [9,27,40]. In case of impossibility of an awake fiberoptic-guided intubation the procedure should be performed while spontaneous breathing is maintained. Difficulties can occur even when using LMA devices [41].

Despite pre-oxygenation patients desaturate very fast. Patients further may suffer from an unusually collapsible larynx, trachea and/or bronchi. Some authors recommend placement of high-flow nasal cannula for continuous apneic oxygenation and using prophylactic bronchodilators prior to induction of anesthesia [24]. The patients also may be difficult to ventilate after intubation. Weaning from ventilator also may be delayed [42].

In the reports on unproblematic intubations in patients with achondroplasia, a small and short trachea is mentioned. The following rule applies: the size of the tube should be chosen according to the body weight (not as usual according to the age) [2,3,6,8,9,19,43,44]. Mechanical ventilation should be adjusted to 6 cc/kg ideal body weight for height. In case of indication of a tube thoracostomy smaller intercostal spaces and anatomical variations should be anticipated [45].

Due to the fact that regional procedures do not always offer a safe alternative, also in these cases the airway management should be planned very well before the operation.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

There are no reports on a particular thrombosis prophylaxis in case of achondroplasia. In general, after these patients have entered puberty an adequate thrombosis prophylaxis has to be taken into consideration, particularly if they have to undergo an extended period of immobilization and lower extremity surgery.

One case report describes a severe and lethal intraoperative fat embolism as a consequence of a lower extremity intervention [16].

Particular precautions for positioning, transportation and mobilization

Greatest care is required in order not to risk damages caused by patient positioning in case of anatomical particularities (above all spine and extremities). Frequently, these patients have joint contractures. Some of them are unable to lie either in a prone or supine position [41].

Case reports on damages caused by positioning do exist (e.g., two cases of brachial plexus palsy [8], one case of visual loss after prone positioning during spine surgery [37]).

As compared to the size of the body, the head is relatively big and due to the relatively increased body surface area, there is a good chance of a significant drop in body temperature. Especially in the case of children, early thermal management has to be remembered.

Interactions of chronic disease and anesthesia medications

Not reported.

New drug treatments to increase bone growth are available but their long-term effects and potential drug interactions are still unknown [46].

Anesthetic procedure

Premedication: Whereas some authors refrain from sedation medication when a difficult intubation has to be expected or when the patient is diagnosed with a sleep apnea syndrome [9], other authors describe that anxiolysis is helpful to these patients who are often very anxious [2]. For patients with severe adiposity, ranitidine and metoclopramide or sodium citrate are frequently administered in terms of aspiration prophylaxis [4,5,9].

Anesthesia: if intravenous access is difficult, inhalational induction of anesthesia can be considered. Due to excessively lax skin, soft tissue and joint flexion deformities the surgical exposure of a vein can be required [41]. The subclavian and jugular access can be challenging as well [45].

Regarding the use of anesthetic medication calculated according to the body weight, no particularities are reported [2,3]. However, in case of a slim achondroplastic patient a dosage in this manner probably can lead to underdosing [47]. Patients with severe hypersalivation can be given a vagolytic drug – in most cases, secretion aspiration is sufficient.

One should avoid negative inotropic medication [1].

Regarding other drugs which are generally used preoperatively, there are no absolute contraindications.

There are no signs indicating an increased tendency toward malignant hyperthermia.

Particular or additional monitoring

Monitoring should be oriented towards the patient's pre-existing, organ-specific diseases. In most cases, a routine monitoring corresponding to the surgical intervention is described [4]. The choice of the appropriate blood pressure cuff can present a challenge.

In the case of pre-existing cardio-respiratory problems, invasive blood pressure measurement is recommended [24].

Possible complications

- Difficult airway management (including smaller tube size)
- Hypersalivation
- Frequent respiratory tract infections
- Risk of cervicomedullary compression or spinal cord ischemia
- Difficult regional anesthesia with partly unpredictably high spread in neuraxial techniques; increased risk of neurological sequelae
- Increased obesity rate
- Tendency towards sleep apnea syndromes (obstructive and/or central)
- Increased cardiovascular risk
- High risk of intraoperative damage caused by positioning.

Postoperative care

Primarily, postoperative care is based upon the intervention and the patient's pre-existing conditions. Even without anesthesia, the tendency towards central and obstructive sleep apnea is held responsible for the increased mortality rate, above all in early childhood [14-16,34,42]. The risk for postoperative respiratory complications is increased [47]. For this reason, particularly in the case of children it is recommended to carry out pulse oximetry monitoring after surgery [17] – this applies above all when opioids are administered. Moreover, an extended stay in the anesthetic recovery room should be scheduled. A stay in intensive care is not mandatory but has proven its value in bariatric surgery [9].

Disease-related acute problems and effect on anesthesia and recovery

Typical differential diagnostics refer above all to the neurological aspects of the disease:

- Potential neurological failures after regional anesthesia (Differential diagnosis: disease-related neurological symptoms versus nerve damage caused by regional anesthesia).
- Possibly increased risk of an ascending neuraxial blockade versus sleep apnea due to a central cause.
- Postoperative hypopnea / apnea (Differential diagnosis: of central sleep apnea corresponding to the underlying disease versus residual opiate effect).

– 25,6% of the patients suffer from chronical pain in the lower limbs. This is often associated with a depression [48] (Differential diagnosis: postoperative pain versus chronic pain).

Ambulatory anesthesia

The hitherto existing literature does not provide any recommendations regarding outpatient procedures in patients with achondroplasia. As a rule, anesthesia on an outpatient basis should be avoided due to the above mentioned possible postoperative problems. This applies above all to pediatric patients. Especially in the first year of life the risk of sudden death is significantly higher than in the general population even without anesthesia [47].

Obstetrical anesthesia

Delivery beyond 32 weeks should be by Cesarean section. Vaginal delivery might be appropriate in some clinical circumstances. There is no increased risk for preterm birth, but an induced preterm birth might be required for maternal reasons. Pregnant women should be assessed for deterioration of respiratory, cardiac and skeletal functions. Patients should receive an anesthesiology consultation at an early stage to discuss the individual anesthesia options [24,35].

Many articles concerning neuraxial procedures in case of achondroplasia deal with anesthesia in Cesarean section. Due to a disproportion between the infant's head and the mother's pelvis, pregnant women with achondroplasia have a high rate of scheduled Cesarean sections [5,26].

Most articles indicate the anesthetic dilemma of a potentially difficult respiratory system and a possibly difficult regional anesthesia [4,13,27,28,30]. Close to the spinal cord, preference should rather be given to epidural anesthesia of low-dose CSE [27,31], because of the superior titratability. In case of emergency, also spinal anesthesia has been carried out with success [4]. With respect to these pregnant women, general anesthesia has to be planned particularly well. This procedure is favored by some authors [1,10,43]. Pre-existing alterations of the respiratory system become even more difficult to handle. Moreover, a reduction of FRC has to be encountered – clearly exceeding the reduction which is considered to be normal in pregnant women – as a consequence of a thoracic hypoplasia and a possibly restrictive lung function, resulting in intrapulmonary shunts. This means that in addition to an altered respiratory system, these women have a very limited pulmonary reserve, implying a great risk of hypoxia [26]. Phenotypically speaking, these patients appear in the 16th week of gestation like other women in the 30th week of gestation [5]. This might also involve an (earlier) increased risk of aspiration.

The decision for a certain anesthetic procedure has to be taken in each individual case after a detailed risk-benefit analysis. There is a shift away from general anesthesia towards a (ultrasound-guided) neuraxial anesthesia with height-based dosing and careful titration when possible [48].

TAP blocks are suitable for postoperative analgesia after Cesarean section to reduce morphine consumption in patients with achondroplasia [41].

Even moderate blood loss can lead to hemodynamic impairment. At the same time, there is a risk of fluid overload because pregnant patients with achondroplasia have less maternal blood volume than average. It is essential to replace fluids and blood products carefully [24].

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Date last modified: **February 2026**

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

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Disclosure: The reviewers have no financial or other competing interest to disclose.

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