orphanaesthesia

Anesthesia recommendations for

Larsen Syndrome

Disease name: Larsen Syndrome

ICD 10: Q74.8

OMIM: 150250

ORPHAcode: 503

Synonyms: -

Disease summary: First described in 1950, Larsen Syndrome (LS) is a rare hereditary condition, characterized by multiple joint dislocations and characteristic facial, limbs and spinal abnormalities [1]. LS can be presented by both autosomal dominant and recessive forms, although the former is more commonly seen. The incidence of disease is 1:100,000 live births, with equal gender distribution [2]. The autosomal dominant form is caused by mutations of the gene encoding filamin B, in region containing human type VII collagen. These mutations lead to abnormal collagen formation resulting in musculoskeletal and cardiac anomalies [3]. The vertebrae are often affected and may manifest as cervical instability and kyphoscoliosis [4]. Cardiac abnormalities have been reported, including aortic root dilatation, valvular disease and congenital cardiac shunts, resembling connective-tissue disorders such as Marfan syndrome [5]. The decreased in cartilage rigidity often results in laryngomalacia, tracheomalacia, and bronchomalacia [6]. Patient with LS often has higher risk of hypoxia and atelectasis post-op due to poor respiratory reserve [7]. Given the multisystem involvement, a comprehensive pre-op evaluation of airway, cervical, cardiovascular, respiratory and neurological function is essential. Careful airway planning, minimized cervical spine movement and patient positioning are critical to ensure safe anesthesia.

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**	High risk of difficult airway (cleft palate, midface hypoplasia, macroglossia). Review previous anesthetic records (Cormack-Lehane grade, airway equipment used). Cervical instability is the major concern: minimize neck movement with manual in-line stabilization. Videolaryngoscopy or fiberoptic intubation usually preferred. Supraglottic devices can be considered for short, uncomplicated procedure.
B	**BLOOD PRODUCTS (COAGULATION)**	No inherent association with coagulation disorder. Routine coagulation test is sufficient. Group & safe or crossmatch according to procedural bleeding risk. Tranexamic acid if not contraindicated.
C	**CIRCULATION**	Cardiovascular involvement has been reported, including aortopathy, valvular abnormalities, and congenital cardiac shunts. Pulmonary hypertension may occur in severe restrictive lung disease. Preoperative cardiology review and/or echocardiography if cardiac murmur detected, patient symptomatic or known cardiac history. Consider invasive monitoring in complex cases. Avoid excessive fluid in cardiac failure, avoid increase in pulmonary vascular resistance.
D	**DRUGS**	No proven association with malignant hyperthermia. In patients with significant restrictive lung disease, opioids should be titrated carefully due to the risk of respiratory depression.
E	**EQUIPMENT**	Airway equipment: videolaryngoscopy, fiberoptic bronchoscope, smaller endotracheal tubes, pediatric bougie, suction catheter. Pressure-relieving mattress and meticulous padding of pressure points.

Typical surgery and procedures

Talipes correction and craniofacial surgery, including cleft palate repair, are typically performed in early life. ENT procedures related to associated craniofacial and airway abnormalities may also be required. Patients with LS may require repeated orthopedic surgeries for the management of joint dislocations and limb deformities. Spinal surgery, such as cervical spine fusion and scoliosis correction, is commonly performed later in life, and multiple revision procedures may be required due to progression of deformity [8].

Type of anesthesia

General and regional anesthesia can be used, although the disease involvement of the spine makes the latter technically challenging. Both intravenous and gas induction are safe. While there was one case report of malignant hyperthermia due to volatile agents, the evidence for this association was strongly disputed in the same journal [9, 10]. There is no contraindication to common anesthetic drugs. Regional analgesic techniques such as caudal blocks have been described [11].

Necessary additional preoperative testing (beside standard care)

Additional tests are guided by a thorough assessment of the airway, cervical spine, respiratory, cardiovascular, neurological and musculoskeletal systems. A thorough evaluation of the airway is necessary in these children. Nasal fiberoptic endoscopy can be considered by ENT surgeons to assess airway dynamics if there are significant concerns. Due to the frequent involvement of the cervical spine, cervical radiograph is a reasonable and practical first step to identify structural abnormalities. Further cervical spine imaging, such as CT or MRI should be done if there are positive findings on radiograph of the cervical spine or in the presence of neurological signs. Cardiovascular abnormalities resembling connective-tissue disorders have been described in LS. In view of the potential for aortopathy, valvular disease and congenital cardiac shunts, a low threshold for pre-operative cardiac assessment, including echocardiography, is appropriate – particularly in the presence of a murmur, symptoms, or known cardiac disease.

Particular preparation for airway management

Difficult intubation should always be anticipated. Equipment such as pediatric bougies, supraglottic airway devices, videolaryngoscopes and fiberoptic endoscopes should be available. Previous anesthetic charts should be reviewed due to the likelihood of repeated surgeries. Manual in line stabilization of the cervical spine is recommended even in the absence of neurological signs pre-operatively.

For short and uncomplicated procedures, consider the use of facemask or supraglottic airway devices to avoid the need for tracheal intubation [11]. This would avert the risk associated with intubations and minimize manipulation of the neck. However, preparation for difficult intubation should remain in place.

Particular preparation for transfusion or administration of blood products

No special requirements for transfusion have been reported. Blood loss should be anticipated in complex and prolonged orthopedic procedures.

Particular preparation for anticoagulation

There is no known association between LS and intrinsic coagulation disorder.

Particular precautions for positioning, transportation and mobilization

Careful positioning of patients with LS is extremely important. The cervical spine needs to be handled with care, especially during prone positioning for vertebral surgery. Large joints are at risk of dislocations and needs to be carefully positioned. Prone positioning can be particularly challenging in patients with poor chest wall compliance, as it may significantly increase intrathoracic pressure, reduce venous return, and precipitate a low cardiac output state. Cases of cardiac arrest related to these physiological changes have been reported in the literature [7].

Interactions of chronic disease and anesthesia medications

Not reported.

Anesthetic procedure

Premedication is generally safe and useful, particularly in anxious children. Both intravenous and gas induction can be used. Once asleep, cervical in line stabilization should be maintained and difficult airway anticipated. In the presence of laryngotracheomalacia, airway patency may be compromised following induction; careful planning of induction and the timing of neuromuscular blockade is therefore required. Common anesthetic agents are safe to use. Positioning and transfer of patient need to be done carefully to minimize risk of dislocations. Extubation requires careful planning due to the risk of airway compromise, including laryngotracheomalacia [12].

Particular or additional monitoring

For surgery involving the spine, intraoperative neurophysiological monitoring may be used, such as somatosensory or motor evoked potentials, to minimize the risk of spinal cord damage during surgery [13]. Invasive monitoring should be considered if the patient has severe cardiac involvement.

Careful monitoring of patient positioning during prolonged procedures would help to reduce the risk of musculoskeletal injury.

Possible complications

Complications arise mainly from known risks. Cervical injury due to excessive neck manipulation can occur, particularly if tracheal intubation is difficult. There have been numerous reports on respiratory complications after surgery [7,14]. Post-extubation airway edema may cause croup / stridor. The presence of laryngotracheomalacia or subglottic stenosis may further contribute to respiratory complications in the postoperative period. Bronchomalacia and lung hypoplasia may contribute to respiratory failure during the post-operative period. Musculoskeletal injury can occur due to suboptimal positioning. There was one case report of intraoperative cardiac arrest during spinal surgery under sevoflurane anesthesia [15]. This was attributed to a combination of a known pre-existing cardiac disease and stress of scoliosis surgery.

Postoperative care

High dependency or intensive care unit admission should be considered if the patient has significant organ involvement of the disease, or if surgical procedure is prolonged and complex. Patients with severe kyphoscoliosis may require prolonged and additional respiratory support post-extubation [16].

Disease-related acute problems and effect on anesthesia and recovery

None reported.

Ambulatory anesthesia

There are no reported day case procedures in the literature. However, this can be considered depending on the preoperative condition of the patient and type of surgery.

Obstetrical anesthesia

Due to pelvic and hip abnormalities in LS, planned caesarean sections may be considered. General anesthesia is best avoided. Pregnancy induced changes to the airway and respiratory system would compound the problems in LS. However, spinal or epidural insertions may be technically challenging due to vertebral abnormalities. If time permitting, a regional technique consisting of an epidural catheter with gradual titration of local anesthetic is ideal. This reduces excessive rostral spread and minimizes the risk of respiratory complications. Difficult airway equipment should be prepared in case a general anesthetic is required. Neonatal cervical spine protection during delivery may be required if prenatal screening reveals a likelihood of baby having LS [17].

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Internet links:

1. National Organisation for Rare Diseases https://rarediseases.org/rare-diseases/larsen-syndrome/

2. Patient support in the UK : http://www.cafamily.org.uk/medical-information/conditions/l/larsen-syndrome/

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