

## Anaesthesia recommendations for **Alport syndrome**

**Disease name:** Alport syndrome

**ICD 10:** Q87.81

**Synonyms:** Hereditary nephritis

**Disease summary:**

The Alport syndrome is a rare inherited form of progressive renal failure with an incidence of one in 10000 newborns. It is due to genetic mutations of collagen IV  $\alpha 3$ -4-5 network that is the major collagenous constituent of basement membranes in glomerulus, cochlea, lens and retina. Inheritance is X-linked in 80% of affected patients, with a more severe clinical course in males. It can lead to end-stage renal disease requiring dialysis and transplantation. Autosomal recessive and dominant variants arise in 15% and 5%, respectively. Low prevalence of dominant cases can be due to their high variability in the phenotype, from mild symptoms to clinical patterns comparable to the X-linked disease, although renal function deterioration occurs more slowly, resulting in several unrecognized dominant cases. Loss of renal function – due to the progressive glomerulosclerosis and tubulointerstitial fibrosis – is the most important clinical manifestation of the syndrome with haematuria, proteinuria and hypertension. Sensorineural hearing loss and ocular abnormalities are common especially in X-linked and autosomal recessive forms of Alport syndrome. Leiomyomatosis in respiratory, gastrointestinal and female reproductive tracts is found in 2-5% of patients with X-linked genotype. The main anaesthetic problems in the treatment of patients with Alport syndrome are related to chronic renal failure with haemorrhagic diathesis and abnormalities in heart conduction due to hyperkalaemia and altered calcium metabolism. Circulatory collapse or difficulties in ventilation due to the presence of mediastinal leiomyomas compressing heart, large vessels and airway is a possible risk as well as the presence of concomitant comorbidities.

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Medicine is in constant progress; new clinical knowledge may not be in this guideline.



Recommendations are not rules or laws; they are a framework for clinical decision-making.

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

The diagnosis may be wrong; if questionable, the diagnosis should be confirmed.

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

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## Typical surgeries

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Renal biopsy; renal transplantation; eye surgery; hearing aids implantation; leiomyomas removal.

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## Type of anaesthesia

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Both general and regional anaesthesia can be performed in cases with Alport syndrome.

Doses of sedatives (i.e. midazolam) and opioids should be reduced and titrated to effect in patients with renal failure since these agents may have delayed metabolism and excretion. Moreover, distribution volume and plasma protein binding of anaesthetic drugs may be altered, resulting in higher than expected plasma concentrations.

Hypnotic agents (i.e. propofol) should be carefully administered as a bolus to avoid hemodynamic and myocardial impairment in these patients who are often hypovolemic and with coexisting heart failure.

Succinylcholine can be safely used as neuromuscular blocking agent only in absence of electrocardiographic changes and if the serum potassium concentration is <5.5 mEq/L.

Regional anaesthesia may allow to limit the risks of deep narcosis and the use of intravenous drugs in patients with multiple comorbidities. It can be performed taking into account: 1) the altered platelet function induced by renal failure; 2) the residual effects of heparin administered during dialysis.

If possible, monitored anaesthesia care (MAC) – in which patient undergoes a procedure in local anaesthesia plus sedation and analgesia - is preferred in those subjects with end-stage renal disease related to Alport syndrome.

There are not specific pain management methods. However, some adjustments are required in patients who develop renal impairment: 1) non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated; 2) opioids (i.e. tramadol) must be administered at lower doses to avoid plasmatic accumulation and subsequent respiratory depression.

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

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Alport syndrome is often associated with cardiovascular diseases (hypertension, arrhythmias, heart failure) and progressive renal failure and these possible pathologies must be specifically investigated:

1. cardiac function test, such as electrocardiography and echocardiography, should be performed to exclude cardiomyopathy;
2. pulmonary picture should be evaluated, at least with chest radiography, to exclude oedema or pleural effusion;
3. renal function, serum electrolytes and acid–base balance should be always evaluated to assess the degree of the renal failure, the need of perioperative dialysis and to early adjust electrolytic and acid-base disorders;
4. standard coagulation tests should always be investigated, since haemorrhagic diathesis is a known risk. In end-stage renal disease patients, the use of thromboelastography (TEG) or rotational thromboelastometry (ROTEM) could be particularly indicated.

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

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No defined guidelines referring to the patient's airway management and position exist.

Major attention should always be given to airway management in patients with X-linked Alport syndrome due to the high incidence of upper airway lesions that characterize these patients. A preoperative careful airway assessment, possibly benefiting from a more specific examination by otorhinolaryngologist, is hence crucial in planning the best approach for anaesthesia induction.

In patients undergoing oesophageal leiomyoma removal surgery - a frequent complication of Alport syndrome - the lateral position could be particularly indicated to avoid tracheal and major vessels compression during anaesthesia induction. Fibrobronchoscopy could help in performing oro-tracheal intubation.

Since a case report describing a bilateral vocal cord paralysis following coronary artery aneurysmectomy in Alport syndrome has been published, pointing out the neural vulnerability in all renal failure patients, but especially in those with Alport syndrome, it is advisable for the surgeons to pay close attention to the risk of damage to the vocal cords.

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

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Alport syndrome patients developing renal failure may have an elevated risk of intraoperative bleeding due to the altered coagulation process and inhibited platelet function induced by uraemia, impaired vessel reactivity and anaemia. Consequently, higher need of blood products could be observed during surgery.

Preoperative dialysis has been reported to improve platelet function in patients with end-stage renal disease, reducing the bleeding risk during surgery. In case that there is no time for dialysis, desmopressin could be useful to facilitate platelet aggregation.

Major attention should always be paid to residual heparin in the four hours following dialysis. Protamine could help to reverse heparin in the case of emergency surgery.

Even in absence of definite recommendations for administration of blood products in patients with Alport syndrome, all uremic and actively bleeding patients should be treated with platelet concentrates immediately before or during surgery, regardless of the platelets count.

### **Particular preparation for anticoagulation**

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If heparin has been used in patients with Alport syndrome on dialysis, coagulation parameters normalization, usually lasting four hours, should be awaited before surgery. Protamine can anyhow reverse the heparin effect.

### **Particular precautions for positioning, transport or mobilisation**

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Patients with important oesophageal leiomyomas associated to Alport syndrome should be subjected to cautious postural changes and remain in the lateral position to avoid airway, heart and major vessels compression by the mediastinal masses.

No other suggestions for positioning, transport or mobilization have been reported.

## **Interaction of chronic disease and anaesthesia medications**

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In Alport syndrome dialysis-dependent patients, the recommendations concerning the use of anaesthetic agents are comparable to those of patients with end-stage renal disease.

### **Anaesthetic procedure**

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In patients with renal failure due to the Alport syndrome:

1. midazolam and opioids (especially morphine) should be avoided or titrated to effect due to their delay in metabolism and excretion possibly resulting in prolonged respiratory depression;
2. hypnotic agents (i.e. propofol) and volatile agents must be carefully administered in patients with myocardial impairment and/or at risk of hypovolemia due to dialysis;
3. non-depolarizing neuromuscular blocking agents (NMBA) - such as atracurium and cisatracurium – should be preferred to succinylcholine, whose metabolism by cholinesterase is reduced in end-stage renal disease. Rocuronium may be used in longer surgery or if sugammadex is available, since its partial renal excretion.

In patients requiring rapid sequence of induction and intubation, succinylcholine could be used if serum potassium concentration is <5.5 mEq/L and electrocardiographic alterations are not evident.

In patients requiring total intravenous anaesthesia (TIVA), such as in neurosurgery, continuous infusion of propofol and short-acting opioids (i.e.: remifentanyl) is not contraindicated.

Regional anaesthesia is safe and feasible, when appropriate, in patients with Alport's syndrome considering that the onset of action of local anaesthetics is slower in end-stage renal disease due to low serum bicarbonate levels and reduced protein binding.

Particularly suggested is the use of combined spinal-epidural anaesthesia to perform renal transplantation in Alport syndrome patients. In fact, a low dose of intrathecal heavy bupivacaine in addition to an epidural volume extension of analgesia during and after the procedure has been reported to provide the necessary motor block and the best pain management, with a low risk of adverse events and no impact on hemodynamic and respiratory muscles activity.

### **Particular or additional monitoring**

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Due to the high risk of arrhythmias possibly induced by elevated serum potassium, at least 5-lead, better 12-lead, electrocardiogram (ECG) should be used during surgery in patients with Alport syndrome.

Non-depolarizing muscular blockage should be always monitored due to the variability in pharmacokinetic of NMBAs in end-stage renal disease patients.

In case of high-risk surgery, invasive tools and monitoring, such as arterial cannulation for invasive blood pressure measurement and central venous line placement, are recommended.

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### **Possible complications**

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Severe cases of Alport syndrome are characterized by a high risk of fatal arrhythmias, hyperkalaemic cardiac arrest, heart failure and intraoperative bleeding. Over-administration of intravenous fluids during surgery may lead to pulmonary oedema, while under-administration may cause hemodynamic instability. Sedative drugs (i.e.: midazolam) and NMBA's may induce severe and prolonged respiratory depression.

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### **Post-operative care**

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Postoperative care and monitoring depends on patient and surgical characteristics.

The great majority of Alport syndrome patients could return home after outpatient procedures or be discharged to a regular surgical ward after inpatient surgery.

Admission to intermediate or Intensive Care Unit could be indicated in dialysis-dependent patients who are hemodynamically unstable after major surgical procedures or in presence of severe perioperative comorbidities. All severe cases of Alport syndrome and all end-stage renal disease patients should be adequately monitored in the postoperative period due to the high risk of electrolytic disorders, pulmonary oedema and bleeding.

Major attention should be given to those patients undergoing narcosis due to their slower drug metabolism and excretion, monitoring the breathing capacity.

Patients requiring dialysis should receive renal replacement therapy as soon as the risk of surgery-induced fluid shifts and bleeding has been reduced.

Postoperative analgesia should be guaranteed with a multi-modal approach, such as regional anaesthetic techniques and wound infiltration with local anaesthetics in order to reduce the need of intravenous analgesics and to avoid NSAIDs.

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### **Disease-related acute problems and effect on anaesthesia and recovery**

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The emergency-like situations in patients with Alport syndrome are fatal arrhythmias mainly related to end-stage renal disease.

There are evidences supporting the need of standby extracorporeal life support (ECLS) during oesophageal leiomyomas removal surgery due to the risks of critical hemodynamic and/or breathing problems possibly induced by mediastinal mass compression on heart, major vessels and airway.

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### **Ambulatory anaesthesia**

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Ambulatory anaesthesia is indicated during early phases of Alport syndrome taking into account renal function, electrolytic and acid-base balance and coagulation profile.

If outpatient procedures are necessary in patients with end-stage renal disease, anaesthesiologists should be aware of the recommendations about narcosis drugs and potential complications detailed above.

## **Obstetrical anaesthesia**

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Not specific recommendations are reported.

Since X-linked inheritance is the most frequent form, females with Alport syndrome have often a disease phenotype less severe than males. It is uncommon for end-stage renal disease due to X-linked Alport syndrome to characterize pregnant women since the risk of severe renal failure arises with increasing age, achieving a 30% probability by the age of 60. On the contrary, the chronic kidney disease and the consequent myocardial impairment may occur in women with autosomal dominant forms during the childbearing age.

However, central neuraxial block (spinal or epidural) may be safely used for labour analgesia and caesarean surgery in patients on dialysis.

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