European Reference Network
for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)

VASCERN DO'S AND DON'TS FACTSHEETS FOR RARE VASCULAR DISEASE PATIENTS FACING FREQUENT SITUATIONS

Loeys-Dietz syndrome

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Co-funded by the Health Programme of the European Union

VASCERN

VASCERN, the European Reference Network on Rare Multisystemic Vascular Diseases, is dedicated to gathering the best expertise in Europe in order to provide accessible cross-border healthcare to patients with rare vascular diseases (an estimated 1.3 million concerned). These include arterial disease (affecting aorta to small arteries), arterio-venous anomalies, venous malformations, and lymphatic diseases.

VASCERN gathers 31 expert teams from 26 highly specialized multidisciplinary HCPs, plus 7 Affiliated Partner centers, from 16 EU Member States, as well as various European Patient Organisations and is coordinated in Paris, France.

Through our 5 Rare Disease Working Groups (RDWGs) as well as several thematic WGs and the ePAG – European Patient Advocacy Group, we aim to improve care, promote best practices and guidelines, reinforce research, empower patients, provide training for healthcare professionals and realise the full potential of European cooperation for specialised healthcare by exploiting the latest innovations in medical science and health technologies.

More information available at: https://vascern.eu

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Abbreviations

ARD: Aortic Root Diameter

LDS: Loeys-Dietz syndrome

IVF: In vitro fertilization

ß-blockers: beta-blockers

Introduction

These factsheets are in part based on existing LDS management guidelines (McCarrick et al, 2014) and have been reviewed and adjusted by the experts of the VASCERN HTAD-WG. Diagnostic criteria for LDS are currently under development.

The HTAD-WG agrees with the recommendations but wishes to emphasize that these are recommendations made by consensus at expert level. We would recommend that these factsheets be used as a guide to implement locally agreed policies.

These factsheets are meant for patients as well as for caregivers. Implementing these recommendations should go hand in hand with strategies to educate patients about medical situations where specific care is required and about relevant symptoms and how to act when they occur.

Pregnancy, Delivery and Postpartum Care

Women with LDS can tolerate and have successful pregnancies and deliveries, although pregnancies should be considered high risk. Currently few data are available specifically for LDS, so current recommendations are also based on experience with Marfan syndrome.

1.1 Before Pregnancy

WHAT IS RECOMMENDED

- Address the issue of pregnancy in both male and female Loeys-Dietz syndrome (LDS) patients of childbearing age in a systematic manner to inform them of the options of prenatal/pre-implantation diagnostics when genetics is known. Inform women as well about specific management and care recommendations - also include the optimal conditions of follow-up and a written delivery plan.
- As soon as a pregnancy is being considered by someone suspected of having LDS, refer him and/or her to a specialized centre, if this has not already been done, for a full assessment and pre-pregnancy counselling.
- Plan the pregnancy in collaboration with the specialized centre.
- Assess the risk of aortic dissection before pregnancy by measuring the aortic diameter.
    - < 40 mm: pregnancy allowed.
    - 40-45 mm: pregnancy allowed on a case by case basis.
    - >45 mm: contra-indication for pregnancy with limited evidence. This aortic diameter may warrant prior surgery.
- No data is available on the effect of hormonal procedures (IVF). The same thresholds as for pregnancy (contra-indicated when ARD >45 mm) should be used.

Pregnancy, Delivery and Postpartum Care

1.2 During Pregnancy

The risk of aortic dissection is increased during pregnancy, delivery and the postpartum period.

WHAT IS RECOMMENDED

- Treatment with β-blockers throughout the entire pregnancy and in the postpartum period. Check the type of β-blocker: atenolol is the least favourable; propranolol, metoprolol and labetalol are preferred.
- Monitor the aortic diameters (including abdominal diameters) by ultrasound at least twice during pregnancy: 20-24w and 32-36w. More examinations may be considered if the aortic diameter is above 40 mm or when increased growth is noted.
- Monitor blood pressure on a regular basis (target <130/80 mm Hg).
- Fetal growth should be monitored carefully to assess the effect of β-blockers.

WHAT YOU SHOULD NOT DO

- Prohibit pregnancy for all women with Loeys-Dietz Syndrome.
- Stop treatment with β-blockers during the pregnancy or at delivery.

Pregnancy, Delivery and Postpartum Care

1.3 Delivery

WHAT IS RECOMMENDED

- Assess the risk of aortic dissection before delivery based on the aortic diameter
    - <40mm: vaginal delivery. Shorten the duration of stage 2 of labour with vacuum-extractors, etc.
    - 40-45 mm: delivery on a case by case basis (contact the expert centre).
    - >45 mm: Caesarean section and plan the delivery by limiting the duration of the third trimester, the period of maximum risk. A tailored delivery should be formalized. Different factors should be taken into account: distance of home to hospital, aortic diameter, etc... Labour should be limited to a minimum.
- Adequate epidural anesthesia should be performed with caution, considering dural leakage and in some cases dose adjustment. MRI can be considered prior to epidural.

WHAT YOU SHOULD NOT DO

- Administer an epidural without first checking the condition of the spine with imaging (scoliosis, spondylolisthesis, dural ectasia).
- Stop treatment with β-blockers.

Pregnancy, Delivery and Postpartum Care

1.4 Postpartum care

WHAT IS RECOMMENDED

- Cardiac ultrasound in the mother within 48 hours postpartum and after 6 weeks.
- Depending on the heart rate of the baby at birth, additional monitoring can be decided by the paediatrician.

Breastfeeding

- Breastfeeding is not contraindicated.

Anaesthesia

General anaesthesia does not pose any particular problems, apart from an interaction with β-blocker treatment or anticoagulants (www.orphananesthesia.eu).

WHAT YOU SHOULD NOT DO

- Expose the patient to blood pressure fluctuations.

Aortic Dissection

WHAT IS RECOMMENDED

- Consider aortic dissection if chest pain/back pain/abdominal pain is present in a patient with Loeys-Dietz syndrome or a LDS-related syndrome.
- Treat the dissection as an emergency, following the same protocols as with a non-LDS patient.
- For type A dissections, the sinuses of Valsalva should not remain in place (either Bentall or valve sparing are preferred).

WHAT YOU SHOULD NOT DO

- Use a stent as a first option in the presence of a dissection of the descending aorta if other options are possible.

Acute coronary syndrome

Spontaneous coronary artery dissection (SCAD) occurs more frequently in LDS patients.

WHAT IS RECOMMENDED

- A coronary dissection can be seen in LDS, and this diagnosis should also be considered in a young person.
- Ensure that there is no aortic dissection.
- Adhere to general recommendations that are available for treatment of SCAD.

Extra-aortic peripheral arterial dissections

Extra-aortic aneurysms do occur more frequently in LDS.

WHAT IS RECOMMENDED

- Ensure that there is no evidence of aortic dissection.
- Contact expert centre to seek advice for management.

Spontaneous haemoperitoneum

WHAT IS RECOMMENDED

- Rule out aortic dissection.

Stroke

The incidence of stroke is increased in patients with Loeys-Dietz syndrome due to the presence of intracranial, carotid and vertebral aneurysms.

WHAT IS RECOMMENDED

- Management and treatment are identical for LDS and non-LDS patients.
- Perform additional cerebral imaging when alarm symptoms are present.
- Rule out aortic dissection with extension to the supra-aortic trunks.
- The presence of cervical or cerebral aneurysms should prompt evaluation by neuroradiology or neuro-interventional specialists.

WHAT YOU SHOULD NOT DO

- Stop treatment with β-blockers.
- Delay management and modify treatment as a result of a diagnosis of Loeys-Dietz Syndrome.

Pulmonary embolism

There is no particular risk of pulmonary embolism associated with Loeys-Dietz syndrome.

WHAT IS RECOMMENDED

- Follow standard treatment protocols for pulmonary embolisms (including anticoagulant treatment).

Pneumothorax

Pneumothorax is associated with Loeys-Dietz syndrome and is the most frequent respiratory manifestation of the disease.

No particular issues except in cases of anticoagulant treatment, as in the general population.

WHAT IS RECOMMENDED

- Indications and treatments are identical for LDS and non-LDS patients.
- Perform aortic imaging if there is the slightest suspicion of aortic dissection

WHAT YOU SHOULD NOT DO

- Stop treatment with β-blockers.
- Delay care as a result of the diagnosis of LDS.

Abdominal/gastrointestinal/ gynaecological emergencies

Intestinal ruptures have been reported in Loeys-Dietz syndrome.

Particular attention should be given in case of anticoagulant treatment.

WHAT IS RECOMMENDED

- Rule out aortic dissection if there is the slightest doubt or in the event of unexplained pain.
- Indications and treatments are identical in LDS and non-LDS patients.

WHAT YOU SHOULD NOT DO

- Administer a spinal anaesthetic without first checking the condition of the spine (scoliosis, spondylolisthesis, dural ectasia).
- Stop treatment with β-blockers.
- Delay treatment as a result of the diagnosis of Loeys-Dietz Syndrome.

Colonoscopy, gastroscopy, laparoscopy or fibroscopy

Due to increased tissue fragility in LDS, there is a theoretical risk of perforation, although this has not been observed commonly. Alternative imaging procedure should be considered when feasible.

Particular issues in cases with dissection of the descending aorta.

WHAT IS RECOMMENDED

- Endoscopic or fibroscopic procedures should be carried out with caution
- A high degree of caution in cases with dissection of the descending aorta due to the high risk of blood pressure variations.

WHAT YOU SHOULD NOT DO

- Expose the patient to blood pressure fluctuations.

Antiplatelet agents and anticoagulants

WHAT IS RECOMMENDED

- Indications and contraindications for antiplatelet and anticoagulant treatments are identical in LDS and non-LDS patients.

WHAT YOU SHOULD NOT DO

- Modify the prescription of antiplatelet agents or anticoagulants as a result of a diagnosis with Loeys-Dietz Syndrome.

Contraindicated medications

WHAT IS RECOMMENDED

- QT prolongation should be checked on the electrocardiography prior to proposing QT prolonging drugs.
- The use of fluoroquinolones is advised against because of increased risk of aortic dissection.
- There are no specific contraindications to Bromocriptin, or any other drug, in patients with LDS.

Infiltrations

No particular issues except in cases of anticoagulant treatment.

Physical activity

Sports can be of great value considering body weight, blood pressure and fitness of the patient. Many symptoms like aches, pains and migraines may benefit from exercise. Sports can also be dangerous if they are accompanied by a significant increase in arterial blood pressure.

WHAT IS RECOMMENDED

- Endurance sports such as swimming, walking, running, and cycling.
- The physical activity level should be adjusted by the cardiologist based on the evaluation of aortic dimensions and valvular function, both in children and adults.

WHAT YOU SHOULD NOT DO

- Abrupt, isometric exercises, such as sit-ups, pull-ups or weightlifting.
- Contact/competitive sports such as football, basketball, handball, and tennis.
- Exercising to the point of exhaustion.
- Activities with rapid acceleration/deceleration should be discouraged as these may increase the risk of vessel dissection.

Retinal detachment

LDS patients have increased incidence of blue sclerae and eyes muscle problems such as strabismus/amblyopia/exotropia. Ectopia lentis is not commonly seen in Loeys-Dietz patients. Retinal detachment and cataract can also occur.

WHAT IS RECOMMENDED

- Cataract and retinal detachment are treated as per non-LDS protocols.

Odontology/dentistry

No specific issues with management and treatment, even though patients can have a very narrow jaw. Dental enamel defects also occur at higher frequency in LDS.

WHAT IS RECOMMENDED

- Regular monitoring.
- Early orthodontic follow-up due to dental misalignments.
- The prevention of endocarditis, as in the general population (only in the case of a history of valve surgery or if previous history of endocarditis).

Allergies and anaphylactic shock

LDS has been associated with a high prevalence of immunologic features including asthma, food allergies, eczema, and allergic rhinitis. Symptoms range from acute, life-threatening reactions to more chronic gastro-intestinal symptoms.

WHAT IS RECOMMENDED

- Avoidance of food triggers or environmental allergens.
- Antihistamines should be used to treat cutaneous or milder reactions.
- Asthma treatment as per standard protocols.
- EpiPens should be retained only for life-threatening reactions because they rapidly constrict blood vessels and could be harmful for individuals with underlying vascular disease.

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