

A&I

ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

Offizielles Organ: Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e.V. (DGAI)
Berufsverband Deutscher Anästhesisten e.V. (BDA)
Deutsche Akademie für Anästhesiologische Fortbildung e.V. (DAAF)
Organ: Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin e.V. (DIVI)



Camp(t)omelic dysplasia

Fabry disease

orphan**a**nesthesia

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

SUPPLEMENT NR. 4 | 2020

OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesisten damit keine Erfahrungen gesammelt haben, so dass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

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orphananesthesia

Anaesthesia recommendations for Fabry disease

Disease name: Fabry disease

ICD 10: E75.2

Synonyms: Morbus Fabry, Anderson Fabry disease (AFD), Fabry syndrome, angiosarcoma corporis diffusum, α -galactosidase A deficiency

Disease summary: Fabry disease is a rare lysosomal storage disease of X-linked recessive inheritance, which was first described in Germany and the United Kingdom in 1898 [1,11,50]. Due to mutations in the GLA gene, located on the X chromosome (Xq22.1), patients show a partial or complete deficiency of ceramidtrihexosidase, also referred to as α -galactosidase A (α -Gal A) [3,50]. The biochemical aetiology of this condition was discovered several years later [4,22]. Because of this mutation, sphingolipids accumulate in various tissues. Particularly globotriaosylceramide (Gb3) accumulates in skin, eye, heart, kidney, brain, vascular and nervous systems [50]. Accordingly, Fabry disease is a multisystem disease.

The disease can be divided into a severe, classical phenotype and a generally milder non-classical phenotype. In the severe form, there is typically no residual enzyme activity [3]. The non-classical type, also referred to as late-onset or atypical Fabry disease, often demonstrates a more variable disease severity and progression. Disease manifestations are often limited to a single organ with mainly isolated renal or cardiac manifestation [3]. Males tend to develop greater disease severity than females [50]. Skewed X inactivation might be responsible for the variability of the phenotype in women [3,10].

The overall incidence in new-born children varies between 1/40,000 or 1/117,000 in men up to much higher incidences with about 1/3100 to 1/1000 in high-risk populations, and even 1:875 in male and 1:399 female live births in Taiwan. It seems to differ between various countries [8,18,29,30,42,45].

In a cohort of 98 male patients, the mean age of diagnosis was 21.9 years [27]. The mean median cumulative survival seems to be 50 ± 8 years for males and up to 72 years for females. [5,27,46] The disease may present at any age and generally is progressive [38].

The diagnosis can be difficult, because patients present with nonspecific complaints such as headaches, limb or abdominal pain plus diarrhoea. The definitive diagnosis is most commonly made following severe complications such as stroke, heart and kidney failure [35].

Typical facial features include periorbital fullness, prominent lobules of the ears, bushy eyebrows, recessed forehead, pronounced or prominent nasal angle, generous nose or bulbous nasal tip, prominent supraorbital ridges, shallow midface, full lips, prominent nasal bridge, broad alar base, coarse features, posteriorly rotated ears and prognathism [35]. Other features include short fingers, prominent superficial vessels of hands, 5th digit brachydactyly or clinodactyly [35].

► **Citation:** Gaik C, Wiesmann T: Fabry disease. AnästH Intensivmed 2020;61:S74–S82. DOI: 10.19224/ai2020.S74

Fabry disease may present with cardiac abnormalities, which occur in up to 60% of male patients with the classical form of Fabry disease [39]. The pre-dominant finding is concentric left-ventricular hypertrophy (LVH). Furthermore, the left-ventricular mass index seems to be inversely correlated with α -Gal activity [49]. Moreover, Fabry patients often present with left-sided valvular dysfunction and conduction disturbances (bradycardia, atrioventricular block, various forms of ventricular and supraventricular arrhythmias, in particular atrial fibrillation) [9,25,39]. However, the right ventricle is occasionally affected, resulting in systolic and diastolic dysfunction [21,26].

End-stage renal disease and cerebrovascular events are not uncommon, largely due to glycolipid deposits in the glomeruli. The chronic kidney disease is characterised by glomerulosclerosis, tubular atrophy and interstitial fibrosis leading to proteinuria and chronic renal insufficiency [2]. The central nervous system has an increased incidence of stroke [39]. Mild cognitive abnormalities are only rarely described [43].

Pulmonary manifestations include obstructive airflow limitation [6,14].

Impaired autonomic and endocrinal function is also common. Gastrointestinal manifestations include abdominal pain or episodic diarrhoea, and are not uncommon. Besides, headaches and fever of unknown origin are frequently reported [37]. Fever of unknown origin as well as reduced saliva and tear formation may occur [7]. Hypohydrosis often leads to decreased exercise tolerance in Fabry patients [38]. Some of these symptoms as well as fatigue, dry skin or vague gastrointestinal complaints are also signs of hypothyroidism, which is a common co-finding in patients with Fabry disease [12,17].

The involvement of the peripheral nervous system leads to neuropathic pain or painful sensations in the extremities and arthralgia and myalgia might result in a decrease in quality of life. These symptoms can be triggered by changes in environmental or body temperature, exercise or emotional stress [37].

Other manifestations of Fabry disease may be corneal opacities (cornea verticillata), angio-keratoma, tinnitus or hearing loss [36,44].

In recent years, enzyme replacement therapy (ERT) has been offered as a treatment for Fabry disease and may halt disease progression [50]. The Mainz Severity Score Index (MSSI) was developed and may help to measure the severity of AFD and to monitor the clinical course of the disease in response to ERT [47].

Medicine is in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong



Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

Dermatology: typical vascular skin lesions termed angiokeratoma [16].

Ophthalmology: corneal opacities (cornea verticillata) and other ophthalmological changes [28].

Cardiac surgery: valve repair or replacement, implantation of a pacemaker or internal cardiac defibrillator, cardiac assist devices, resynchronisation therapy and heart transplantation [34,38,39].

Neurology and Neurosurgery: cerebrovascular strokes in small or large vessels [31,32].

Surgery: arteriovenous fistula for haemodialysis, cadaveric renal transplantation [33].

Traumatology: fractures or injuries due to seizures [39].

Type of anaesthesia

General anaesthesia and regional anaesthesia techniques might present potential problems in Fabry patients.

Ideally, these patients require assessment and anaesthesia care by a senior anaesthetist. The involvement of different organs and tissues means that pre-operative assessment needs to be thorough and organ dysfunction should be assessed carefully [24].

General anaesthesia has been described in very few patients. The use of fentanyl, propofol, rocuronium and cisatracurium for induction of general anaesthesia was reported as uneventful [23,40]. There is one case report on a Fabry patient with transient bronchospasm after induction of general anaesthesia using fentanyl, propofol and atracurium. An anaphylaxis was excluded [48]. In case of pre-terminal or terminal renal insufficiency, a relevant prolongation of elimination times must be expected for certain drugs which undergo renal clearance.

For maintenance, sevoflurane, desflurane, propofol as well as remifentanyl and fentanyl (boli) were reported as uneventful [24,48].

Post-operative pain management may be difficult due to episodic or chronic pain in the patient's medical history. For analgesia, morphine, metamizole, paracetamol as well as lidocaine were reported as being without incident [24,41].

To minimise post-operative nausea and vomiting, dexamethasone and ondansetron have been described not to cause any problems [24].

Neostigmine and glycopyrrolate were administered to reverse neuromuscular block [24].

In patients with severe cardiac, renal or other organ dysfunctions, regional anaesthesia techniques might be the optimal approach whenever applicable.

Necessary additional pre-operative testing (beside standard care)

There is no general recommendation or protocol for an ideal pre-operative assessment. In consideration of various manifestations and a peculiarity of symptoms, the pre-operative assessment must identify the specific pattern of symptoms present in the individual patient [24]. The assessment should focus on identifying organ dysfunction, particularly with special reference to lung, heart, brain and kidneys [41].

Patients with existing chronic pain require careful consideration of the peri-operative pain treatment plan [24].

Pre-operative evaluation of functional capacity status using an objective tool is likely to be helpful in identifying significant cardiorespiratory disease (e.g. cardiopulmonary exercise testing, 6-minute walk test) [6].

With regard to frequent cardiac involvement in Fabry disease, a 12-lead ECG as well as transthoracic echocardiography may prove useful to identify valvular disease and assess global ventricular function [41]. Some authors recommend a high index of suspicion of occult disease and suggest the use of non-invasive cardiac stress tests in patients over 30 years of age and relevant symptoms [48].

Laboratory analysis is recommended to identify patients with impaired kidney function [41].

Particular preparation for airway management

Airway examination should be performed carefully and with particular attention to the patient's anatomic and dysmorphic features, with a focus on head and neck anatomy to evaluate potential airway problems [41]. Difficult airway management should be anticipated and strategies for airway management should be carefully planned in advance. Prognathism or physical features of midface, lips and nose may hinder an optimal mask ventilation. Pulmonary impairment might also aggravate ventilation. Laryngoscopy and intubation may be challenging. [41]

Overall, the evaluation and preparation for airway management in patients with Fabry disease should follow common practice standards for airway management.

Particular preparation for transfusion or administration of blood products

No specific recommendations are given. No typical bleeding disorders were reported for Fabry patients.

Particular preparation for anticoagulation

There are no specific suggestions for Fabry disease. Subject to cardiac and valvular surgery, arrhythmias, strokes or other cardiovascular events in the patient's anamnesis, anticoagulation should be considered after operation according to current recommendation.

Particular precautions for positioning, transportation and mobilisation

Extreme positioning for specific operations, e.g. a (reverse) Trendelenburg positioning, might lead to haemodynamic impairment if there is severe cardiac involvement. Due to chronic pain disorders in some patients, positioning and mobilisation must be tailored on an individual basis.

Interactions of chronic disease and anaesthesia medications

Not reported. Especially enzyme replacement therapy does not interfere with any of the reported drugs used [24].

Anaesthetic procedure

Pre-operative evaluation: see details above.

Pre-medication: might be performed weighing the benefits and risks in individual patients. Enzyme replacement therapy should be continued following regular prescription when undergoing general anaesthesia.

Prophylaxis for endocarditis: should be performed on patients with an indication for prophylaxis (mainly after cardiac valve surgery) according to current international guidelines and after discussion with the responsible cardiologist [15].

Patient positioning & monitoring: act with caution due to haemodynamic impairment if there is a severe cardiac involvement and long-lasting chronic pain anamnesis.

Vessel cannulation: might be difficult due to vascular impairment or large-area haemangioma [41].

Anaesthesia: induction of anaesthesia should be performed with consideration of patient-specific risk factors and with attention to cardio-pulmonary involvement. With regard to physical features and pulmonary impairment, difficult airway management should be anticipated, particularly bag-mask ventilation, laryngoscopy and intubation. Using established drugs (see details above) for induction and maintenance of anaesthesia has been reported as uneventful. Total intravenous or balanced anaesthesia using volatile anaesthetics appears to be safe. The dosage of drugs should be adapted to renal function.

There are no reports of regional or neuraxial anaesthesia in patients with Fabry disease. However, the use of regional anaesthesia techniques might be favourable in patients with relevant organ disorders if applicable.

Particular or additional monitoring

A cardiopulmonary evaluation might include invasive blood pressure and non-invasive cardiac output measurement for both intra-operative fluid management as well as blood pressure management as in other patients according to the patient's status and scheduled surgical procedure [41].

Possible complications

Complications in airway management (bronchospasm, laryngoscopy, ventilation) have been reported [41,48]. Post-operative pain management may be challenging and has been reported as such. Haemodynamic instability due to underlying cardiovascular impairment has been reported.

Post-operative care

Post-operative care should be tailored to the individual's disease severity and type of surgery. A stay in intermediate or intensive care unit is not mandatory but might be reasonable if severe organ dysfunctions exist or post-operative dialysis is necessary.

Disease-related acute problems and effect on anaesthesia and recovery

Desaturation and hypoxia: allergic genesis, pulmonary embolism, endotracheal disconnection or other technical problems.

Haemodynamic deviation: anaphylactic genesis, myocardial infarction, bleeding complications.

Ambulatory anaesthesia

Ambulatory anaesthesia is possible and might be performed in institutions with adequate resources and expertise. Depending on pre-existing cardiac, respiratory and renal dysfunction and the procedure itself, this should be discussed on a case-by-case basis. A longer period in the post-anaesthesia care unit (PACU) due to prolonged drug effects may be anticipated. There are no general recommendations regarding outpatient procedures due to the lack of reports in the literature.

Obstetrical anaesthesia

Patients with Fabry disease are fertile. Due to the lack of reports on spinal or epidural anaesthesia in Fabry patients, recommendations cannot be provided. Haemangioma can occur over the medial spine and should be considered [20]. There is one case report of a spontaneous spinal epidural haematoma in a non-pregnant woman with Fabry disease [19]. Although cerebrovascular events are common in Fabry disease, there are no cases of vertebral dissection or spinal cord infarction documented in the literature to date [23]. However, in patients without relevant bleeding anamnesis and with normal coagulation lab results, regional anaesthesia may be considered. Few reports with small cohorts of pregnant women with Fabry disease, who underwent continued or reinitiated enzyme replacement therapy during pregnancy, observed no adverse events either in the mothers or their children [13]. Complications during pregnancy, which led to an emergency Caesarean section, have been reported. They include eclampsia with proteinuria, hypertensive crisis and seizures, pathologic cardiotocographic monitoring or premature birth [13,20].

References

1. Anderson W. A case of angiokeratoma. *Br J Dermatol* 1898;18:113–117
2. Alroy J, Sabins S, Kopp JB. Renal Pathology in Fabry Disease. *J Am Soc Nephrol* 2002;13: S134–138
3. Arends M, Wanner C, Hughes D, Mehta A, Oder D, Watkinson OT, et al. Characterization of Classical and Nonclassical Fabry Disease: A Multicenter Study. *J Am Soc Nephrol* 2017; 28:1631–1641
4. Brady RO, Gal AE, Bradley RM, Martensson E, Warshaw AL, Laster L. Enzymatic Defect in Fabry's Disease. *New Engl J Med* 1967;276:1163–1167
5. Branton MH, Schiffmann R, Sabnis SG, Murray GJ, Quirk JM, Altarescu G, et al. Natural History of Fabry Renal Disease. *Medicine (Baltimore)* 2002;81:122–138
6. Brown LK, Miller A, Bhuptani A, Sloane MF, Zimmerman MI, Schilero G, et al. Pulmonary Involvement in Fabry Disease. *Am J Respir Crit Care Med* 1997;155:1004–1010
7. Cable WJ, Kolodny EH, Adams RD. Fabry disease: impaired autonomic function. *Neurology* 1982;32:498–502
8. Chien YH, Lee NC, Chiang SC, Desnick RJ, Hwu WL. Fabry Disease: Incidence of the Common Later-Onset α -Galactosidase A IVS4+919G – A Mutation in Taiwanese Newborns – Superiority of DNA-Based to Enzyme-Based Newborn Screening for Common Mutations. *Mol Med* 2012;18:780–784
9. Desnick RJ, Bliden LC, Sharp HL, Hofschire PJ, Moller JH. Cardiac valvular anomalies in Fabry disease. Clinical, morphologic, and biochemical studies. *Circulation* 1976;54:818–825
10. Echevarria L, Benistan K, Toussaint A, Dubourg O, Hagege AA, Eladari D, et al. X chromosome inactivation in female patients with Fabry disease. *Clin genet* 2016;89:44–54
11. Fabry J. Ein Beitrag zur Kenntnis der Purpura haemorrhagica nodularis (Purpura papulosa haemorrhagica Hebrae). *JAMA Dermatol* 1898;43:187–200
12. Faggiano A, Pisani A, Milone F, Gaccione M, Filipella M, Santoro A, et al. Endocrine Dysfunction in Patients with Fabry Disease. *J Clin Endocrinol Metab* 2006;91:4319–4325
13. Fernández P, Fernández SO, Gonzalez JGM, Fernández T, Fernández CC, Fernández SP. Enzyme Replacement Therapy in Pregnant Women with Fabry Disease: A Case Series. *JIMD Rep* 2019;45:77–81
14. Franzen D, Haile SR, Kasper DC, Mechtler TP, Flammer AJ, Kraysenbühl PA, Nowak A. Pulmonary involvement in Fabry disease: effect of plasma globotriaosylsphingosine and time to initiation of enzyme replacement therapy. *BMJ Open Respiratory Research* 2018; 5:e000277
15. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. ESC Scientific Document Group. ESC Guidelines for the management of infective endocarditis 2015: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;3075–3128
16. Hashimoto K, Gross BG, Lever WF. Angiokeratoma Corporis Diffusum. Histocemical and Electron Microscope Studies of the skin. *J Invest Dermatol* 1965;44:119–128
17. Hauser AC, Gessl A, Lorenzi M, Voigtländer T, Födinger M, Sunder-Plassmann G. High prevalence of subclinical hypothyroidism in patients with Anderson–Fabry disease. *J Inher Metab Dis* 2005;28:715–722
18. Inoue T, Hattori K, Ihara K, Ishii A, Nakamura K, Hirose S. Newborn screening for Fabry disease in Japan: prevalence and genotypes of Fabry disease in a pilot study. *J Human Genet* 2013;58:548–552
19. Iwafuchi Y, Oyama Y, Narita I. Heterozygous Fabry disease complicated by acute onset paralysis. *Clin Exper Neurol* 2017;21:941–942
20. Kalkum G, Macchiella D, Reinke J, Kölbl H, Beck M. Enzyme replacement therapy with agalsidase alfa in pregnant women with Fabry disease. *Eur J Obstet Gynecol Reprod Biol* 2009;144:92–93
21. Kampmann C, Baehner F, Whybra C, Bajbouj M, Baron K, Knuf M, et al. The right ventricle in Fabry disease. *Acta Paediatr* 2005;94:15–18
22. Kint JA. Fabry's Disease: Alpha-Galactosidase Deficiency. *Science* 1970;167(3922):1268–1269
23. Kolodny E, Fellgiebel A, Hilz MJ, Sims K, Caruso P, Phan TG, et al. Cerebrovascular Involvement in Fabry Disease. Current Status of Knowledge. *Stroke* 2015;46:302–313

24. Krüger S, Nowak A, Müller TC. General Anesthesia and Fabry Disease: A Case Report. *Anesth Analg Case Rep* 2017;8:247–249
25. Linhart A, Ubanda JCL, Alecek TP, Ultas JB, Aretova DK, Edinova JL, et al. Cardiac manifestations in Fabry disease. *J Inherit Metabol Dis* 2001;24:75
26. Linhart A. The heart in Fabry disease. In: Mehta A, Beck M, Sunder-Plassmann G, (eds.): *Fabry Disease: Perspectives from 5 Years of FOS*. Oxford PharmaGenesis 2006
27. MacDermot KD, Holmes A, Miners AH. Anderson-Fabry disease: clinical manifestations and impact of disease in a cohort of 98 hemizygous males. *J Med Genet* 2001;38:750–760
28. Macrae WG, Gosh M, McCulloch C. Corneal changes in Fabry's disease: A clinicopathologic case report of a heterozygote. *Ophthalmic Paediatr Genet* 1985;5,3:185–190
29. Masson C, Cissé I, Simon V, Insalaco P, Audran M. Fabry disease: a review. *Joint Bone Spine* 2004;71:381–383
30. Meikle PJ, Hopwood JJ, Clague AE, Carey WF. Prevalence of Lysosomal Storage Disorders. *JAMA* 1999;281:249–254
31. Mitsias P, Levine SR. Cerebrovascular complications of Fabry's disease. *Ann Neurol* 1996;40:8–17
32. Moore DF, Kaneski CR, Askari H, Schiffmann R. The cerebral vasculopathy of Fabry disease. *J Neurol Sci* 2007;15;257:258–263
33. Ojo A, Meier-Kriesche HU, Friedmann G, Hanson J, Cibrik D, Leichtmann A, et al. Excellent outcome of renal transplantation in patients with Fabry's disease. *Transplantation* 2000; 15;69:2337–2339
34. Pierre-Louis B, Kumar A, Frishman WH. Fabry Disease. Cardiac Manifestations and Therapeutic Options. *Cardiol Rev* 2009;17:31–35
35. Ries M, Moore DF, Robinson CJ, Tiffet CJ, Rosenbaum KN, Brady RO, et al. Quantitative dysmorphology assessment in Fabry disease. *Genet Med* 2006;8:96–101
36. Ries M, Kim HJ, Zalewski CK, Mastroianni MA, Moore DF, Brady RO, et al. Neuropathic and cerebrovascular correlates of hearing loss in Fabry disease. *Brain* 2007;130:143–150
37. Ries M, Gupta S, Moore DF, Sachdev V, Quirk JM, Murray GJ, et al. Pediatric Fabry Disease. *Translational Pediatrics* 2016;5:37–42
38. Schiffmann R. Fabry disease. *Handb Clin Neurol* 2015;132:231–248
39. Sheppard MN. The heart in Fabry's disease. *Cardiovasc Pathol* 2011;20:8–14
40. Sims K, Politei J, Banikazemi M, Lee P. Stroke in Fabry Disease Frequently Occurs Before Diagnosis and in the Absence of Other Clinical Events. *Stroke* 2009;40:788–794
41. Sorbello M, Veroux M, Cutuli M, Morello G, Paratore A, Sidoti MT, et al. Anaesthesiologic protocol for kidney transplantation in two patients with Fabry Disease: a case series. *Cases J* 2008;1:321
42. Spada M, Pagliardini S, Yasuda M, Tükel T, Thiagarajan G, Sakuraba H, et al. High Incidence of Later-Onset Fabry Disease Revealed by Newborn Screening. *Am J Hum Genet* 2006;79:31–40
43. Tuttolomondo A, Pecoraro R, Simonetta I, Miceli S, Pinto A, Licata G. Anderson-Fabry Disease: A Multiorgan Disease. *Curr Pharm Des* 2013;19:5974–5996
44. van der Tol L, Cassiman D, Houge G, Janssen MC, Lachmann RH, Linthorst GE, et al. Uncertain Diagnosis of Fabry Disease in Patients with Neuropathic Pain, Angiokeratoma or Cornea Verticillata: Consensus on the Approach to Diagnosis and Follow-Up. *J Inherit Metabol Dis Rep* 2014;17:83–90
45. van der Tol L, Smid BE, Poorthuis BJHM, Biegstraaten M, Lekan Deprez RH, Linthorst GE, et al. A systematic review on screening for Fabry disease: prevalence of individuals with genetic variants of unknown significance. *J Med Genet* 2014;51:1–9
46. Vedder AC, Linthorst GE, van Breemen MJ, Groener JEM, Bemelman FJ, Strijland A, et al. The Dutch Fabry cohort: Diversity of clinical manifestations and Gb3 levels. *J Inherit Metabol Dis* 2007;30:68–78
47. Whybra C, Kampmann C, Krummenauer F, Ries M, Mengel E, Baehner F, et al. The Mainz Severity Score Index: a new instrument for quantifying the Anderson-Fabry disease phenotype, and the response of patients to enzyme replacement therapy. *Clin Genet* 2004; 65:299–307
48. Woolley J, Pichel AC. Peri-operative considerations for Anderson-Fabry disease. *Anaesthesia* 2008;63:96–107
49. Wu JC, Ho CY, Skali H, Abichandani R, Wilcox WR, Banikazemi M, et al. Cardiovascular manifestations of Fabry disease: relationships between left ventricular hypertrophy, disease severity, and α -galactosidase A activity. *Eur Heart J* 2010;31:1088–1097
50. Yuasa T, Takenaka T, Higuchi K, Uchiyama N, Horizoe Y, Cyaen H, et al. Fabry disease. *J Echocardiogr* 2017;15:151–157.

Date last modified: **November 2019**

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Disclosure The authors have 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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Verlag & Druckerei

Aktiv Druck & Verlag GmbH

An der Lohwiese 36 |
97500 Ebelsbach | Deutschland
www.aktiv-druck.de



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Paumgartnerstraße 28 | 90429 Nürnberg
E-Mail: mazyblue@klaus-steigner.de
www.klaus-steigner.de

Erscheinungsweise 2020

Der 61. Jahrgang erscheint jeweils zum
Monatsanfang, Heft 7/8 als Doppelausgabe.

Bezugspreise (inkl. Versandkosten):

• Einzelhefte	30,- €
• Jahresabonnement:	
Europa (ohne Schweiz)	258,- €
(inkl. 7 % MwSt.)	
Schweiz	266,- €
Rest der Welt	241,- €

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Impressum auf www.ai-online.info

Indexed in **Current Contents®/Clinical
Medicine, EMBASE/Excerpta Medica;
Medical Documentation Service;
Research Alert; Sci Search; SUBIS
Current Awareness in Biomedicine;
VINITI: Russian Academy of Science.**

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