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REVIEW ARTICLE

Anaesthetic management of patients with myopathies

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The anaesthetic management of patients with myopathies is challenging. Considering the low incidence and heterogeneity of these disorders, most anaesthetists are unfamiliar with key symptoms, associated co-morbidities and implications for anaesthesia. The pre-anaesthetic assessment aims at the detection of potentially undiagnosed myopathic patients and, in case of known or suspected muscular disease, on the quantification of disease progression. Ancillary testing (e.g. echocardiography, ECG, lung function testing etc.) is frequently indicated, even at a young patient age. One must differentiate between myopathies associated with malignant hyperthermia (MH) and those that are not, as this has significant impact on preoperative preparation of the anaesthesia workstation and pharmacologic management. Only few myopathies are clearly associated with MH. If a regional anaesthetic technique is not possible, total intravenous anaesthesia is considered the safest approach for most patients with myopathies to avoid anaesthesia-associated rhabdomyolysis. However, the use of propofol in patients with mitochondrial myopathies may be problematic, considering the risk for propofol-infusion syndrome. Succinylcholine is contra-indicated in all patients with myopathies. Following an individual risk–benefit evaluation, the use of volatile anaesthetics in several non-MH-linked myopathies (e.g. myotonic syndromes, mitochondrial myopathies) is considered to be well tolerated. Perioperative monitoring should specifically focus on the cardiopulmonary system, the level of muscular paralysis and core temperature. Given the high risk of respiratory compromise and other postoperative complications, patients need to be closely monitored postoperatively.

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Background

The anaesthetic management of patients with myopathies is challenging. Given the low incidence and heterogeneity of these disorders, most anaesthetists are unfamiliar with the key symptoms, associated co-morbidities and implications for anaesthesia.

Myopathies include a wide variety of disorders impairing the function, metabolism and structural integrity of muscle tissue. Over 800 separate entities are classified as neuromuscular diseases. Most of them are very rare, yet their entire cluster has a cumulative prevalence of 1 : 1500. Considering the extensive disease spectrum, this review will focus on primary myopathies, including dystrophinopathies [e.g. Duchenne's muscular dystrophy (DMD)], myotonic disorders (e.g. myotonic dystrophy), congenital myopathies (e.g. central core disease) and mitochondrial myopathies (e.g. Kearns–Sayre syndrome) (Table 1). Most myopathies are associated with progressive weakness and fatigue. This functional loss may be caused by a lack or dysfunction of contractile proteins (dystrophinopathies), a shortage of energy (mitochondrial myopathies), or other complex aberrations of muscle cell structure, ion channelopathies (myotonic syndromes) or intracellular metabolism. In addition to weakness, patients suffering from myotonic syndromes present with episodes of involuntarily prolonged muscle contractions. Apart from peripheral muscle tissue, myopathies also usually cause weakness and fibrous or fatty transformation of cardiac, respiratory, pharyngeal and ocular muscles leading to cardiomyopathies, conduction defects, respiratory failure and prolonged ventilatory support. Severe limb and spinal contractures resulting from immobilisation and pathologic changes in tissue structure are common in advanced stages of the disease. Neurologic symptoms, ranging from intellectual impairment and early dementia to ataxia and seizure disorders, are frequently part of mitochondrial myopathies. Considering this vast spectrum of co-morbidities, the impact on anaesthetic management is significant (Table 1).

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Table 1 Overview of primary myopathies and associated co-morbidities

Myopathy	Risks		Cardiac			Lungs		Neurology				Ocular		Other		Musculoskeletal			
Legend: ■ = common, ■ = occasional, □ = not reported K = kidney, L = liver	MH-Susceptibility	Risk for rhabdomyolysis	Cardiomyopathy	Arrythmias	Sudden cardiac death	Respiratory weakness	Recurrent pneumonia	Epilepsy	Ataxia	Dysarthria	Neuropathy	Ophthalmoplegia	Ptosis	Kidney/ Liver impaired	Difficulty swallowing	Exercise intolerace	Muscle weakness	Myotonia/ -spasm	Spinal deformities
Muscular dystrophies (MD)																			
Duchenne's MD		■	■			■	■									■	■		■
Becker's MD		■	■			■	■									■	■		
Emery-Dreifuss (EDMD)		■	■	■	■												■		■
Congenital MD		■				■		■									■		
Distal MD		■	■							■					■		■		
Fascioscapulohumeral MD		■	■	■													■		■
Limb-girdle MD		■	■	■						■					■		■		
Oculopharyngeal MD		■					■			■		■	■		■		■		
Scapuloperoneal MD		■															■		
Myotonic syndromes																			
Dystrophia myotonica (Steinert)		■	■	■	■	■	■				■	■	■		■	■	■	■	
Chondrodystrophic myotonia		■															■	■	■
Myotonia congenita (Thomson)		■											■					■	
Myotonia congenita (Becker)		■																■	
Neuromyotonia (Isaacs-Mertens syndrome)		■								■					■	■	■	■	
Paramyotonia congenita (von Eulenburg's)		■													■		■	■	
Congenital myopathies																			
Central core disease	■	■													■		■		■
Multi-/ Minicore disease	■	■				■						■			■		■		■
Myotubular (centronuclear) myopathy		■				■					■	■	■				■		
Nemaline myopathy	■	■	■							■					■		■		■
Fiber-type disproportion		■	■									■	■		■		■		■
Evans syndrome	■	■											■				■		■
King-Denborough syndrome	■	■											■				■		■
Mitochondrial mypathies																			
Kearns-Sayre syndrome		■	■	■					■			■	■	K			■		
Leber's disease		■		■													■		
Leigh's encephalopathy (MILS)		■				■			■			■		K	■		■		
Mitochondrial DNA depletion syndrom ADS)		■						■		■				L	■		■		
Mitochondrial encephalomyopathy, lactic sis, strokelike episodes (MELAS)		■	■	■				■								■	■		
Mitochondrial neurogastrointestinal encephalop (MNGIE)		■	■								■	■	■	L	■		■		
Myoclonus epilepsy with ragged red fibers (MERRF)		■						■	■								■	■	
Neuropathy, ataxia and retinitis pigmentosa (NARP)		■							■		■					■	■		
Pearson syndrome		■	■	■					■			■	■				■		
Progressive external ophthalmoplegia (PEO)		■							■		■	■	■			■	■		

Age of disease onset, symptom severity, life expectancy and medical management of most myopathies vary tremendously depending on the subtype of mutation and zygosity at the genetic locus. Accordingly, data provided in Table 1 are not intended to be exhaustive; however, it aims to characterise common forms of clinical presentations and associated disorders relevant to the anaesthetic management. Individual symptoms and co-morbidities may vary depending on subtypes of causative mutations and disease progression. Moreover, the same clinical presentation can be produced by mutations in different genes: this makes genetic diagnosis very important to obtain for therapeutic, prognostic and genetic counselling purposes. Given the rarity and heterogeneity of these conditions, the overview of co-morbidities (Table 1) and most recommendations are based on case series, case reports and expert opinion.

Preoperative anaesthetic assessment and risk stratification

Considering the genetic origin of most myopathies, the chances are that affected families will test their children early and may present with a precise diagnosis at the preoperative anaesthetic assessment. Although this facilitates anaesthetic management significantly, there is always a risk of undiagnosed myopathic patients

presenting for routine operations, especially children and patients with subclinical or late-onset symptoms. Moreover, it should be kept in mind that many mutations occur *de novo* (up to 50% in DMD) and that a positive family history is not always present. Given the extensive variety of myopathies and their clinical presentations, it cannot be expected of anaesthetists that they should diagnose or differentiate subgroups on their own. The knowledge of key clinical symptoms, however, is essential for identifying potentially undiagnosed patients in need of further investigations.

History and physical examination

In myopathies with late-onset, minor or subclinical manifestations, the family history may be the only possibility of identifying patients at risk. Detailed inquiries about muscle tissue disorders and anaesthetic complications in relatives over several generations are essential. Reported weakness of muscle groups, myalgia, cramping, inability to voluntarily relax a hand shake, exercise intolerance, fatigue, gait disturbances, reports of brown urine following strenuous exercise, impaired cognitive or motor development should prompt further evaluations, especially in children. Early manifestations of myopathies are potential causes for 'floppy baby' syndrome. A delay in walking (>2 years of age), the use of the Gower's manoeuvre (the sign describes a patient who has to use their hands and arms to 'walk' up their own body from a squatting position due to lack of hip and thigh muscle strength) and a waddling gait are highly suggestive of muscular dystrophies. In myotonic dystrophy, the inability to relax a muscle group after a contraction does not usually appear before the age of 5 to 6 years. Patients often do not report this symptom spontaneously as they are used to it, and therefore this should be specifically evaluated by the practitioner during the preoperative visit. Histories of relatives with short statures, extremity or facial contractures, spinal deformities, confinement to a wheelchair or in need of mechanical ventilatory support may be indicative of myopathic disorders. Suspicious reports of anaesthetic complications include episodes of intraoperative fever (MH) or cramping/stiffness (muscle rigidity or myotonia), postoperative discoloured/brownish urine (rhabdomyolysis, myoglobinuria) or long-term stays in the intensive care unit (prolonged mechanical ventilatory support).

It is important to note that patients with myopathies or MH susceptibility (MHS) (Table 1) may have undergone general anaesthesia 3 to 9 times, with concomitant administration of volatile anaesthetics or succinylcholine, before eventually developing a clinically apparent MH-episode or rhabdomyolysis.[1,2] Therefore, reports of uneventful previous anaesthetic exposures cannot be used to rule out a pre-disposition to MH or anaesthesia-induced rhabdomyolysis (AIR). The review of systems and physical examination should focus on the extent of associated co-morbidities (Table 1). In particular, impairment of the cardiopulmonary system (signs of dyspnoea on exertion, fatigue, oedema, palpitations, tachycardia, syncope, inadequate sputum clearance, coughing efficacy), and increased risk of aspiration (dysphagia, recurrent pneumonias, myotonic episodes) have direct impact on anaesthetic management. The extent of peripheral muscle weakness correlates poorly with the strength of cardiac or respiratory muscle tissue.[3] In advanced disease stages, patients may be confined to wheel chairs or be entirely immobilised. This may impair the ability to classify cardiac function by history taking alone, as the potential for exertion may be significantly limited (e.g. dyspnoea on exertion, metabolic equivalent of task, etc.). To assess the severity of respiratory muscle weakness, complaints of orthopnoea may indicate advanced diaphragmatic dysfunction. Reports of snoring, morning headache and daytime sleepiness are indicators for sleep-related breathing disorders, which may also occur in children. A difficulty swallowing liquids can be an early indicator of pharyngeal involvement and bulbar muscle weakness. Several myopathies may present with neurological (e.g. ataxia, neuropathy) or ophthalmological disorders (e.g. ophthalmoplegia, ptosis) (Table 1). These preoperative findings should be documented carefully, as they could otherwise be confused with serious disorders in the postoperative environment (e.g. stroke) or perioperative iatrogenic complications (e.g. nerve damage). Especially before regional anaesthetic techniques, the current neurologic status and motor function should be documented carefully. Also, spinal deformities (e.g. scoliosis), usually resulting from contractures, accompany many myopathies. Whenever neuraxial regional techniques are planned, careful examination of the spine is essential. In experienced hands, ultrasound may be helpful to identify suitable spinal puncture sites and identify the best pathway for the block needle. As muscle contractures and dysmorphic features may also affect the patient's head and cervical spine, increased vigilance for signs of a difficult airway (restricted mouth opening <3 cm, thyromental distance <6 cm, restricted cervical spine mobility, elevated Mallampati score etc.) is required. In Emery–Dreifuss myopathy, there have been reports of contractures severely limiting cervical reclination.[4] Furthermore, most of these diseases are progressive, meaning that the percentage of pathologic features is increasing over the patient's life time.

In patients with suspected undiagnosed myopathies, a referral to neurologic or neuropaediatric specialists is mandatory. Diagnosis is usually confirmed by muscular biopsies and electromyography. Genetic testing (e.g. DNA sequencing) is essential for identifying causative mutations and differentiating subtypes of disease. Establishing the correct genetic diagnosis has significant impact on the patient's medical treatment (e.g. availability of specific genetic therapies), anaesthetic management

(e.g. potential risk of MH in RYR-1 mutations) and overall prognosis. Given the progressive course of most myopathies, genetic testing should be performed early on (e.g. in infancy). In case of emergency, the most likely diagnosis should be established by a neurologist on clinical grounds. In addition, obtaining a baseline plasma creatine kinase level is useful.

Ancillary testing and consultations

Cardiac testing

As the myocardium is also a muscle, echocardiography and ECG should be performed at the time of diagnosis in every muscle disease. It should be repeated regularly thereafter depending on the disease and the initial cardiac involvement. In myopathies commonly associated with cardiac disorders (e.g. DMD), routine echocardiographic examinations should be initiated at the time of diagnosis or at 6 years of age. Cardiac function should be re-evaluated every 2 years in patients under 10 years of age and annually in older patients.[5] Furthermore, cardiological consultations are recommended for all patients as cardiac function correlates poorly with the overall clinical impression of the patient and may be significantly affected.[6] Cardiac medication is common, even in paediatric patients. Angiotensin converter enzyme inhibitors are considered to be the first-line agents for the treatment of cardiomyopathy.[5,7] Given the high risk of conduction defects and arrhythmias in cardiomyopathy, pacemakers and cardioverter defibrillators are frequently implanted. The correct functional status of implanted devices should be confirmed preoperatively.

Pulmonary testing

Pulmonary dysfunction is another significant anaesthesia-related risk factor. Preoperative pulmonary testing will focus on three major aspects, the evaluation of respiratory muscle strength, gas exchange and the presence of occult pulmonary infection.

Lung function testing is helpful to quantify limitations of respiratory function and can serve as an indicator for disease progression, when compared with earlier records. Pathological findings are recorded frequently (73%) in myopathies with respiratory involvement (e.g. DMD).[8] Restrictive lung function patterns are highly prevalent. Of note, a significant decrease (>50%) in muscle strength usually precedes relevant changes in vital capacity. Diaphragmatic involvement should be suspected, if vital capacity values decrease by more than 25% when moving from a standing to a supine position.[9] Oscillations in forced inspiratory and expiratory flow are indicators of upper airway muscular weakness.[10]

Arterial or capillary blood gas analysis is helpful for quantifying a baseline for alveolar gas exchange. Patients are considered high risk for pulmonary complications, if the forced vital capacity is less than 50%.[6] Hypercarbia indicates advanced respiratory muscle weakness and typically develops when muscle strength falls below 30% of normal values.[11]

Chest radiographs are useful for detecting atelectasis, cardiomegaly or pneumonic infiltrates.

Blood testing

A creatine kinase elevation could indicate an undiagnosed myopathy and should prompt further investigations, as it has been recognised as a marker for dystrophinopathies and MHS.[12–15] Creatine kinase (CK) testing alone, however, is unsuitable as a screening tool for myopathies and should only be used in case of adequate pre-test probability of disease, provided by careful history taking and physical examination, especially in toddlers and older children. In patients with diagnosed myopathies, measuring creatine kinase, serum myoglobin and lactate levels before or at the beginning of anaesthesia provides a baseline for comparison, in case of postoperative hyperCKaemia or suspected rhabdomyolysis. Inflammatory markers (white cell count, C-reactive protein, procalcitonin) may provide valuable information on the presence of (occult) respiratory infections. Although these blood tests are applicable to all primary myopathies, some patients may require additional specialised testing. In myotonic dystrophy, the endocrine system (thyroid and adrenal hormones) may be affected. Measuring appropriate hormone levels may help determine the need for preoperative replacement therapy (i.e. corticosteroids or thyroid hormones). Mitochondrial myopathies may be associated with lactic acidosis (Table 1). Baseline pH and lactate levels should be recorded for future reference.

Risk stratification

The association of malignant hyperthermia and myopathies

For years, myopathies in general were assumed to be associated with malignant hyperthermia (MH). It is now understood that MH-like reactions in most myopathies are in fact a separate disease entity that follows a different pathophysiologic pathway. This syndrome occurs following exposure to the same triggering substances as MH (succinylcholine, halogenated agents) and its initial signs, like tachycardia, rhabdomyolysis, hyperkalaemia, myoglobinuria and arrhythmias are almost indistinguishable from MH-episodes, especially in the early phases of symptom onset.[16] Its treatment, however, is different.

Even though mutations of the *RYR1*-gene are regarded as the most common reason for congenital myopathies,[17] only a minority of those are linked to MH-susceptibility. Examples for such congenital MH-linked myopathies are central core disease, King–Denborough disease and Evans myopathy (Tables 1 and 2).[18,19] Subtypes of nemaline and multi-minicore myopathies with underlying mutations of the *RYR-1*-gene have been suspected of being associated with MHS.[19,20]

Table 2 MH-susceptible myopathies

MH-susceptible myopathies
Central core disease
King–Denborough syndrome
Multi/Minicore disease
Nemaline myopathy
Evans myopathy

In patients with other neuromuscular diseases, the risk of developing MH or rhabdomyolysis from exposure to volatile anaesthetics is estimated to be 1.09%.[21]

There are multiple theories for the development of MH-like reactions in non-MH-linked myopathies.

In case of muscular dystrophies, like Duchenne's, it is assumed that a defect in the dystrophinglycoprotein complex causes a chronic instability of muscle cell membranes, that are further destabilised by trigger substances, especially succinylcholine or halogenated agents, leading to acute rhabdomyolysis. In other myopathies, upregulation of acetylcholine-receptors outside the muscle endplate is a cause for severe hyperkalaemia following succinylcholine administration.[22] It is crucial to understand that the use of dantrolene is ineffective in case of AIR and that intensive treatment of rhabdomyolysis and hyperkalaemia is essential.[23] Considering the current evidence, muscular dystrophies, myotonic and mitochondrial myopathies are not suspected to be associated with MH. AIR is very rare in mitochondrial diseases, unless there is significant muscular involvement and succinylcholine is used.

Role of regional anaesthesia

As general anaesthesia is associated with an inherent potential for severe complications in myopathic patients, regional anaesthetic techniques should be chosen whenever possible.[24] Pre-existing respiratory insufficiency, however, can be exacerbated in cases of high spinal anaesthesia.

Preoperative anxiolysis and sedation

Whenever possible, preoperative sedatives (i.e. oral benzodiazepines) should be avoided, as they may increase the risk for respiratory insufficiency in myopathic patients, who commonly present with an increased sensitivity to anaesthetics and sedatives, pre-existing respiratory muscle weakness and a pathologic respiratory drive.[19] On the other hand, stress and anxiety may exacerbate myopathic symptoms. For example in myotonic syndromes, they may trigger severe myotonic reactions. Clonidine or dexmedetomidine could serve as suitable alternatives. If the anaesthetist feels that preoperative anxiolysis and sedation with benzodiazepines is strictly required, short-acting agents (i.e. midazolam) should be chosen in a monitored setting.

Intraoperative anaesthetic management

Scheduling and preparations

Myopathic patients should be the first to be anaesthetised on a given day, considering that the anaesthesia workstation must be free of volatile anaesthetics remnants, especially when patients are susceptible to MH or AIR.

In addition, there are disease-specific aspects to consider. In patients suffering from mitochondrial myopathies, fasting times should be as short as possible, as the use of fatty acid as a source of energy may be impaired. Therefore, glucose should be supplemented by infusions during the perioperative period, until adequate oral intake is possible. Equally, stress and hypothermia should be avoided as they increase metabolic demands. There is also a high risk of atrioventricular block.[25,26] Hence, if a permanent pacemaker is not already in place, immediate access to a transcutaneous pacemaker should be available. In severe myopathies (e.g. muscular dystrophies), glucocorticoids are used to slow down disease progression and preserve pulmonary function. As daily steroid treatment is more effective, the patient's regular treatment intervals should be preserved.[27] Additional perioperative steroid substitution may be necessary depending on the patient's regular steroid dose and the type of surgery.

Myocardial dysfunction is frequently present in DMD and predisposes patients to increased perioperative blood loss. Apart from having a low threshold to type and cross match several red blood cell units preoperatively, the prophylactic use of tranexamic acid has been shown to decrease intraoperative blood loss and transfusion requirements in patients undergoing major spinal surgery.[28]

In cases in which exposure to a halogenated agent is best avoided (MHS, risk of AIR) (Table 1), performing a trigger-free anaesthetic also includes removing any remains of volatile anaesthetics from the anaesthesia workstation.[29] This can be achieved by removing volatile anaesthetic vapourisers, as well as exchanging the respirator tubing and carbon dioxide absorbent and flushing the circuit with high-flow oxygen according to the cleaning instructions provided by the manufacturers. (These vary depending on the anaesthesia machine used). For example, internal structures of modern anaesthesia machines absorb volatile anaesthetics and require prolonged decontamination times (i.e. >100 min).[30] Active charcoal filters attached to the tubing may significantly shorten these intervals.[30] The goal of decontamination is to decrease halogenated agent content within the anaesthetic machine to lower than 5 ppm. This value has been arbitrarily defined. To date, the exact safety threshold of volatile anaesthetics is unknown. Even though several authors have described using inhalational agents in myopathic patients, decontamination is not trivial, as there is at least one case report of rhabdomyolysis in a child with muscular dystrophy most likely caused by inadequate

flushing prior to anaesthesia.[31] Even after decontamination, a high fresh gas flow should be used during anaesthesia to avoid a rebound increase in trace levels of halogenated agents in the breathing circuit.

Pharmacologic management

To choose well tolerated pharmacological agents for general anaesthesia, one must differentiate between myopathies that are clearly linked to MH or are at high risk for AIR, and all other 'low-risk' myopathies (no MHS, AIR uncommon) (Tables 1 and 2).

Patients, who are suffering from MH-linked myopathies (Table 2), or are at a high risk of AIR, require the performance of a trigger-free anaesthetic, which means the strict avoidance of succinylcholine and volatile anaesthetics. Trigger-free agents like propofol, barbiturates, etomidate, benzodiazepines, opioids, nitrous oxide, xenon and non-depolarising muscle relaxants can be used safely.[29,32] Ketamine is often very useful in these situations. As usual, titration to effect is essential. The prophylactic use of dantrolene is considered obsolete, as it does not prevent MH-episodes and may cause adverse reactions.[33,34] For example, its properties as a muscle relaxant may exacerbate respiratory muscle weakness.

In most patients with adequate venous access who are high risk of AIR (e.g. DMD), there are no convincing arguments for using volatile anaesthetics, considering there are well tolerated intravenous anaesthetic alternatives that are suitable for virtually all clinical scenarios. In case venous access is challenging (e.g. poor peripheral circulation, cold extremities) or airway management is expected to be difficult in paediatric patients, several authors consider use of inhalational agents for the induction of anaesthesia to be well tolerated in myopathies that are not predisposed to MH-susceptibility.[30,35,36] In these specific situations, an individual risk assessment is required. The risk of harming the patient by using inhalational anaesthetics (e.g. 1.09% risk for MH/rhabdomyolysis) needs to be carefully weighed against potential complications that could ensue if these agents are avoided (e.g. risk of hypoxia in a difficult airway, cardiodepressant effects of propofol in patients with cardiomyopathy).

In myopathies considered low risk for MH or AIR (e.g. myotonic syndromes, mitochondrial myopathies), succinylcholine is also contra-indicated due to the risk of hyperkalaemia. The uncritical use of propofol, however, is a topic of controversial debate. Although propofol is considered well tolerated in patients with muscular dystrophies and congenital myopathies, there are specific concerns regarding its use in patients with mitochondrial myopathies and myotonic syndromes. In theory, the lipid carrier of propofol may exert negative effects on the respiratory chain and fatty-acid oxygenation in mitochondrial myopathies, increasing the risk of propofol-infusion syndrome. It has been suggested that propofol should be avoided in this patient population, especially since the association of mitochondrial myopathies and MH has mostly been discarded.[37,38] Volatile anaesthetics are regarded to be well tolerated alternatives to propofol in mitochondrial myopathies.[38] In patients with myotonic syndromes, propofol may induce severe myotonic reactions. Other commonly used agents like succinylcholine, barbiturates, anti-cholinestase inhibitors, potassium chloride and fibrates may precipitate similar effects. Severe myotonic states can be unresponsive to muscle relaxants and may cause significant thoracic rigidity and challenging intubating conditions. For most myotonic myopathies, including myotonic dystrophy, there is no evidence to suggest that inhalational agents are dangerous.[22] Yet, there are case reports of MH-like reactions in patients with myotonia congenita.[39,40] It is unclear, however, whether these incidents were true cases of MH, AIR, unrelated drug side effects or merely exacerbated generalised myotonic reactions.

In undiagnosed myopathic patients, the risk of MH and/or rhabdomyolysis is uncertain. In case of emergency, volatile anaesthetics and succinylcholine are best avoided. In general, propofol and rocuronium are considered well tolerated, except for patients suspected of suffering from mitochondrial myopathies (e.g. elevated lactate, neurologic symptoms). For these patients, benzodiazepines, barbiturates, ketamine or volatile anaesthetics may be more suitable.

In general, myopathic patients are more sensitive to anaesthetics, opioids and muscle relaxants.[41] An upregulation of endorphin receptors has been discussed as a potential reason for increased opioid sensitivity.[42] Accordingly, to minimise the risk of postoperative compromise of the respiratory drive, whenever feasible, short acting agents (propofol, remifentanil) should be chosen. Apart from a potentially negative impact on the postoperative pulmonary function, when determining appropriate doses it must be taken into account that cardiodepressant effects of most anaesthetics (intravenous and inhalational) are usually more pronounced, especially in patients with cardiomyopathies.[43]

Considering the high prevalence of muscle weakness in most myopathies, it is not surprising that the sensitivity to muscle relaxants and the duration of action are markedly increased. There is conflicting evidence, whether these effects are less pronounced with short acting muscle relaxants like mivacurium or atracurium.[44,45] Neuromuscular monitoring (i.e. train-of four) is strictly necessary to guide muscle relaxant dosing requirement, as the latter is markedly reduced compared with non-myopathic patients.[24] Given the heterogeneity of reactions to paralytics in myopathic patients, neuromuscular monitoring is the only reliable way to determine the state of muscle relaxation, especially regarding its potential negative impact on postoperative respiratory function. The

monitored muscle group should be chosen depending on the individual disease pattern. A baseline train of four (TOF) value should be obtained to quantify the patient's individual muscle response to neuromuscular stimulation before administering any muscle relaxant. Even minor residual paralysis must be excluded by neuromuscular monitoring (TOF-ratio target of 1.0), before any extubation attempts are made. In patients with myotonic syndromes, reliable monitoring of neuromuscular blockade may be impossible, as the electrical stimulation may trigger myotonic reactions, which might falsely suggest full reversal of residual muscle paralysis.

Furthermore, the specific type of myopathy and the extent of generalised muscle weakness may influence the muscle relaxant's duration of action. In case of myopathies with localised muscle weakness (e.g. oculopharyngeal muscular dystrophy), recovery times were unchanged after cisatracurium administration.[46] However, in myopathies typically presenting with severe generalised muscle weakness, such as DMD, a reduction in the induction dose of rocuronium by 50% (0.3 mg kg^{-1}) still led to a prolonged duration of action.[47] There is little evidence outlining optimal dosing of muscle relaxants in myopathic patients. Taking this into account, the use of rocuronium has one major advantage: any remaining muscle paralysis, which could easily exacerbate a pre-existing impairment of the respiratory reserves can safely and effectively be antagonised with sugammadex.[48] Considering the potential muscarinic side effects of neostigmine (e.g. bradycardia, bronchoconstriction, nausea/vomiting, QT interval prolongation) in addition to its delayed peak effect (10 min) and short duration of action (20 to 30 min), neostigmine is not an ideal reversal agent for neuromuscular blockade in myopathic patients.[49] In addition, there are reports of unpredictable reactions to neostigmine, ranging from acute muscle spasm to prolonged weakness.[50] The risk of postoperative residual paralysis or recurarisation must be minimised, as patients with myopathies are already predisposed to pulmonary complications, especially in the presence of bulbar or respiratory muscle weakness. Moreover, neostigmine requires at least partial recovery from full neuromuscular blockade (e.g. detection of two twitches in response to train-of-four stimulation) to work effectively. In light of these potential disadvantages of neostigmine, despite its increased costs, the use of rocuronium/sugammadex may be beneficial in myopathies. Its safety and efficacy in this patient collective has been demonstrated in numerous cases.[48,51]

Even though most myopathies are associated with increased sensitivity to muscle relaxants, reports of a resistance to paralytics in patients with mitochondrial myopathies also exist.[52]

Temperature management

Tight temperature management and prevention of hypothermia are strongly indicated in all myopathic patients. Avoiding hypothermia and shivering is important, especially in patients with myotonic myopathies, as it can induce severe myotonic reactions or paradoxical paralysis. Hypothermia may also prolong the duration of action of anaesthetics. Owing to increased energy demands during rewarming, patients with mitochondrial myopathies are especially in need of perioperative normothermia.

Airway and aspiration risk

Myopathies may affect smooth muscle cells and the gastrointestinal tract as well. Bulbar muscle weakness, dysphagia and delayed gastric emptying predispose to an increased aspiration risk. Given the risk of myotonic reactions and generalised muscle spasms, supraglottic airway devices may not provide sufficient airway protection in patients with myotonic syndromes. A rapid sequence induction with rocuronium would be an alternative in this group of patients.

In other myopathies, laryngeal mask airways may be beneficial as endotracheal intubation and subsequent muscle paralysis could be entirely avoided. It has been argued that it might be preferable for initial intubation attempts to be performed without any muscle relaxation. However, this is not without significant risks. Whenever muscle relaxants are omitted, intubating conditions are markedly worse.[53–55] Accordingly, the risk of vocal cord injuries and postoperative hoarseness is increased.[53] Studies demonstrating the feasibility of intubating without muscle relaxation commonly used specific induction regimens with high doses of intravenous or inhalational anaesthetics and opioids.[56,57] These methods, however, may be unsuitable for myopathic patients, considering previously mentioned risks for rhabdomyolysis, an increased sensitivity to anaesthetic agents and the subsequent risk for cardiovascular compromise.

Awake fibreoptic or (awake) videolaryngoscopic intubations may be advantageous alternatives for airway management without muscle relaxation.

Monitoring

As in all other groups of patients, standard monitoring, including ECG, blood pressure measurements and pulse oximetry is mandatory. Even though the constant use of waveform capnometry is already part of standard intraoperative monitoring, in patients with MH-linked myopathies especially it serves as an early indicator of hypermetabolic states.

Considering the high prevalence of cardiac co-morbidities, there should be a low threshold to implement intensified cardiovascular surveillance techniques. Invasive blood-pressure monitoring is recommended for patients with cardiomyopathy, as cardiodepressant effects of most anaesthetics are more pronounced. Also, immediate access to blood gas samples ensures early

detection of postoperative pulmonary dysfunction (i.e. hypercarbia).

Close monitoring of the metabolic state is required, specifically in patients with mitochondrial myopathies. Blood glucose, pH and lactate levels should be checked in regular intervals, as lipid metabolism as an energy source may be severely impaired.[58]

Postoperative care and disposition

In light of the high prevalence of co-morbidities, myopathic patients are a high-risk population and often require intensive postoperative monitoring. Judging by the fact that 26.5% of patients with myopathies affecting the cardiac and respiratory system experience postoperative complications, surveillance should focus specifically on the early detection of cardiopulmonary compromise.[59]

In addition to potential cardiopulmonary complications, episodes of MH and AIR may occur in the postoperative period.[60] To detect early signs of rhabdomyolysis, screening for myoglobinuria has been suggested.

Especially in progressive stages of disease, patients are regularly in need of nocturnal non-invasive ventilatory support. These devices should accompany the patient throughout the entire hospital stay (ward, anaesthesia recovery area, an intermediate care (IMC) or ICU). For these patients, postoperative disposition to an ICU or IMC is recommended, as the need for non-invasive ventilation is usually more pronounced after general anesthesia. Furthermore, given the elevated sensitivity to opioids and anaesthetics in combination with impairments of central respiratory drive, continuous monitoring of cardiopulmonary status is essential. Considering the unpredictable impact on the patient's respiratory drive, patient-controlled opioid infusion pumps should only be used in a closely monitored setting with markedly reduced dosing.

Apart from potential pulmonary complications, several myopathies are associated with cardiomyopathy and conduction deficits. Hence, prolonged postoperative ECG monitoring is indicated, especially in myopathies with an increased risk of arrhythmias (Table 1). Patients with preexisting cardiomyopathies need to be closely evaluated for early signs of cardiac decompensation. Postoperative immobilisation should be as short as possible, as it negatively influences residual muscle strength. Hence, early initiation of respiratory and general physiotherapy are important to restore and maintain muscle strength and reduce the risk for pulmonary complications.

Take home messages

(1) The prevalence and severity of myopathy-associated co-morbidities vary greatly, but may have significant impact on anaesthetic management.
(2) The pre-anaesthetic assessment aims at the detection of potentially undiagnosed myopathic patients and on the quantification of the impairment of the cardiopulmonary system, which is a common reason for perioperative complications.
(3) Only few myopathies are clearly associated with MH or AIR. Nevertheless, if regional anaesthetic techniques are not possible, total intravenous anaesthesia is considered the safest approach, especially in high-risk patients.
(4) Following an individual risk/benefit evaluation, the use of volatile anaesthetics in several non-MH-linked myopathies (e.g. myotonic syndromes, mitochondrial myopathies) is considered to be well tolerated.
(5) Succinylcholine is contra-indicated in all patients with myopathies.
(6) Perioperative monitoring should specifically focus on the cardiopulmonary system, the level of muscular paralysis and core temperature.
(7) Given the high risk of respiratory compromise and other complications, patients need to be closely monitored postoperatively.

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