Perioperative Implications

- No clinical trials studying the effects of anesthetic agents and techniques and incidence of intraop and postop complications in pts with mitochondrial disorders. The current available data consist of level 4 evidence.

Preoperative Preparation

- Communication with the pt's neurologist is crucial; a targeted preop assessment should be done because the organ systems affected in mitochondrial disorders are highly variable among individuals.
- Optimize nutritional state and pulmonary function.
- Consider premedication with prokinetic agents and nonparticulate antacid.
- Continue all medications and supplements for mitochondrial disorder up to day of surgery.
- Minimize duration of fasting, ensure normoglycemia, and avoid dehydration; list as first case of the day.
- Risk counseling.

Induction

- RSI in pts at high risk of aspiration.
- Consider avoidance of depolarizing neuromuscular blockers in view of risk of hyperkalemia.
- Reasonable to consider use of rocuronium with sugammadex available on standby.
- Propofol has been associated with decoupling of oxidative phosphorylation; experience is scarce on whether it should be avoided, but has been used successfully.

Monitoring

- Standard mandatory monitoring.
- Consider intra-arterial line: Continuous BP monitoring for pts with cardiomyopathy, early detection of arrhythmias, and frequent blood sampling for electrolytes, lactate, and glucose.
- Consider temp monitoring, especially for prolonged procedures greater than 2-h duration.
- Urinary cath to monitor urine output for adequacy of organ perfusion and fluid balance.
- Neuromuscular monitoring (unpredictable response to nondepolarizing neuromuscular blockers, aids timing of reversal and extubation).

Maintenance

- The association between mitochondrial myopathy and malignant hyperthermia remains unproven in current literature. Malignant Hyperthermia Association of the United States recommends volatile agents not be routinely avoided and succinylcholine to be used with care
- Consider increasing depth of inhalational and concurrent use of remifentanil to avoid depolarizing neuromuscular blockers
- Concerns: Acute decompensation with lactic acidosis, electrolyte abnormalities, acute encephalopathy, neuromuscular weakness, and cardiac dysfunction or arrhythmias.
- Avoid IV fluids containing lactate.

Extubation/Postoperative Period

- Ensure adequate reversal of neuromuscular blockers and extubate awake.
- Comanagement with neurologist.
- Avoid postop respiratory compromise; early and aggressive chest physiotherapy and early mobilization.
- Avoid decompensation: ensure adequate hydration, maintain normoglycemia and normothermia, and monitor for and correct electrolyte abnormalities.
- Adequate analgesia; use of multimodal approach.
- Appropriate postop placement; high dependency ward or ICU as indicated.
- Thromboembolic prophylaxis as appropriate.

Mitochondrial Myopathy

Jerry H. Kim | Jeremy M. Geiduschek

Risk

- More common than previously thought. Prevalence ranges from 1:7000–15,000.
- Occurrence is usually sporadic or maternally inherited.

Perioperative Risks

- Metabolic acidosis
- Respiratory and cardiac insufficiency/failure
- Delayed emergence

Worry About

- Respiratory failure following sedation.
- Consider aspiration risk.
- Metabolic acidosis.
- Hypotension during induction.

Overview

- Clinically heterogeneous collection of diseases with myopathy of mitochondrial origin as common trait. Defects can be in electron transport, fatty acid, and amino acid metabolism.
- Commonly associated with encephalopathy.
- Nomenclature rapidly changing to reflect discovery of specific genetic mutations. The following all are mitochondria-based disorders that may include a myopathic component: Kearns-Sayre syndrome (KSS); Pearson syndrome (PS); maternally inherited Leigh syndrome (MILS); late-onset Leigh syndrome; mitochondrial encephalomyopathy, lactic acidosis, and stroke-like symptoms (MELAS); myoclonic epilepsy with ragged red fibers (MERRF); Leber hereditary optic neuropathy (LHON); chronic progressive external ophthalmoplegia (CPEO); and neuropathy, ataxia, and retinitis pigmentosa (NARP).
- Onset is variable. Most severe phenotypes present in infancy.
- Most common symptom is muscle weakness, and most common sign is lactic acidosis, resulting from the inefficient metabolism of pyruvate and shift to anaerobic respiration.
- Muscle biopsy often used for suspected cases. Hallmark is appearance of ragged red fibers.
- Biochemical analysis of mitochondria often needed to make exact diagnosis.
- Anesthetic sensitivity may manifest as decreased MAC of inhaled anesthetics (e.g., complex I disorders), increased respiratory insufficiency from sedatives and narcotics, and decreased hepatic clearance or renal excretion of IV agents.

Etiology

- Genetic variation in either mtDNA or nDNA.
- Large-scale mtDNA deletions (e.g., KSS, PS, PEO) are most often acquired sporadically.
- Single-base mtDNA changes (e.g., MELAS, MERRF, MILS, LHON) are often inherited maternally and usually affect mitochondrial protein synthesis (via mRNA, tRNA, or rRNA) or components of the electron-transport chain (i.e., complex I, III, IV, V).
- Single-base nDNA changes (e.g., late-onset Leigh syndrome) are often inherited in mendelian patterns (autosomal dominant or recessive).

Usual Treatment

- Supportive measures
- Dietary vitamins and supplements, coenzyme Q

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Dysphagia	Coughing, choking, aspiration with feeding	Sialorrhea	Swallow study
CV	Cardiomyopathy Conduction defects (KSS)	Symptoms of CHF	Murmur, gallop, crackles	CXR, ECHO ECG, exercise testing (VO_2 max)
RESP	Disorganized respiratory muscle effort	Hypoventilation, hypoxia following sedative use	Rhonchi	CXR
GI	Chronic diarrhea Exocrine pancreatic failure (PS)	Dehydration Steatorrhea		Serum lytes
ENDO/METAB	Lactic acidosis Hepatic insufficiency	N/V Prolonged Rx effects	Hyperventilation	Serum lactate, CSF pyruvate/lactate ratio
GU	Renal tubular defects (PS), nephropathy	Urinary changes		Urinalysis Serum BUN, Cr, lytes
CNS	Encephalopathy (MILS) Ophthalmoplegia (CPEO, KSS) Stroke (MELAS) Seizure (MELAS, MERRF) Retinopathy, ataxia (NARP), blindness (LHON), deafness	Developmental delay Poor visual tracking Poor coordination Vision loss	Decreased ROM of extraocular mm Decreased visual acuity, ptosis Focal neurologic deficits Signs of seizures Pigmented retinas	Head CT or MRI Ophtho exam
PNS	Peripheral neuropathy	Weakness, clumsiness	Decreased strength	
MS	Hypotonia, weakness Myoclonus (MERRF)		Decreased strength	Muscle biopsy (ragged red fibers)

Clinical findings listed above may be characteristic of one or more mitochondrial myopathies. A specific disorder may follow in parentheses if the finding is a primary feature.
Key Reference: Niezgoda J, Morgan PG: Anesthetic considerations in patients with mitochondrial defects, *Paediatr Anaesth* 23(9):785–793, 2013.

Perioperative Implications

Preoperative Preparation
- Assess for cardiomyopathy and conduction defect.
- Preop anticholinergic for excessive oral secretions.
- Avoid prolonged fasting and dehydration, which can worsen acidosis.
- When possible, start IVF at NPO time, allow for late (2 h prior) clear fluid intake, and book as first case.

Airway
- Possible aspiration risk

Monitoring
- Routine, assuming no severe cardiomyopathy or CHF
- Consider BIS monitor prior to induction for possible increased anesthetic sensitivity

Induction
- Avoid lactate-containing IVF (e.g., lactated Ringer).
- Consider dextrose-containing IVF (e.g., 2–5% dextrose in normal saline).
- Avoid succinylcholine for uncharacterized myopathy or in face of neuropathy.

Maintenance
- Many techniques have been used safely.
- Avoid prolonged infusion of IV anesthetics, especially propofol, which is a known electron transport chain decoupler, due to worsened acidosis and reduced ATP production.
- Hepatic and renal insufficiency may increase IV anesthetic half-life and prolong elimination.
- If NMB agent is required, consider careful titration with shorter-acting agents.
- Implement aggressive temp control; recommend active warming techniques.
- Avoid tourniquets.

Extubation
- Muscle weakness and anesthetic sensitivity may delay extubation.

Regional Anesthesia
- Used successfully, but caution in those with underlying cardiac conduction block.
- Local anesthetics have potential to decouple electron transport chain.

Postoperative Period
- Close monitoring of respiratory function.
- For cases of longer duration, consider serum electrolytes or blood gas to assess acidosis.
- Some have reported increased incidence of PONV.

Anticipated Problems/Concerns
- Generally not associated with MH; however, scenario of critical ATP depletion may lead to muscular contraction mimicking MH.
- Although succinylcholine is not contraindicated as in Duchenne or Becker MD, acidosis and neuropathy may predispose to accentuation of hyperkalemia.

Mitral Regurgitation

Luiz Maracaja | Raj K. Modak

Risk
- Mitral regurgitation affects more than 2 million people in USA.
- Incidence of moderate/severe mitral regurgitation: Nearly 20% for age >55 y.
- Mitral valve prolapse is the primary form of myxomatous degeneration of the valve.
- Mitral valve prolapse is the most frequent diagnosed valve abnormality.
- Incidence in females is slightly higher than in males.

Perioperative Risks
- Acute mitral regurgitation
- Atrial arrhythmias (tachycardia, atrial fibrillation, atrial flutter)
- LV dysfunction yielding reduced cardiac output, acute CHF, pulm edema, and acute RV failure
- Bacterial endocarditis

Worry About
- Worsening symptoms of fatigue, orthopnea, dyspnea on exertion
- Acute or chronic mitral regurgitation
- New-onset atrial fibrillation
- Hemodynamic instability in setting of poor LV function and acute MI

Overview
- The mitral valve allows one-way blood flow through the left heart.
- During diastole, it acts as an open conduit for blood flow from the LA to the LV During systole, it closes preventing backflow while the heart contracts.
- With mitral regurgitation, retrograde flow occurs from the LV to the LA during systole. This can occur as an acute or chronic process.
- The acute form results in sudden elevations in LA pressure. Elevated pressures in the pulm vasculature resulting in pulm edema and RV strain and possible failure.
- Chronic mitral regurgitation is tolerated well. LV hypertrophy is followed by dilation and failure. Similar changes in the RV and pulm circulation occur, as in the acute form, but are better tolerated over the longer time period.
- As a general rule, the more precipitous the onset, the more significant the sequelae.

Etiology
- Acute: Myocardial ischemia or MI causing papillary muscle dysfunction, ruptured chordae causing a flail mitral valve from infarction or endocarditis, trauma, prosthetic valve dysfunction.