OSTEOGENESIS IMPERFECTA

Surgical Specialty:	Orthopedic Surgery
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Background:

- General Considerations[1,2,3,4]
  - Osteogenesis Imperfecta (OI) is a heterogeneous connective tissue disorder that may result in skeletal deformities, short stature, bone fragility, hypermobile joints, blue sclera, dentinogenesis imperfecta, and coagulopathy. Global prevalence is ~1/ 20,000. It is also called Lobstein syndrome, Porak and Durante disease, or brittle bone disease.
  - Patients with OI may frequently present for surgery due to bone fractures. Surgery may be urgent depending on the type and severity of the fracture.
  - The underlying pathophysiology of the most common types of OI is caused by a defect in type I collagen synthesis due to a gene mutation.
    - It may be inherited in an autosomal dominant or autosomal recessive manner or associated with new gene mutations encoding for type I collagen.
    - Type I collagen is the primary type found in bone, skin, sclera, and teeth.
  - There are four main types of OI, but up to 17 forms have been described, each with varying severity.
    - **Type I** – Most common (60% of cases) and the *mildest* form. These patients may present with blue sclera, hearing loss, and varying bone fragility.
    - **Type II** – 10% of cases. *Most severe* form and is evident in utero or at birth. Often results in neonatal death.
    - **Type III** – 20% of cases. *Severe* form and may result in death in childhood or adolescence due to cardiopulmonary complications. Early and frequent fractures result in progressive skeletal deformities.
    - **Type IV** – Less than 10% of cases. *Moderate* in severity (between Type I and Type III). Frequent fractures and possible dentinogenesis imperfecta.
- Patient Considerations
  - Disease Specific Considerations
    - Perioperative challenges such as difficult airway, difficult intravenous (IV) access, difficult neuraxial anesthesia placement, perioperative fracture, and significant intraoperative blood loss are more common in patients with severe OI types (Types III and IV).[1]
    - Care must be taken when moving and positioning patients and when using a non-invasive blood pressure cuff or tourniquet, as bone fractures may occur with minimal pressure or trauma.[1,2,4]

        - Most OI patients have normal cognition. However, patients with OI may be hard of hearing due to deformities of the inner ear.[1,2,4]
    - Associated Comorbidities/Syndromes[1,2,3,4]
        - Patients with OI may have a difficult airway due to facial dysmorphism, decreased cervical spine mobility, concern for cervical spine and mandibular fracture with airway manipulation, and brittle teeth.
        - Basilar invagination, described as the upward displacement of basilar and condylar portions of the occipital bone, causing an infolding of the foramen magnum and leading to a translocation of the upper cervical spine into the brainstem, is a serious complication in OI patients.
        - Patients with OI may have restrictive lung disease, pulmonary hypertension, and/or right ventricular dysfunction due to scoliosis or thoracic skeletal deformities.
        - Sleep-disordered breathing may affect children with OI, particularly in those with compromised walking autonomy, high BMI, trunk deformities, and severe OI types.[5]
        - Patients with OI may exhibit increased surgical bleeding due to platelet dysfunction and capillary fragility.
            - Platelet dysfunction is related to abnormal collagen and its effects on platelet-endothelial cell interactions.
        - Patients with OI may demonstrate a hypermetabolic state and hyperthermia. Although previously controversial, it is widely accepted that an association between OI and malignant hyperthermia (MH) does not exist.

Anesthetic Planning:

- Pre-Anesthetic Evaluation
    - A medical history should be elicited, and a physical exam should be performed.
        - Medical history should include exercise tolerance, symptoms that may indicate basilar invagination or restrictive lung disease, history of fractures with precipitating causes, and any complications with prior surgeries.
            - Symptoms of basilar invagination include occipital headaches, limitations of neck range of motion due to weakness, proprioception disturbances, paresthesias, or other signs of increased intracranial pressure.[4]
        - Physical exam should focus on the following:
            - General appearance of the patient, including obvious skeletal deformities and signs that indicate a bleeding or bruising tendency.
            - An airway evaluation, including neck range of motion, symptoms of cranio-vertebral junction pathology with neck extension, and defective dentition.
            - A musculoskeletal examination, including range of motion of extremities and fixed flexion or extension of extremities.
    - Additional labs/tests indicated during work-up
        - Echocardiography may be indicated, especially in patients with severe OI types. It may demonstrate evidence of pulmonary hypertension, ventricular dysfunction, mitral valve prolapse, aortic regurgitation, or aortic root dilation.[2,4]

        - Type I collagen makes up 85% of cardiac muscle. Decreased collagen diameter and amount may lead to alterations in the structure and mechanics of the myocardium and valves.[4]
    - A complete blood count, coagulation studies, and type and screen may be indicated due to increased risk for surgical bleeding.[1,2,4]
        - Approximately 30% of OI patients have abnormal bleeding times.[2]
  - Discussions to have with surgeon/family
    - Risks, benefits, and alternatives to surgery should be discussed with the patient, the patient's family, and the surgeon, given the patient's risk for increased blood loss, perioperative fractures, and potential for injury to the cervical spine and dentition with airway management.
    - Consent to transfuse blood products should be discussed depending on the type of surgery.
    - Patient positioning should balance optimizing surgical exposure while minimizing pressure to prevent fractures.
    - Post-operative pain management should be discussed prior to surgery.
    - Code status
- Specific or Unique Room Set-up Requirements
  - Airway[1,2,4]
    - Patients with OI may have a difficult airway due to facial dysmorphism, large head, short neck, decreased cervical spine range of motion, thoracic skeletal deformities, and brittle dentition.
    - In-line stabilization of the cervical spine should be maintained throughout airway management. A supraglottic airway or endotracheal tube (ETT) may be utilized depending on the patient and procedure, and video laryngoscopy or fiberoptic intubation should be considered if placing an ETT to minimize cervical spine extension.
        - If mask ventilation requires significant neck extension or forceful pressure on the maxilla or mandible, a supraglottic airway may be placed as a temporizing measure.
            - Cervical spine fracture or atlantoaxial subluxation may occur with excessive neck manipulation or extension. Maxillary or mandibular fracture may occur with pressure to the maxilla or mandible.
        - Dental guards may be used if brittle dentition is present.
  - Drugs/Infusions
    - Avoidance of succinylcholine is recommended, as fasciculations may result in fractures.[1,4]
        - In cases where succinylcholine is necessary, pretreatment with a nondepolarizing muscle relaxant will attenuate fasciculations.
        - In patients with severe skeletal deformities or with recurrent fractures that cause immobility, succinylcholine may result in hyperkalemia due to up-regulation of acetylcholine receptors.
    - A case of lactic acidosis has been described in a child who received total intravenous anesthesia (TIVA) with propofol.[6]
    - Patients with OI may demonstrate a hypermetabolic state, manifested as diaphoresis, hyperthermia, tachycardia, and tachypnea.[1,2,3] Atropine or glycopyrrolate should be used judiciously if hyperthermic.[2]

- Monitors[1,2,4]
  - Standard American Society of Anesthesiologists monitors should be employed. However, if there is a concern for fracture with inflation of a non-invasive blood pressure cuff, an arterial line may be placed. Of note, cases of iatrogenic fracture due to blood pressure cuff inflation are not commonly described.
    - If a standard non-invasive blood pressure cuff is utilized, one should consider cycling less frequently if hemodynamics permits.
  - The use of a tourniquet to facilitate IV placement may result in fracture. An ultrasound may be employed to facilitate IV placement without using a tourniquet, or gentle manual circumferential pressure may be employed in place of a tourniquet.
- Blood Availability
  - Packed red blood cells, fresh frozen plasma, and platelets should be available depending on the surgical procedure, as OI patients are at risk for increased bleeding due to platelet dysfunction and capillary fragility.[1,2,4]
- PICU Bed Availability
  - PICU admission may be necessary depending on the patient and surgical procedure, specifically in patients who have restrictive lung disease.

Intraoperative Considerations:

- General
  - Most occurrences of difficult airway, difficult IV access, perioperative fractures, and significant intraoperative blood loss occur in patients with severe OI types.
    - Patients with OI Type III have a 5.6-fold increased overall risk of anesthetic complications compared to patients with OI Type I.[1]
  - General anesthesia and/or neuraxial or regional anesthesia may be utilized depending on the patient and procedure.
    - There is insufficient evidence to validate or refute the risks of neuraxial and regional anesthesia in patients with OI. Still, the potential for difficult placement due to anatomical abnormalities, increased surgical bleeding, and platelet dysfunction should be considered when choosing an anesthetic technique.[7]
      - If performing neuraxial anesthesia, platelet count and coagulation studies should be obtained.
      - If performing a peripheral nerve block, nerve stimulation may lead to contraction-induced fractures; therefore, ultrasound guidance is preferred.
- Induction
  - Inhalational induction versus intravenous induction depends on patient-specific factors.
    - If performing an inhalational induction, pressure on the maxilla and mandible should be avoided to prevent fracture.
    - If possible, succinylcholine should be avoided, given the potential for fasciculation-induced fractures.[1,4]
- Positioning
  - Extreme care must be taken when moving and positioning patients to prevent fractures. Padding of pressure points is essential.[1,2,4]

- Maintenance
    - Volatile agents are often used if there is no separate concern for MH, although TIVA is an option.
    - Monitoring neuromuscular blockade with a twitch monitor should be done with caution, as skeletal contraction with monitoring may cause fractures.
- Hemodynamic/Physiologic goals
    - Maintain age-appropriate hemodynamic parameters.
    - Patients with OI may demonstrate a hypermetabolic state, manifested as diaphoresis, hyperthermia, tachycardia, and tachypnea. However, one should maintain a broad differential diagnosis as the cause for vital sign abnormalities and monitor and treat based on such a broad differential.[1,2,3,4]
- Surgical Considerations
    - If a tourniquet is indicated on the operative extremity, the risk of iatrogenic fracture with a tourniquet must be weighed against increased surgical bleeding without the use of the tourniquet. Consider a lesser degree of tourniquet inflation if it is to be used.
- Emergence/Disposition
    - The decision to extubate post-operatively should be based on patient comorbidities and surgical factors. Most patients without severe restrictive lung disease can be extubated and recover in PACU.
- Post-op Care
    - Non-opioid analgesics, opioids, muscle relaxers, and neuraxial or peripheral nerve catheters may be utilized to manage pain postoperatively.

Case-Specific Complications/Pitfalls

- The hallmark of the management of OI patients is to be gentle, as even minimal pressure or trauma can result in fractures.[1,2]
- Identifying the type and severity of OI preoperatively will aid in intraoperative preparedness, as complications related to airway management, IV access, perioperative fracture, and surgical blood loss are influenced by the severity of OI.[1]
- Positioning, airway management, IV access, and performance of neuraxial and regional anesthesia may become more challenging as skeletal deformities progress and the range of motion declines.
- OI patients may have perioperative anxiety due to frequent surgeries. In addition to pharmacologic anxiolysis, the involvement of child life specialists or parental presence during induction may minimize perioperative anxiety.
- Although previously controversial, it is widely accepted that an association between OI and MH does not exist. However, patients with OI may demonstrate a hypermetabolic state, resulting in hyperthermia, tachycardia, and tachypnea. Nevertheless, one should consider a separate diagnosis of MH if the clinical picture permits.[1,2,3,4]

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