

Anesthetic considerations in children with Hutchinson-Gilford progeria syndrome: A narrative review

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Abstract

Background: Hutchinson-Gilford progeria syndrome is a rare disease in childhood that results in premature aging. The presence of multisystem derangements including skin, bone, and joint diseases and possibly a difficult airway makes the anesthetic management challenging. Because of the extremely low prevalence, experience is limited even for experienced pediatric anesthesiologists.

Objective: To review the available literature on anesthesia for patients with Hutchinson-Gilford progeria syndrome and to give recommendations for establishing the best practice for patients with Hutchinson-Gilford progeria syndrome.

Design: A narrative review of the rare existing literature.

Date sources: CENTRAL (Cochrane), EMBASE, Google Scholar, MEDLINE and PubMed.

Eligibility criteria: Articles addressing anesthesia in patients with Hutchinson-Gilford progeria syndrome were included.

Results: An overview of the current literature was made on anesthesia care for patients with Hutchinson-Gilford progeria syndrome. After screening the literature, only ten articles were found to be of interest and include some case reports and a correspondence. The focus points on how to perform anesthesia care in patients with Hutchinson-Gilford progeria syndrome and the entire perioperative care are suggested. The available data are limited and results need to be interpreted with caution.

Conclusion: The patients with Hutchinson-Gilford progeria syndrome are not just “frail” patients. Awareness concerning intubation difficulties is mandatory, and airway strategies must be addressed in advance. Although these patients present with the physiology of an elderly with accompanying comorbidities, emotionally they are only children and should be approached as such.

KEYWORDS

anesthesia, Hutchinson-Gilford progeria syndrome, progeria

1 | BACKGROUND

Hutchinson-Gilford progeria syndrome (HGPS), commonly referred to as progeria, was first described in 1886 by Dr Hutchinson and later

in 1901 by Dr Gilford. It is a rare childhood syndrome (incidence 1 in 8 million live births) that results in premature aging, severe growth failure, and very early-onset atherosclerosis,¹⁻⁴ resulting in cardiovascular comorbidity as main cause of death.⁵ HGPS belongs to a

group of progeroid laminopathies, which are characterized by a mutated form of LMNA, known as progerin.⁶ The LMNA gene contains 12 exons and is located on chromosome 1q21.2-q21.3.⁷ Mutations in other parts of the LMNA gene result in at least seven further distinct disorders with partly overlapping phenotypes to HGPS.⁷ There exist other progeroid syndromes such as Cockayne (progeroid dwarfism) and Rautenstrauch-Wiedemann (neonatal progeria) which are not linked to mutations of LMNA but are also the result of defective repair of DNA damage and share signs and symptoms with HGPS.^{8,9}

Progerin is a key factor in DNA signaling leading to defects in DNA repair with premature cell senescence.¹⁰

Currently, there is no treatment available for HGPS and mean life expectancy is only 13 years.^{2,6} A new treatment with lonafarnib has shown to be associated with a lower mortality rate after 2.2 years of follow-up; however, its use is still experimental.¹¹ There are only a small number of case reports in literature discussing the anesthetic management of HGPS.^{1-4,6,12-14} Because of the severity of the syndrome, patients often require surgery during their short lives.³ Although these patients present as an elderly person with accompanying comorbidities, it is important to interact with them at the appropriate developmental mental level.¹³

The presence of multiorgan derangements, possible difficult airway, and associated skin, bone, and joint disease makes the anesthetic management challenging.^{3,15} Because of the extremely low prevalence, experience is limited even in the hands of experienced pediatric anesthesiologists.⁶

Key points

- Given the comorbidities of HGPS linked to premature aging, the clinician must approach these patients with increased vigilance.
- Tracheal intubation of a patient with HGPS is often difficult: The upper airway should thus be carefully evaluated, and airway management should be addressed in advance.
- In almost all the HGPS cases reported, spontaneous ventilation was maintained until easy controlled ventilation by facemask was proven.
- Although these patients present with the physiology of an elderly with accompanying comorbidities, emotionally they are only children and should be approached as such.

This review was prompted with the personal experience of the first author with a 14-year-old boy with HGPS scheduled for interventional cardiac catheterization. Following discussion with the anesthesiologist, cardiologist, parents, and the patient, it was decided to proceed with local anesthesia in the groin combined with monitored anesthetic care. The procedure was uneventful, was completed within 1 hour, and the patient did not require any sedation.

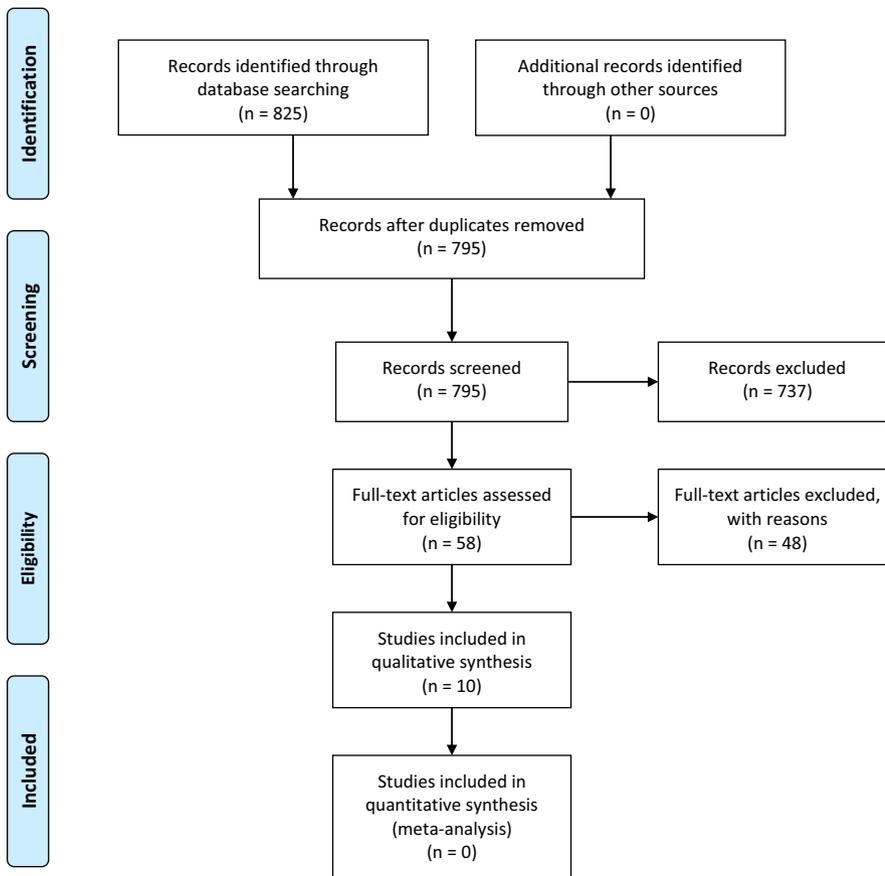


FIGURE 1 PRISMA flow diagram

2 | MATERIALS AND METHODS

2.1 | Search strategy and study selection

A review of the literature regarding anesthesia care in patients with HGPS was conducted using the PRISMA guidelines, used for systematic reviews. Two authors (NK and HD) performed a comprehensive literature search using the CENTRAL (Cochrane), EMBASE, MEDLINE, PubMed, and Google Scholar databases. Study identification and selection is summarized in a PRISMA flow diagram (Figure 1).¹⁶ The characteristics of the included articles can be found in Table 2.

2.2 | Assessment of study quality

We assessed the risk of bias in the included studies. No randomized controlled trial was available, nor meta-analysis. Only case reports and a correspondence on anesthesia for HGPS were available.

3 | RESULTS

3.1 | Preoperative assessment

A thorough preoperative assessment is mandatory in patients with HGPS. They are known to develop diseases associated with aging and frailty during the first or second decade of life.^{4,6} Preoperative evaluation by a cardiologist is preferable due to cardiovascular decline.^{2,15} Left ventricular diastolic dysfunction is the most prevalent abnormality,⁵ sometimes in combination with degenerative calcification of the mitral and/or aortic valves.^{2,15} Severe atherosclerosis with coronary artery and cerebrovascular disease is frequently seen.^{2,15} The preoperative cardiologic investigation should include an ECG, echocardiography, and an exercise-stress test.² However, due to joint disease, exercise-stress testing is not always possible. In literature, the use of stress echocardiography and dipyridamole-thallium SPECT is described as an alternative in the noninvasive

assessment of coronary artery disease in children.² Diabetes mellitus can also be present.²

Although patients have premature aging, they also suffer from severe growth failure which causes an average height of 100 cm and weight of <12-15 kg.³

3.2 | Airway management and induction

Airway management should be of significant concern. Most existing case reports mention a difficult airway management due to the typical airway features of children with HGPS (Table 1 and Figure 2).

Various techniques of securing the airway have been described in anesthesia including laryngeal mask airway in combination with fiberoptic intubation.^{17,18} However, there are only a small number of case reports discussing the airway management of HGPS (Table 2).

In almost all the HGPS cases reported, spontaneous ventilation was maintained until easy controlled ventilation by facemask was proven. This can be achieved either by using inhalational induction with a volatile anesthetic or IV propofol accompanied by carefully titrated (remi-) fentanyl. We admit that spontaneous

TABLE 1 Typical airway features of children with HGPS

Abnormal dentation due to crowding or delayed eruption ^{2,4,12,13}
Retrognathia ^{2,6} and/or micrognathia ^{2,3,6,12,13}
Mandibular hypoplasia ³
Small mouth opening ^{1-3,6}
Narrow glottic opening ⁴
High-arched palate ¹
Skin changes due to sclerodermatous and loss of subcutaneous tissue resulting in inelastic tissue ^{2-4,13}
Pointed beak-like nose due to its narrow shape and small nostrils ^{2-4,13}
Joint stiffness with decreased flexibility of neck and temporomandibular joints ¹⁻³
Decreased neck mobility ¹



FIGURE 2 A photo of a HGPS patient

TABLE 2 Included articles

Article	Type of article	Anesthesia type	Airway management	Type of surgery
Chapin et al ⁴ (1979)	Case report girl, 10 years old (1 patient underwent four times general anesthesia)	General anesthesia induced with halothane and N ₂ O or enflurane and N ₂ O or with thiopental. No muscle relaxants were used.	Mask ventilation during surgery without preoperative problems. Due to fear of laryngeal edema, no attempts of intubation were performed.	Indication: dislocated hip. Initially, a closed reduction was performed. Open reduction of the dislocated hip was accomplished, followed by two cast changes.
Nguyen et al ¹ (2001)	Case report girl, 5 years old (1 patient underwent two times general anesthesia)	General anesthesia induced with halothane and N ₂ O. No muscle relaxants were used.	It was difficult to maintain adequate mask ventilation. Direct laryngoscopy was difficult, and an uncuffed oral tracheal tube was blindly placed using the patient's breath sounds as a guide.	Indication: diagnostic CT scan, auditory evoked potentials, and examination of the tympanic membranes for hearing loss and a second time a tympanoplasty.
Liessmann CD ² (2004)	Case report boy, 12 years old	General anesthesia induced with sevoflurane at 100% O ₂ . Anesthesia was maintained with isoflurane, N ₂ O, O ₂ , and intermittent fentanyl.	Mask ventilation was successful. The best view by laryngoscopy was obtained with a Bellhouse laryngoscope blade and external manipulation of the larynx, getting a Cormack-Lehane grade III. Flexible fiberoptic intubation was conducted with the use of a guidewire and a bougie.	Indication: multiple dental extractions.
Arai et al ¹² (2002)	Correspondence not specified	General anesthesia Not further specified.	Face mask assisted ventilation. Not further specified.	Indication: pericardiocentesis.
Russo-Menna et al ¹³ (2010)	Case report girl, 4 years old	General anesthesia induced with sevoflurane and 100% O ₂ .	Mask ventilation was successful. Under inhaled anesthesia, the patient was nasally intubated with a 3.5-mm uncuffed endotracheal tube. Sufficient prepping of the small nostril by 2% lidocaine gel and nasal airway dilation was performed.	Indication: dental extraction and dental restoration.
Esparandar et al ¹⁴ (2012)	Case report girl, 12 years old	Intravenous sedation. Not further specified.	Not further specified.	Indication: closed reduction for left shoulder and left hip.
Hansda et al ³ (2013)	Case report boy, 7 years old	General anesthesia induced by inhalational anesthesia. Anesthetics not further specified.	Mask ventilation quality not explicitly specified. Direct laryngoscopy in a spontaneously breathing patient revealed a Cormack-Lehane grade III. After some attempts, it was possible to secure the airway with the help of an intubating stylet over an endotracheal tube.	Indication: extradural hematoma surgery.
Kumar et al ¹⁹ (2013)	Case report girl, 14 years old (1 patient underwent four times general anesthesia)	The first time general anesthesia induced by inhalation of sevoflurane and 100% O ₂ . The next time intravenous induction of general anesthesia with adequate preoxygenation was conducted.	Mask ventilation was easily established, but placement of an appropriately sized laryngeal mask proved difficult, and eventually, a size 1.5 mask was inserted. In one of the occasions, an laryngeal mask could not be placed successfully and anesthesia was maintained by mask ventilation.	Indication: closed reduction in the hip (four times).

(Continues)

TABLE 2 (Continued)

Article	Type of article	Anesthesia type	Airway management	Type of surgery
Borse et al ²⁰ (2015)	Case report girl, 11 y old	General anesthesia was induced intravenously using thiopentone sodium 100mg and suxamethonium 35mg. Anesthesia was maintained using halothane and N ₂ O.	Mask ventilation quality is not explicitly specified. The patient was intubated with a cuffed endotracheal tube with the aid of external laryngeal manipulation.	Indication: cataract surgery.
Herd et al ¹⁵ (2015)	Database research: boy, 6 y old boy, 14 y old boy, 21 y old	General anesthesia induces with volatile anesthetics and IV medication with nondepolarizing muscle relaxant. Not further specified. General anesthesia with volatile and IV anesthetics. Not further specified. General anesthesia induces with volatile anesthetics and IV medication with nondepolarizing muscle relaxant. Not further specified.	Easy direct laryngoscopy and intubation. Not further specified. Preexisting tracheostomy. Intubated in emergency department—no record of difficulty.	Indication: otorhinolaryngology Indication: esophagogastroduodenoscopy Indication: Urologic operation
Vreeswijk et al ⁶ (2016)	Case report boy, 11 y old	General anesthesia induced by sevoflurane. Anesthesia was maintained with propofol 6 mg/kg/h and remifentanyl 0.17 mg/kg/min.	Mask ventilation was successful. Direct laryngoscopy with a Macintosh blade 2 revealed a Cormack-Lehane grade IV. Nasopharyngeal intubation was conducted by flexible fiberoptic intubation.	Indication: dental extraction and dental restoration.

ventilation, especially with opioids, is not always easily achievable in reality. However, the authors agree that spontaneous ventilation should be aimed for until we know that ventilation is possible.

Failed direct laryngoscopy seems fairly common in children with HGPS although most appear easy to ventilate by mask despite decreased subcutaneous fat presence in the facial area.^{2,4} As a consequence, multidisciplinary collaboration and the use of more advanced airway techniques are recommended. As mouth opening is often limited, the use of a supraglottic airway or videolaryngoscope can be difficult if not impossible.^{3,21}

Advanced airway planning and assembling equipment for difficult intubation should be done prior to induction. Initial selection of endotracheal tube size should best be based on the patient's height.^{6,22} The use of ultrasound for measurements of the subglottic area may also be of great help in choosing the correct endotracheal tube diameter.⁵ It should be noted that nasal intubation can be challenging due to the anatomy of the nose.

Attention should be paid if an oropharyngeal airway is used as a bite block because, due to local tissue frailty, it can result in labial and buccal tears.² We propose the use of softer, more patient-friendly, bite block to prevent this from happening. Awake extubation is generally preferred.^{1,6}

3.3 | Preoperative management

Atherosclerotic disease and myocardial fibrosis with associated heart failure are very common in children with HGPS.¹ Therefore, full ASA monitoring is mandatory during anesthesia with intraoperative 5-lead ECG monitoring for ST-segment changes assessing leads II and V5.² Invasive monitoring is appropriate in particular cases, however not standard.² Hypovolemia, hypoperfusion, and hypothermia should be avoided.¹

Cerebrovascular disease and carotid and cerebral aneurysm have been reported which need to be taken into account during anesthesia.¹ Because of alopecia and a decreased layer of subcutaneous fat, measures to prevent hypothermia should be taken prior to induction of anesthesia.¹ Blood glucose levels should be controlled perioperatively, and careful manipulation and positioning is needed to avoid injury to the fragile patient.⁴ In case of preexisting hypertriglyceridemia, total intravenous anesthesia with propofol should be used cautiously during long-duration surgery because it could increase further blood triglyceride levels with a risk of hypertriglyceridemia-associated acute pancreatitis.²³ In summary, one needs to be mindful of the physiological changes and multi-derangements of aging in patients with HGPS.³

3.4 | Postoperative management

Postoperative pain management should be based on a multimodal approach adapted to the patient's developmental level and

physiologic status, including regional anesthesia. Postoperative monitoring should be adapted to the invasiveness and duration of the procedure.^{2,13,24}

3.5 | Locoregional anesthesia

To date, no awake locoregional anesthesia case in patients with HGPS has been reported. However, due to risks related to general anesthesia in this population locoregional anesthesia techniques, combined if necessary with mild sedation, could be a good alternative. Dosing of local anesthetics should be based on the patient's body weight.

4 | CONCLUSION

HGPS is a rare childhood syndrome and anesthetic experience with it is limited. Given their comorbidities linked to premature aging, the clinician must approach these patients with increased vigilance. Tracheal intubation is often difficult: The upper airway should thus be carefully evaluated and airway management should be planned. Last but not least, although these patients present as an elderly person, they are children and should be approached as such.

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

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