ORIGINAL CLINICAL RESEARCH REPORT

Anesthetic Management and Outcomes of Patients With Epidermolysis Bullosa: Experience at a Tertiary Referral Center

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BACKGROUND: Epidermolysis bullosa (EB) is a group of rare epithelial disorders caused by abnormal or absent structural proteins at the epidermal-dermal junction. As a result, patients experience blisters and wounds from mild shearing forces. Some forms of EB are complicated by resultant scarring and contractures. The perioperative anesthetic management of patients with EB is complex and requires a systems-based approach to limit harm. We reviewed our experience with providing general anesthesia to patients at our tertiary EB referral center, including adverse events related to anesthetic care, outcomes in the immediate perioperative period, and details of anesthetic management.
METHODS: We retrospectively reviewed the charts of all patients with EB anesthetized at the Children's Hospital Colorado between January 2011 and December 2016. A subset of pediatric anesthesiologists cared for all patients using a standardized clinical care pathway. Patient demographics, detailed anesthetic methods, immediate perioperative outcomes, and adverse events were characterized.
RESULTS: Over a 6-year period, 37 patients underwent 202 general anesthetics. Most patients (75.7%) had dystrophic EB (DEB). Female patients comprised 48.6%. The majority (56.7%) traveled >50 miles to receive care, and many (35.1%) traveled >150 miles for their care. Common adaptations to care included avoidance of electrocardiogram leads (88.6%) and temperature probes (91.6%). Nasal fiberoptic intubation (n = 160) was performed, or natural airway/mask (n = 27) was maintained for most patients. Supraglottic devices were not used for airway management during any of the anesthetics. Anesthesia preparation time was longer (average 25.8 minutes [standard deviation {SD} = 12.7]) than our average institutional time (14 minutes). Succinylcholine was never used, and nondepolarizing muscle relaxants were used in only 1.5% of patient encounters. Blood was transfused in 16.3% of cases and iron infused in 24.8%. Average length of stay in the postanesthesia care unit was comparable to our institutional average (average 40.1 [SD = 28.6] vs 39 minutes). New skin or mucosal injury occurred in 8 encounters (4%), and desaturation occurred in 43 cases (21.3%). There were no major adverse events.
CONCLUSIONS: By using a specialized team and a standardized clinical care pathway, our institution was able to minimize adverse events caused by the anesthetic and surgical care of patients with EB. We recommend natural airway or nasal fiberoptic airway management, meticulous avoidance of shear stress on the skin, and a multidisciplinary approach to care. Supportive therapy such as perioperative blood transfusions and iron infusions are feasible for the treatment of chronic anemia in this population. (Anesth Analg 2022;134:810–21)

KEY POINTS

- **Question:** What perioperative outcomes can be expected from a standardized approach to general anesthesia in a patient with epidermolysis bullosa?
- **Findings:** When cared for by a specialized anesthesia team using a standardized approach that is minimally intrusive to the skin and oral mucosa, patients with epidermolysis bullosa have a very low risk of major and minor adverse events and a low incidence of mucosal injury.
- **Meaning:** We offer our specific technique of performing anesthesia in patients with epidermolysis bullosa to avoid adverse events and minimize skin and mucosal injury.

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GLOSSARY

BP = blood pressure; **CI** = confidence interval; **DEB** = dystrophic EB; **DL** = direct laryngoscopy; **EB** = epidermolysis bullosa; **EBS** = EB simplex; **ECG** = electrocardiogram; **EKG** = electrocardiogram; **Epic** = Epic Systems Corporation; **ETT** = endotracheal tube; **FLACC** = Faces, Legs, Arms, Consolability and Cry; **FOI** = fiberoptic intubation; **GI** = gastrointestinal; **ICU** = intensive care unit; **IV** = intravenous; **JEB** = junctional EB; **KS** = Kindler syndrome; **nETT** = nasal endotracheal tube; **NIBP** = noninvasive blood pressure; **OR** = operating room; **PACU** = postanesthesia care unit; **PICC** = peripherally inserted central catheter; **PICU** = pediatric intensive care unit; **RAE** = Ring, Adair, and Elwyn; **RDEB** = recessively inherited DEB; **SD** = standard deviation; **SpO_2** = oxygen saturation

Epidermolysis bullosa (EB) is a family of hereditary skin disorders in which mild shear forces on the skin and mucous membranes result in blisters and open wounds. In some cases, these wounds heal with scarring and contractures. These disorders result from abnormal or absent structural proteins that cause weak or absent connections between the epithelium and underlying layers of the skin and mucosa.[1] EB and related skin diseases are classified into 4 main types based on the ultrastructural location of blistering: EB simplex (EBS), junctional EB (JEB), dystrophic EB (DEB), and Kindler syndrome (KS).[2] EB occurs in approximately 20 per 1 million live births.[3,4]

EB severity is wide ranging. Some patients can lead a relatively normal life, whereas others die in early infancy. Multiple organ systems are affected in a predictable fashion.[5–10] In the most severe yet survivable subtypes, functionality declines progressively owing to contractures of the skin and mucosal surfaces, chronic anemia, and infections. Chronic anemia in this population is multifactorial and includes anemia of chronic disease, blood, iron, and protein loss from open wounds on the skin, erosions in the intestinal tract, poor iron intake, and poor nutrient absorption. The blisters and wounds heal slowly, and extensive skin loss, scarring, and sepsis are common. Contractures can develop on the flexor surfaces of the neck, limbs, and digits. The fingers and toes fuse together, causing a mitten-type deformity called pseudosyndactyly that restricts dexterity and has a major impact on function (Figure 1B, C). Further, accompanying anemia of chronic disease often necessitates regular venipuncture, transfusions, and iron infusions. Finally, malignancy, most commonly aggressive squamous cell carcinoma, is the leading cause of death in adolescents and adults with recessively inherited DEB (RDEB). Other causes of death in patients with severe forms of EB include malnutrition, sepsis, and respiratory failure. The mucosa in the mouth is histologically similar to that of the skin, except that superficial keratin is absent.[1] Simple mastication erodes the mucosa, resulting in progressive and severe microstomia and ankyloglossia with scarring (Figure 1A). Patients with RDEB experience recurrent and progressive esophageal stricture formation leading to dysphagia, malnutrition, and need for gastrostomy tube. Esophageal strictures in patients with RDEB often require serial balloon dilation with fluoroscopic guidance.[9,11,12] These airway and esophageal changes result in progressively difficult airway management, deterioration of nutritional status, and poor dental hygiene.[10,13] General anesthesia is frequently required to manage these gastrointestinal disease manifestations, as well as procedures for scar and contracture release, pseudosyndactyly release, and dental rehabilitation.[14–21]

In the 1980s, Dr Geoff Lane, MB, BChir, of our institution began developing and teaching methods of caring for patients with EB (Supplemental Digital Content 1, Text 1, http://links.lww.com/AA/D688). Additionally, a few centers of excellence for EB care have been established in the United States.[22] However, largely, the disease process and its clinical manifestations and procedural/anesthetic management are poorly characterized in the literature. The aims of this study were to determine the rate of adverse events related to the anesthetic care of patients with EB, describe patient outcomes in the immediate perioperative period, and review our experience with providing general anesthesia to these patients.

METHODS

Study Design

After obtaining Colorado Multiple Institutional Review Board approval (Protocol 17-0841), and the requirement for written informed consent was waived, we reviewed all anesthetic records for patients age 6 months to 65 years with EB who had procedures requiring anesthesia between January 2011 and December 2016. We defined an anesthetic as care provided by a pediatric anesthesiologist. The database was derived from Epic Systems Corporation (Epic) utilizing the "Slicer-Dicer" function and was cross-referenced with an EB clinical database on patients and their history of anesthetic encounters. We reviewed demographic data, detailed anesthetic encounter information, recovery data, and outcomes. We defined major adverse events as death, cardiac arrest, need for cardiopulmonary resuscitation, permanent injury, and wrong-sided procedure. Study data were collected and managed with REDCap hosted at the University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO.

Figure 1. Clinical images of patients with EB and their care. A, Extremely limited mouth opening and ankyloglossia in a teenage patient with dystrophic EB. B, Peripheral IV placed in the dorsum of the hand of a patient with EB and severe pseudosyndactyly/mitten glove deformity. Note the Mepitac silicone-based tape securing the IV at the skin insertion site. C, Indirect securement of a peripheral IV in the dorsum of the hand. Note that the 1″ gauze roll obscures the IV insertion site but allows for a "touch-free" IV securement. D, Modified nasal trumpet for passive oxygen insufflation during nasal fiberoptic intubation in the nare of a 5-y-old patient with EB. Note also the dressed wounds, chest wrap, and special lubrication on the face in the distribution of the anesthesia mask. E, Preparation of the eyes and face for nETT securement in a patient with EB immediately postintubation. Note that the eyelids were passively closed with folded gauze before placement of the head wrap/turban. F, Final placement of head wrap/turban and cushion to indirectly secure the nETT in a patient with EB. Note that the nETT was elevated with an appropriately sized piece of foam to prevent it from applying pressure or shear force on the nares. EB indicates epidermolysis bullosa; IV, intravenous; nETT, nasal endotracheal tube.

Statistical Analysis

Cohort demographic and clinical characteristics were summarized as mean (standard deviation) and frequency (percent) for continuous and categorical summaries, respectively. Linear mixed effects regression models assuming a random intercept for each patient were used to account for the repeated encounters with each patient and to compare the change in the patient outcome of reported pain scores over the course of an encounter. All analyses and summaries were conducted with R version 3.6.3 software (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org/).

Standardized Anesthetic Clinical Care Pathway

Our patients were cared for by a specialized anesthetic team using a standardized approach that is minimally intrusive to the skin and oral mucosa (Figure 2). More detailed information, including additional images and detailed instructions, can be accessed as Supplemental Digital Content. One of the driving principles in management of patients with EB is the avoidance of friction and shear forces that cause bullae to develop with the resultant complications previously described. We avoid adhesives (tape, electrocardiogram [EKG] leads, and dispersive return electrodes/"grounding pad"),[23] as removal causes significant shearing of the skin. The only acceptable skin contacts are silicone-based, which are hydrophobic and removed easily by moistening with water.

Preoperative Assessment. Surgery, procedures, and repeated venipuncture are risky and stressful events for patients with EB. Careful consideration and tailoring of the anesthetic plan must reflect the competing interests of improved quality of life versus

Preoperative Assessment & Care

- Review goals of procedure, impact on quality of life
- Routine preoperative assessment (history, airway exam, physical exam, document skin condition)
- Targeted testing for new symptoms, anemia, renal/cardiac status (rarely needed)
- Family- or patient-identified site(s) for IV
- Strongly consider premedication (oral, by g-tube, intranasal, IV if GI stricture present)

Preparation

- 'Special lubricant' = 3 packets of surgilube aqueous lubricant + 1 tube of eye ointment; apply liberally to facemask, Anesthesiologist's fingers, tongue surface of blade, nares
- Mepitac silicone tape (Molnlycke Health Care AB)
- 1" rolled gauze
- Webril (Cardinal Health)

Induction & Intravenous access

- Adjunctive environmental strategies: parental presence, allow patient to remain sitting, distraction, mask avoidance via hand-cupping or direct circuit-in-mouth technique
- Inhalational induction and any masking via lubricated mask
- IV placement: single attempt by best operator, tourniquet over clothes or rolled gauze, avoid blind sticks, consider ultrasound or transillumination

Monitoring

- Pulse ox: nonadhesive clip-on probe or adhesive probe with transparent dressing applied to neutralize sticky surface
- BP cuff: place over clothing or soft bandage (kerlix or webril)
- EKG monitors: deferred or needle electrodes w/ Mepitac silicone tape or disposable gel electrodes with adhesive rim removed

Securing the Airway

- Mask anesthesia for simple, noninvasive cases
- Apply oxymetolazine to bilateral nasal passages
- Apply 4% topical lidocaine to vocal cords by gentle direct laryngoscopy (mac blade lubricated on tongue side) or via fiberoptic scope
- Use passive insufflation of O2 by mask, blow-by, or lubricated nasal airway during intubation
- Spontaneous breathing, asleep nasal fiberoptic intubation (asleep FOI)
- Protect eyes via indirect eye closure and Secure see picture

Emergence

- Awake, smooth emergence from anesthesia
- Gentle oropharyngeal and esophageal suctioning with soft suction under direct visualization only

Post-Anesthesia Care Unit / Post-Operative Care

- Continue with the modified monitoring devices
- Soft suction catheter available
- Immediately available presence of Attending Anesthesiologist
- Liberal use of post-operative pain medications (multimodal analgesia encouraged)

Figure 2. Standardized, detailed, stepwise clinical approach to anesthesia in a patient with EB. This is the clinical care pathway used for every patient with EB by the EB team at Children's Hospital Colorado. BP indicates blood pressure; EB, epidermolysis bullosa; EKG, electrocardiogram; FOI, fiberoptic intubation; GI, gastrointestinal; IV, intravenous.

pain, suffering, and morbidity. Beyond history and physical examination with detailed airway evaluation (Figure 1A), additional routine laboratory testing or medical workup infrequently yields information warranting change to the anesthetic plan. Targeted testing (usually after induction of anesthesia) can address new symptomatology, anemia, renal, or cardiac status with better protection of the patient's skin. In our institution, a 14-specialty multidisciplinary team, including a small, dedicated group of pediatric anesthesiologists, engages regularly for the care of these patients, contributing to successful acute and longitudinal care. The EB anesthesia team is a subset of anesthesiologists with a special interest in caring for this patient population. Membership on the team is voluntary, by self-nomination or nomination by an existing member, and requires willingness to follow our institutional clinical care pathway and internal standards for taking care of these patients. Membership also requires the willingness and energy to serve as a resource for these patients to the department and the hospital, as well as outside institutions who contact our team for advice or consultation. New team members are mentored by experienced team members directly in the operating room for several anesthetics until the new team member has demonstrated proficiency with institutional guidelines and team expectations.

Premedication. Premedication is useful to ensure calm induction of anesthesia, as patient restraint may cause skin damage. Successful preinduction techniques may include liberal use of midazolam, intranasal dexmedetomidine, parental presence at induction, distraction, environmental control in the operating room, and an anesthesiologist familiar to the patient-family unit.

Positioning and Patient Transfer. Positioning and transferring patients with EB requires meticulous attention. Most patients have their extremities wrapped in complex dressings and are therefore protected from contact with the mattress or other hospital bedding. They usually do not require additional padding or protective wraps. Any open wounds may be dressed with Mepilex (Molnlycke Health CareAB), to prevent adherence to the sheets or to the operating room table. When moving patients from a crib/stretcher to the operating room (OR) table (and vice versa), it is essential to avoid sliding a patient across any surface. The patient should be levitated, often with the aid of a draw sheet placed under the patient, moved over, and placed back down without any dragging.

Intravenous Access and Induction. Inhalation induction of anesthesia before intravenous (IV) placement is our preferred approach in most cases. Although often difficult to intubate, these patients are typically easy to mask ventilate with limited-to-no manipulation of the jaw or face. We encourage patients to position themselves comfortably before induction with the aid of family members when possible.

IV access is challenging in patients with EB (Figure 1B, C). Their veins may be relatively easy to visualize, as subcutaneous fat is often minimal due to high metabolic rate and chronic malnutrition. However, their limbs are usually wrapped in multilayered dressings that are difficult to replace. Parents become highly skilled at this task and can serve as an ally in identifying an ideal IV site while keeping most of the bandages intact. Meticulous record keeping from prior venipuncture sites is useful for future access attempts. Occasionally we require transillumination, ultrasonography, or peripherally inserted central catheter (PICC) lines. We have standardized our approach to placing and securing IVs in this patient population (Supplemental Digital Content 2, Figure 1, http://links.lww.com/AA/D689). We secure IV catheters using minimal strip(s) of a special silicon-based dressing, Mepitac (Molnlycke Health CareAB), which separates easily from the skin with water (Figure 1B). We then indirectly secure the IV and tubing by wrapping it with rolled gauze and taping only on the gauze (Figure 1C). It is common practice for the IV site of an EB patient to be obscured by the rolled gauze. Therefore, routine assessment of the IV site is often deferred because it risks losing the IV. Sutures are useful if longer term IV access is warranted.

Monitoring. The choice of monitors is weighed against potential injury caused by removal of adhesives that come in contact with the skin. Pulse oximetry is the most valuable cutaneous monitor. Options include either a nonadhesive clip-on probe or a sticky probe rendered adhesive-free with 3M Tegaderm Transparent Film Dressing or cotton (Supplemental Digital Content 3, Figure 2, http://links.lww.com/AA/D690). In patients who have severe mitten deformity and loss of digits, an alternative protuberance such as the ear lobe, lip, or nose is used.

Blood pressure cuffs are well tolerated when placed over clothing or soft bandages, as the force applied is circumferential and less likely to cause significant shear force (Supplemental Digital Content 4, Figure 3A, http://links.lww.com/AA/D691). Increasing the cycle interval time will further reduce risk to the tissues. Invasive arterial monitoring is seldom required but has been used for complex cases.

If needed for patient risk factors or when performing regional or neuraxial anesthesia/analgesia, the EKG can be monitored by using secured needle electrodes or disposable gel electrodes after the adhesive rim has been trimmed (Supplemental Digital Content 4, Figure 3B, http://links.lww.com/AA/D691). For most procedures and patients, pulse oximetry and noninvasive blood pressure measurements provide adequate information and EKG monitoring is deferred.

Airway Management and Airway Devices. Airway management is nuanced for patients with EB. Both safe airway management and mucosal trauma avoidance must be prioritized.[24–27] Mouth opening becomes increasingly small (as small as millimeters in the most severely affected patients), and recurrent oral instrumentation perpetuates scarring and deformation.[10]

Many procedures can be completed successfully with mask anesthesia alone. Airway obstruction is uncommon because progressive ankyloglossia prevents the tongue from falling back into the oropharynx. Even in difficult or traumatic intubation conditions, patients remain easy to mask ventilate. While optimizing the mask position for ventilation, practitioners should minimize hand contact on the bony jaw surfaces; if needed, a well-lubricated nasal airway is preferable to any oral airway device. Liberally applying a mixture of aqueous and oil-based lubricant helps to prevent most shear forces anywhere the patient must be touched (Supplemental Digital Content 4, Figure 3C, http://links.lww.com/AA/D691). The water-based component ensures that the lubricant is adequately thin. Adding the oil-based lubricant prevents the water-based lubricant from becoming too viscid on the skin as it desiccates.

Asleep nasal fiberoptic intubation is the recommended technique when natural airway or mask anesthesia is not appropriate. The nasal passages are lined with respiratory epithelium, which is less likely to blister than the stratified squamous epithelium of the oral mucosa.[1] External nares and vestibule can be narrowed, so sizing down the nasal endotracheal tube (ETT) with softer microcuffs will minimize trauma and allow for an airway seal. Addition of passive insufflation of oxygen by modified nasal trumpet during nasal fiberoptic intubation (Figure 1D) is our recommended adjunctive technique and is also supported by Pediatric Difficult Airway Registry data.[28] The shape of a preformed cuffed nasal Ring, Adair, and Elwyn (RAE) tube allows for nonadhesive, atraumatic securement of the nasal ETT as well as indirect eyelid closure by using a turban/head wrap/taping method (Figure 1E, F).

Although oral intubation may be possible in some patients, direct laryngoscopy (DL) becomes more challenging as the disease progresses owing to mucosal injury, severely reduced mouth opening, and difficulty obtaining alignment of the oral, oropharyngeal, and tracheal axes. If oral intubation is required for the procedure, we recommend using a fiberoptic bronchoscope. Additionally, securing an airway device with adhesive or cloth ties risks severe shear force injury to the skin from friction. If an oral airway device is needed, suturing or wiring the ETT to a tooth (if present) is an imperfect alternative.

Supraglottic devices (eg, LMA® mask) are never recommended because they require large areas of contact with vulnerable mucosal surfaces; the only acceptable use may be for a true airway emergency in patients with an adequate mouth opening.

Emergence and Extubation. Controlling pain and avoiding agitation and delirium are critical for safe emergence from anesthesia.[29,30] Most patients with EB become tolerant to common analgesics and sedatives; therefore, a stimulus-response–based dosing strategy is paramount. Multimodal analgesia and regional anesthesia are useful in the perioperative setting.

Extubation criteria for patients with EB are the same as those for any patient with a difficult airway. Deep or awake extubation can be performed safely depending on ease of mask ventilation and relative risk of secretion management, aspiration, laryngospasm, emergence agitation, and need for restraint. Periemergence oral and gastric suctioning should be performed gently and under direct visualization, usually with a soft suction catheter passed only to the level of the oropharynx to reduce the risk of esophageal tears or perforation with deeper passage. During upper endoscopy, it is safer to have the gastroenterologist empty the stomach and esophagus with an endoscope.

RESULTS

Our review of anesthetic records identified 202 procedures from 37 patients who met inclusion criteria. One encounter was omitted because data were insufficient. Table 1 summarizes the demographics and clinical details of the study group by patient, and Table 2 summarizes the distribution of EB types and procedures performed by case, as many of our patients have recurrent encounters predictably distributed by type of EB. The preponderance of patients were diagnosed with DEB (75.7%); many fewer presented with EBS (21.6%) or JEB (2.7%) (Table 1). Gender was evenly distributed with 18 female patients (48.6%, Table 1). Most patients were either White, Hispanic/Latino (45.9%) or White,

Table 1. Demographics and Summary of Cases by Patient

Covariate	Overall (N = 37)
Female	18 (48.6)
EB type	
Simplex	8 (21.6)
Dystrophic	28 (75.7)
Junctional	1 (2.7)
Kindler	0 (0.0)
Race/ethnicity	
Asian	3 (8.1)
Native American	1 (2.7)
White, Caucasian	14 (37.8)
White, Hispanic/Latino	17 (45.9)
Unknown	2 (5.4)
State	
Arkansas	1 (2.7)
Colorado	22 (59.5)
Kansas	3 (8.1)
Nebraska	1 (2.7)
New Mexico	2 (5.4)
Oklahoma	2 (5.4)
Utah	6 (16.2)
Number of anesthetics per patient	
1	8 (21.6)
2–5	15 (40.5)
6–10	10 (27.0)
11+	4 (10.8)
Distance to hospital (miles)	
0–50	13 (35.1)
50–150	8 (21.6)
150+	13 (35.1)
Not recorded	3 (8.1)

Values are presented are as n (%).
Abbreviation: EB, epidermolysis bullosa.

Table 2. Demographics and Summary of Cases by Case

Covariate	Overall (N = 202)
Age (mo)	133 (89.9)
Weight (kg)	27.4 (15.2)
Height (cm) (n = 185)	126 (30.5)
Female	102 (50.5%)
GI procedure noted	132 (65.3%)
Anesthesia preparation duration (min)	25.8 (12.7)
Procedure duration (min)	62.5 (47.8)
PACU duration (min) (n = 194)	40.1 (28.6)
Temperature in PACU (°C) (n = 161)	36.7 (0.54)
EB type	
Simplex	16 (7.9%)
Dystrophic	182 (90.1%)
Junctional	4 (2.0%)
Kindler	0 (0.0%)
Monitors used	
Pulse oximetry	200 (99.0%)
ECG	23 (11.4%)
NIBP	200 (99.0%)
Temperature	17 (8.4%)
Method of induction	
Inhaled	170 (84.2%)
IV	32 (15.8%)
Number of IV attempts	
0	1 (0.5%)
Already in place	14 (6.9%)
1	127 (62.9%)
2	29 (14.4%)
3	7 (3.5%)
4+	6 (3.0%)
Not recorded	18 (8.9%)
IV location	
Antecubital	44 (21.8%)
Foot/neck/other	56 (27.7%)
Hand	94 (46.5%)
Not recorded	8 (4.0%)
IV side	
Left	134 (66.3%)
Right	57 (28.2%)
Not recorded	11 (5.4%)
IV size	
18 G	1 (0.5%)
20 G	6 (3.0%)
22 G	164 (81.2%)
24 G	14 (6.9%)
Central line	7 (3.5%)
PICC line	3 (1.5%)
Not recorded	7 (3.5%)
Postoperative recovery place	
Other	1 (0.5%)
PACU	198 (98.0%)
PICU	3 (1.5%)
Disposition	
Floor	66 (32.7%)
Home	133 (65.8%)
ICU	3 (1.5%)
Perioperative blood transfusion	33 (16.3%)
Perioperative iron infusion	50 (24.8%)
Adverse events	56 (27.7%)
Skin injury	1 (0.5%)
Mucosal injury	7 (3.5%)
Desaturation	43 (21.3%)
Emesis	8 (4.0%)
Procedure aborted	1 (0.5%)
Unanticipated admission to floor	5 (2.5%)
Unanticipated admission to ICU	2 (1.0%)

Values are presented are mean (SD) or n (%) where indicated.

Abbreviations: EB, epidermolysis bullosa; ECG, electrocardiogram; GI, gastrointestinal; ICU, intensive care unit; IV, intravenous; NIBP, noninvasive blood pressure; PACU, postanesthesia care unit; PICC, peripherally inserted central catheter; PICU, pediatric intensive care unit.

Caucasian (37.8%; Table 1). Patients originated from many states but were predominantly from Colorado (59.5%, Table 1). A large proportion presented from Children's Hospital Colorado's 7-state catchment area, including Arkansas, Kansas, Nebraska, New Mexico, Oklahoma, and Utah. In fact, only 13 patients (35.1%) presented from the Denver metropolitan area. Twenty-one patients (56.7%) traveled more than 50 miles to receive care, and 35.1% traveled more than 150 miles (Table 1).

The mean age at time of procedure was 133 months (SD, 89.9 months; median, 120.5 months; range, 4–501 months, Table 2), and mean body mass index was 16.4 kg/m^2 (SD, 2.5; median, 16.3; range, 10.3–25.4). Patients with DEB had a mean age of 136 months (SD, 91) and mean weight of 26.8 kg (SD, 13.4), whereas patients with EBS had a mean age of 75.8 months (SD, 57.2) and mean weight of 24.9 kg (SD, 21.3). The median number of procedures per patient was 5, with a minimum of 1 and a maximum of 17. Eight patients (21.6%) had only 1 recorded procedure, 15 patients (40.5%) underwent 2 to 5 anesthetics, 10 patients (27%) underwent 6 to 10 anesthetics, and 4 patients (10.8%) had 11 or more anesthetics (Table 1). The median time between anesthetics was 150 days (range, 0–2330 days), with a trend toward decreased time elapsed between multiple procedures (Figure 3).

Details of each anesthetic encounter are summarized in Table 2 and Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/D692. Notably, the majority of procedures were performed in patients with DEB (90.1%), and most of those were upper endoscopy for esophageal dilation (65.3%). Twenty-five of 202 cases (12.4%) were scheduled and booked as "combo cases," meaning any procedure combined with another procedure under a single general anesthetic.

For this study, we defined anesthesia preparation time as time of entry into the operating room until completion of all tasks for induction, IV securement, and airway management. Average length of anesthesia preparation time in this patient population was 25.8 minutes (SD, 12.7; Table 2). In comparison, examination of normative data from January to July 2014 revealed the average length of anesthesia preparation time to be 14 minutes (SD, 2). Standard monitors used included near-universal application of an adapted nonadhesive pulse oximeter (99.0%) and noninvasive blood pressure cuff (99.0%; Table 2). Less frequently, EKGs (11.4%) and temperature probes (8.4%) were used. General anesthesia was induced by inhalational method in 84.2% of cases and by IV method in 15.8%. Most IVs were placed on the first attempt (62.9%) or second attempt (14.4%). Three or more attempts were required in 6.5% of IV placements. Location of

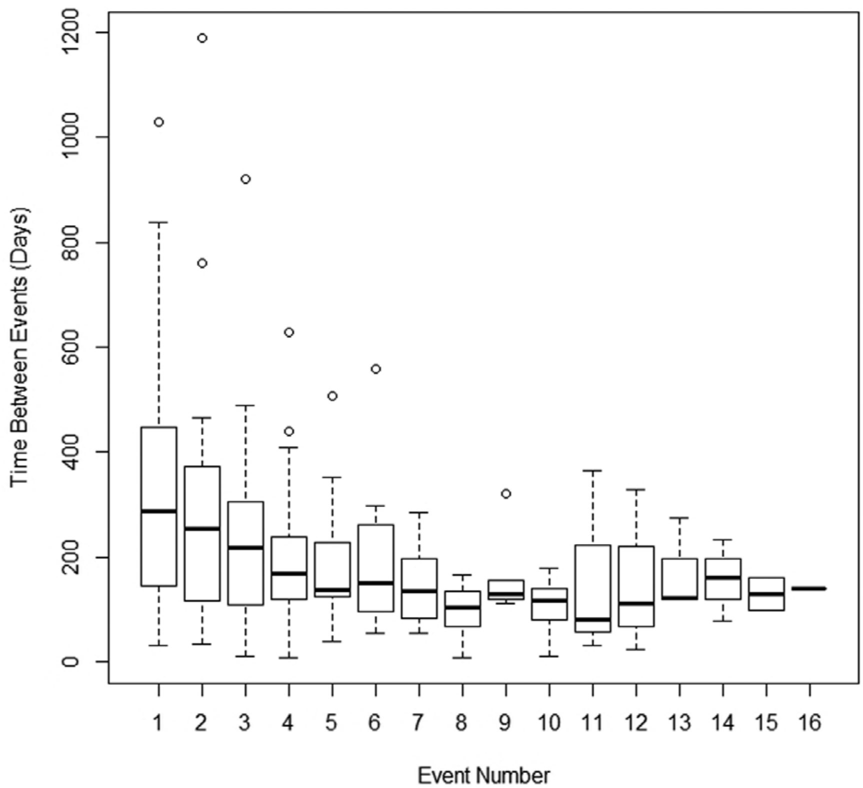

Figure 3. Boxplot of time between anesthetic encounters. The boxplot illustrates the median (central bar in the box), the first and third quantiles (ie, the 25th and 75th percentiles as the box), and potential outliers based on our data (points beyond the whiskers). The data illustrate that the median time between anesthetic events decreases from event 1 to event 8, then oscillates around 100 d. However, the sample size is much smaller at these values. We defined events that occurred within 7 d of one another as a repeat treatment of the same event, so only included events that occurred 8 or more days apart from one another.

IV placement was most frequently the hand (46.5%), followed by foot/neck/other (27%), and antecubital (21.8%). Most IVs were placed on the patient's left side (66.3%). The most common size for IV placement was a 22 gauge (81.2%) or 24 gauge (6.9%). Overall, patients with DEB were more likely to have more than 1 attempt at IV placement (2 attempts 15.4%, 3 attempts 3.8%, >3 attempts 3.3%) when compared to patients with other EB subtypes (Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/D692).

Airway management in patients with EB by case is detailed in Table 3. Notably, none of the 202 anesthetic cases were performed with a supraglottic device (eg, LMA® mask). Most (85.6%) were performed with an ETT, whereas 9.9% were performed with a mask alone, and 3.5% were performed with a natural airway (Table 3). Of the 173 intubations, 165 were performed by asleep nasal fiberoptic technique (95.4%) and only 7 (4%) were performed by DL (Table 3). DL was used for 44% of EBS patients (who have less severe disease) but only 1.8% of patients with DEB (Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/D692).

Most of the ETTs used (91.3%) were cuffed, primarily nasal RAE tubes (66.5%). The 2 largest sizes used were 6.0 (14.5%) and 6.5 (0.6%; Table 3). Very few patients required more than 2 intubation attempts (2.9%), with 77.5% requiring only 1 attempt and 11.6% requiring 2 attempts (Table 3). Of those encounters in which patients were intubated for their procedures, 85% were extubated awake at the conclusion of the procedure/anesthetic (Table 3). For comparison, examination of normative data from January to July 2014 revealed that only 37% of extubations occurred awake at our institution.

Intraoperative medications included sedative/hypnotic agents in 89.1%, opioids in 90.1%, antiemetics in 83.2%, oxymetazoline to the nares in 42.6%, IV lidocaine in 31.7%, topical lidocaine to the airway in 36.1%, and nondepolarizing muscle relaxants in 1.5%. Of note, no patients received succinylcholine and only 1 patient received ephedrine (0.5%). Adjunctive perioperative care was routine for patients with EB. Our study revealed a high rate of perioperative blood transfusion (16.3%) as well as perioperative iron infusion (24.8%; Table 2).

Analysis of postprocedure disposition revealed that 98% of patients recovered in the postanesthesia care unit (PACU) and 1.5% recovered in the intensive care unit (ICU; Table 2). No adverse events were reported in the PACU. Average PACU length of stay, defined as time of arrival until standard criteria were met for phase 1 PACU discharge, was 40.1 minutes (SD, 28.6). For comparison, the average PACU length of stay at our institution is 39 minutes. Patient temperatures in the PACU were obtained for 161 cases and averaged 36.7 °C (SD, 0.54; Table 2). Approximately two-thirds of patients were discharged home from the PACU, and the remaining one-third were admitted (Table 2).

Table 3. Airway Management Summary and Details by Case

Covariate	Overall (N = 173)
Airway type	
Natural	7 (3.5)
Mask	20 (9.9)
Modified nasal trumpet	1 (0.5)
LMA® mask	0 (0.0)
ETT	173 (85.6)
Not recorded	1 (0.5)
Intubation technique	
Direct laryngoscopy	7 (4.0)
Fiberoptic intubation	165 (95.4)
Not recorded	1 (0.6)
Number of intubation attempts	
1	134 (77.5)
2	20 (11.6)
3+	5 (2.9)
Not noted	14 (8.1)
ETT side	
Left naris	71 (41.0)
Oral	7 (4.0)
Right naris	85 (49.1)
Not recorded	10 (5.8)
ETT type	
Uncuffed	7 (4.0)
Cuffed	158 (91.3)
Oral RAE	5 (2.9)
Nasal RAE	115 (66.5)
Straight ETT	16 (9.2)
ETT size	
3	2 (1.2)
3.5	2 (1.2)
4	30 (17.3)
4.5	24 (13.9)
5	47 (27.2)
5.5	37 (21.4)
6	25 (14.5)
6.5	1 (0.6)
Not noted	5 (2.9)
Extubation	
Awake	147 (85.0)
Deep	25 (14.5)
Remained intubated	1 (0.6)
Age (mo), mean [SD]	138 [92.0]
Weight (kg), mean [SD]	27.1 [13.8]

Values are presented as N (%) except where indicated.
Abbreviations: ETT, endotracheal tube; RAE, Ring, Adair, and Elwyn; SD, standard deviation.

We recorded pain with either a verbal scale or the Faces, Legs, Arms, Consolability and Cry (FLACC) scale pre- and postoperatively. Both pain scores increased significantly from preprocedural value to first recorded value in the PACU (verbal: 1.65 increase [95% confidence interval {CI}, 0.82–2.47], P = .0001; FLACC: 0.65 increase [95% CI, 0.09–1.20], P = .0230). Pain scores decreased significantly between the first and last recorded PACU score for patients who were reporting on the verbal scale (1.30 decrease [95% CI], 0.47–2.12; P = .0025) but not for those evaluated by the FLACC scale (0.25 decrease [95% CI, 0.62 decrease to 0.12 increase]; P = .1850).

Adverse events were a primary outcome of this study and are summarized in Table 2 and Supplemental Digital Content 5, Table 1, http://links.lww.com/AA/D692. The overall adverse event rate was 27.7%, and no major adverse events were reported. The most common adverse event was desaturation, which we defined as an oxygen saturation less than 90% at any point during the anesthetic. Desaturation occurred in 21.3% of cases but did not progress to a major adverse event in any patient. Emesis occurred in 4% of cases. Of critical importance to this patient population is mucosal (3.5%) and skin injury (0.5%). The only other adverse events were unanticipated admission to the medical ward (2.5%) or to the ICU (1%). Causes for unanticipated admission included "routine" anesthesia-related complications (pain, nausea/vomiting, and somnolence in the evening hours) as well as a couple of EB-specific complications (unanticipated renal dysfunction on labs, total tongue sloughing from placement of a throat pack, and unexpectedly difficult procedure).

DISCUSSION

Over a 6-year period at our hospital, patients with EB who underwent anesthesia and surgery had a low incidence of both minor and major adverse events, and a very low incidence of skin and mucosal trauma, when cared for with a standardized clinical care pathway. A multidisciplinary approach, natural airway or nasal fiberoptic airway management, and meticulous attention to each step of the anesthesia and procedure were critical to the safe and effective anesthesia for these fragile patients.

In our sample, patients with DEB underwent more procedures than those with other types of EB, required more IV attempts, and experienced more adverse events, including desaturation and skin/mucosal trauma. Another trend noted was that patients with DEB were older, yet weight and height were similar to those of patients with EBS. We attribute these patterns to the fact that patients with DEB have more severe disease, with greater skin fragility, systemic morbidity, and anemia. Additionally, their cutaneous chest involvement contributes to limitation of chest excursion and resultant desaturation after anesthesia induction.

Adverse events were very infrequent and minor when they did occur. Desaturation, which we defined very tightly (oxygen saturation [SpO_2] <90%), was the most common adverse event. Of the 43 desaturation events, 41 occurred in the DEB patient population. Notably, all desaturation events were brief, reversible, and did not result in escalation to any major adverse events. In our clinical experience, we tolerate mild desaturation to allow the time needed to induce anesthesia without restraint or injury, insert an IV atraumatically, manage the airway atraumatically, and emerge a patient calmly. All of these tasks are accomplished with minimal-to-no skin contact, thereby reducing injury risk overall. It should also be recognized that our institution is at 5280 feet of elevation, and altitude may contribute to our observation of increased mild, reversible, desaturation events.

A few details of this analysis warrant emphasis. First, it is critically important that supraglottic devices be avoided to prevent unnecessary oral mucosal trauma and severe airway obfuscation with secretions and blood. Placing a supraglottic device in a patient with EB is not advised, except in a true life-threatening airway emergency (eg, complete inability to mask ventilate per the emergency airway algorithm[31]). However, insertion of a supraglottic device even during life-threatening airway failure may not be possible in patients with EB given their progressively small mouth opening.

With respect to airway management, we performed nasal fiberoptic intubation in 95.4% of our patients. The few exceptions included DL, which was used in 44% of patients with EBS (who have less severe disease), compared to only 1.8% of patients with DEB. It is reasonable to consider DL in patients with EB who are <1 year old, as they have preserved mouth opening, allowing atraumatic access to oral intubation. Additionally, infant naris and airway size, as well as inherent challenges with appropriately sized equipment makes fiberoptic intubation more difficult. We did not use any ETT size larger than 6.0 (14.5%), other than in an adult with DEB undergoing a forequarter amputation who remained intubated postprocedure (6.5 ETT).[23] We chose the smallest possible cuffed ETT even for our adult-sized teenage patients to avoid trauma to the airway or nasal passages while maintaining adequate ETT length and the ability to seal the airway with an inflated cuff.

Available data from the Difficult Airway Registry indicate that the initial success rate is 4% and eventual success rate 21% when a child with a difficult airway is managed by direct laryngocscopy.[28] Although our patient population is known for difficult intubation, we intubated 90% of our patients on the first or second attempt. We attribute our high first- and second-pass success rates to choosing the least traumatic and most effective method of airway management on the first attempt, the routine use of passive oxygen insufflation, familiarity with the patients, a small and experienced team dedicated to this patient population, and access to previous detailed medical records.

We routinely place peripheral 22-gauge IVs (Table 2) because this bore is adequate for the procedure, allows for blood draws, and its small size minimizes skin trauma. Very few patients with EB undergo major procedures, but when they do, we use larger bore IV or central access.[23] We routinely ask patients and families the location of their "best" or preferred vein because many patients are covered with complex dressings, and we recommend leaving as much as possible of their body dressings intact to optimize skin protection. If needed, a second site may also be exposed. Visualizing a possible IV site before induction also allows for wound assessment; we try to avoid placing an IV across interrupted or wounded skin. Thorough documentation of a patient's IV site (particularly location) allows our team to approach the same IV site for subsequent encounters and minimizes disruption of wound dressings—a critical component for long-term care.

For several reasons, we rarely use muscle relaxant as part of the anesthetic care for patients with EB. First, we avoid paralysis because we cannot monitor neuromuscular blockade without impacting skin integrity. Second, induction of anesthesia and the induction sequence in patients with EB is frequently prolonged by the need for meticulous IV placement/securement and lab draws. Patients are rendered very deep under anesthesia before any airway manipulation so muscle relaxant is not necessary. Finally, we prefer to maintain spontaneous ventilation in a patient with a known difficult airway and in whom vigorous mask ventilation is damaging to the skin.

We routinely extubate patients with EB awake in the procedure room, in part to maximize direct care of the patient by an attending anesthesiologist throughout their emergence. Additionally, it allows comprehensive difficult airway management until the patient is fully awake and able to protect their own airway. It also allows us to manage secretions and blood that are associated with the specific procedure and patient's disease process. Pain control is optimized and sedation is used to prevent coughing, bucking, thrashing, or use of restraint during an awake emergence. Most commonly we utilize fentanyl and lidocaine IV.

In general, it is very safe for procedures to be performed during an outpatient/same day surgery visit. Almost all of our patients (98%) went to the PACU, and 68% went home. Patients did have pain associated with their procedures, but this pain was manageable and rarely resulted in unplanned hospital admission. It may be preferable to perform most cases as outpatient to avoid risking exposure to resistant organisms and other infectious diseases in the hospital setting. Despite our recommendation for outpatient disposition whenever possible, serious complications can occur in patients with EB. Access to inpatient and ICU care should be readily available.

In the PACU, patients with EB remained normothermic, likely because their whole-body dressings mitigated the redistributive heat loss that occurs with induction of general anesthesia. We recommend avoiding any method of temperature measurement that could cause friction on the skin. Based on our data analysis, we no longer measure temperature in these patients on arrival to PACU unless we have suspicion of temperature abnormality (unexplained tachycardia, reported chills, observed rigors).

Many of our patients come from a large catchment area and have a long distance to travel for their care. We work directly with our EB team (pediatrician/special care clinic, dermatology, genetics, gastroenterology, dentistry, surgery, orthopedics, nutrition, social work, physical and occupational therapy, wound care, and psychology) to maximize effective care while the patient is under anesthesia. Patients are seen by the members of this multidisciplinary team in a multidisciplinary clinic held twice a month, and the team meets monthly for clinical care conference. All specialties remain available for consultation by the hospital communication system, as well as secure group messaging through Epic. As part of the multidisciplinary approach, our team makes increased efforts to book "combo cases" and minimize the overall number of anesthetics. We also coordinate care to perform lab draws, administer IV iron, and transfuse blood during an anesthetic. Additionally, for unplanned hospital visits, the anesthesiology team is available 24 hours a day, 365 days a year. Every EB patient has a "Best Practice Alert" in the front of the electronic medical record with a description of EB precautions and the direct telephone contact information for communication with the anesthesiology team. We have created a 1-page IV start guide to assist in the preparation, placement, and securement of IVs for these patients. Consolidating care into 1 visit, minimizing procedures/anesthetics, minimizing venipuncture attempts, and providing 24/7 anesthesiology consultation is advantageous for the long-term care of patients with EB.

Limitations of this study include the retrospective nature of the dataset, with some of the data elements missing due to lack of complete documentation during the patient's encounter. Another limitation is that we lacked identification of the person performing airway management and IV placement. In our institution, residents, pediatric anesthesia fellows, and anesthetists routinely perform procedures in these patients under the supervision of an EB anesthesiologist. We recommend using a preprogrammed "macro" in the electronic record that includes many of the critical steps for care of the EB patient; it serves both as a checklist of necessary items and aids in documentation of the anesthetic details more consistently (Supplemental Digital Content 6, Figure 4, http://links.lww.com/AA/D693).

Overall, the complex anesthesia/procedural care of patients with EB can be accomplished safely and effectively with a very low rate of injury to the skin/mucosa and few adverse events. These outcomes are made possible by special consideration paid to each step in the perioperative process and careful attention to every detail of the anesthetic plan. In addition, we provide a high degree of interdisciplinary care coordination with a small and dedicated team.

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DISCLOSURES

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REFERENCES

1. Solovan C, Ciolan M, Olariu L. The biomolecular and ultrastructural basis of epidermolysis bullosa. *Acta Dermatovenerol Alp Pannonica Adriat*. 2005;14:127–135.
2. Has C, Bauer JW, Bodemer C, et al. Consensus reclassification of inherited epidermolysis bullosa and other disorders with skin fragility. *Br J Dermatol*. 2020;183:614–627.
3. Fine JD. Epidemiology of inherited epidermolysis bullosa based on incidence and prevalence estimates from the national epidermolysis bullosa registry. *JAMA Dermatol*. 2016;152:1231–1238.
4. Kelly-Mancuso G, Kopelan B, Azizkhan RG, Lucky AW. Junctional epidermolysis bullosa incidence and survival: 5-year experience of the Dystrophic Epidermolysis Bullosa Research Association of America (DebRA) nurse educator, 2007 to 2011. *Pediatr Dermatol*. 2014;31:159–162.
5. Fine JD, Johnson LB, Weiner M, et al. Pseudosyndactyly and musculoskeletal contractures in inherited epidermolysis bullosa: experience of the National Epidermolysis Bullosa Registry, 1986-2002. *J Hand Surg Br*. 2005;30:14–22.
6. Fine JD, Johnson LB, Weiner M, et al. Genitourinary complications of inherited epidermolysis bullosa: experience of the national epidermylosis bullosa registry and review of the literature. *J Urol*. 2004;172:2040–2044.
7. Fine JD, Johnson LB, Weiner M, et al. Eye involvement in inherited epidermolysis bullosa: experience of the National Epidermolysis Bullosa Registry. *Am J Ophthalmol*. 2004;138:254–262.
8. Fine JD, Johnson LB, Weiner M, et al; National Epidermolysis Bullosa Registry. Inherited epidermolysis bullosa and the risk of death from renal disease: experience of the National Epidermolysis Bullosa Registry. *Am J Kidney Dis*. 2004;44:651–660.
9. Fine JD, Johnson LB, Weiner M, Suchindran C. Gastrointestinal complications of inherited epidermolysis bullosa: cumulative experience of the National Epidermolysis Bullosa Registry. *J Pediatr Gastroenterol Nutr*. 2008;46:147–158.
10. Fine JD, Johnson LB, Weiner M, Suchindran C. Tracheolaryngeal complications of inherited epidermolysis bullosa: cumulative experience of the national epidermolysis bullosa registry. *Laryngoscope*. 2007;117:1652–1660.
11. Gollu G, Ergun E, Ates U, Can OS, Dindar H. Balloon dilatation in esophageal strictures in epidermolysis bullosa and the role of anesthesia. *Dis Esophagus*. 2017;30:1–6.
12. Azizkhan RG, Stehr W, Cohen AP, et al. Esophageal strictures in children with recessive dystrophic epidermolysis bullosa: an 11-year experience with fluoroscopically guided balloon dilatation. *J Pediatr Surg*. 2006;41:55–60.
13. Lindemeyer R, Wadenya R, Maxwell L. Dental and anaesthetic management of children with dystrophic epidermolysis bullosa. *Int J Paediatr Dent*. 2009;19:127–134.
14. Griffin RP, Mayou BJ. The anaesthetic management of patients with dystrophic epidermolysis bullosa. A review of 44 patients over a 10 year period. *Anaesthesia*. 1993;48:810–815.
15. Lin YC, Golianu B. Anesthesia and pain management for pediatric patients with dystrophic epidermolysis bullosa. *J Clin Anesth*. 2006;18:268–271.
16. Goldschneider K, Lucky AW, Mellerio JE, Palisson F, del Carmen Viñuela Miranda M, Azizkhan RG. Perioperative care of patients with epidermolysis bullosa: proceedings of the 5th international symposium on epidermolysis bullosa, Santiago Chile, December 4–6, 2008. *Paediatr Anaesth*. 2010;20:797–804.
17. Van Den Heuvel I, Boschin M, Langer M, et al. Anesthetic management in pediatric patients with epidermolysis bullosa: a single center experience. *Minerva Anestesiol*. 2013;79:727–732.
18. Narejo AS, Khan MU, Alotaibi WM, Khan MM. Anesthetic consideration in dystrophic epidermolysis bullosa. *Saudi J Anaesth*. 2016;10:110–112.
19. Saraf SV, Mandawade NJ, Gore SK, Padhye UD, Pereira CS. Epidermolysis bullosa: careful monitoring and no touch principle for anesthesia management. *J Anaesthesiol Clin Pharmacol*. 2013;29:390–393.
20. Nandi R, Howard R. Anesthesia and epidermolysis bullosa. *Dermatol Clin*. 2010;28:319–324, x.
21. Herod J, Denyer J, Goldman A, Howard R. Epidermolysis bullosa in children: pathophysiology, anaesthesia and pain management. *Paediatr Anaesth*. 2002;12:388–397.
22. Arbuckle HA. Epidermolysis bullosa care in the United States. *Dermatol Clin*. 2010;28:387–389, xiii.
23. Strupp KM, Zieg JA, Johnson B, Szolnoki JM. Anesthetic management of a patient with epidermolysis bullosa requiring major orthopedic surgery: a case report. *A A Case Rep*. 2017;9:73–76.
24. Fitzmaurice BC, Lambert BG. Failed fiberoptic intubation in a child with epidermolysis bullosa, rescued with combined use of the Glidescope®. *Paediatr Anaesth*. 2016;26:455–456.
25. Ida JB, Livshitz I, Azizkhan RG, Lucky AW, Elluru RG. Upper airway complications of junctional epidermolysis bullosa. *J Pediatr*. 2012;160:657–661.e1.
26. Özkan AS, Kayhan GE, Akbaş S, Kaçmaz O, Durmuş M. Emergency difficult airway management in a patient with severe epidermolysis bullosa. *Turk J Anaesthesiol Reanim*. 2016;44:270–272.
27. George M, Martinez AE, Mellerio JE, Nandi R. Maxillary alveolar process fracture complicating intubation in a patient with epidermolysis bullosa. *Paediatr Anaesth*. 2009;19:706–707.
28. Park R, Peyton JM, Fiadjoe JE, et al; PeDI Collaborative Investigators; PeDI collaborative investigators. The efficacy of GlideScope® videolaryngoscopy compared with direct laryngoscopy in children who are difficult to intubate: an analysis from the paediatric difficult intubation registry. *Br J Anaesth*. 2017;119:984–992.
29. Goldschneider KR, Good J, Harrop E, et al; Dystrophic Epidermolysis Bullosa Research Association International (DEBRA International). Pain care for patients with epidermolysis bullosa: best care practice guidelines. *BMC Med*. 2014;12:178.
30. Goldschneider KR, Lucky AW. Pain management in epidermolysis bullosa. *Dermatol Clin*. 2010;28:273–282, ix.
31. Apfelbaum JL, Hagberg CA, Caplan RA, et al; American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. *Anesthesiology*. 2013;118:251–270.