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Management of Mitten-Glove Hand Deformity in Recessive Dystrophic Epidermolysis Bullosa: A Narrative Review of Surgical, Rehabilitation, and Adjunctive Treatment Strategies

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ABSTRACT

Introduction and Objective: Recessive dystrophic epidermolysis bullosa (RDEB) is a serious hereditary condition (mutations within the COL7A1 gene) characterized by chronic inflammation, where the skin is prone to the development of chronic wounds, scarring, and fibrosis that, in the final state, lead to progressive syndactyly, thumb adduction contractures, and mitten hand deformities. This article highlights the latest surgical techniques, rehabilitation methods, and additional therapies, focusing on patients' autonomy, caregiver burden, and social engagement. **Methods used for the literature review in academic style:** A thorough literature review was performed to extract data from journals, guidelines, and regulations of regulatory organizations for the period 1992-May 2026. The literature review concentrated on such themes as RDEB, hand surgery, dressings, splints, occupational therapy, physiotherapy, wound care, pain control, and wound healing innovations. **Current Status:** Surgery produces improvements in function regarding grasping and pinching functions but has a high recurrence rate due to skin fragility and scar formation associated with wound healing. Outcomes rely on proper wound care, minimizing trauma through splinting after surgery, hand therapy, education of caregivers, pain management, and the functional use of the hand. Current wound healing approaches make it possible for wounds to heal but do not reverse existing contractures or pseudosyndactyly. **Conclusion:** Management of the mitten-glove hand in RDEB must be multidirectional, involving surgical management, rehabilitation, occupational retraining, and other adjunctive treatments in order to reduce the burden of the wound and restore function.

Keywords: recessive dystrophic epidermolysis bullosa; mitten-glove hand; pseudosyndactyly; hand surgery; rehabilitation; wound healing.

1. INTRODUCTION

Epidermolysis bullosa (EB) is a group of inherited disorders characterized by fragility of the skin and mucous membranes, resulting in blistering following minor friction or trauma. Dystrophic epidermolysis bullosa (DEB) results from mutations in the COL7A1 gene responsible for encoding the $\alpha 1$ -chain of type VII collagen, which forms the main structural element of anchoring fibrils ensuring adhesion between the epidermis and dermis (Bardhan et al., 2020; Shinkuma, 2015; Chung & Uitto, 2010). Recessive dystrophic epidermolysis bullosa (RDEB), in particular the generalized severe type, is considered one of the most disabling EB manifestations. Extensive blistering of the skin, non-healing ulcers, anemia, malnutrition, mucosal strictures, osteoporosis, musculoskeletal contractures, and SCC are some other manifestations of the disease (Bardhan et al., 2020; Shinkuma, 2015; Nyström et al., 2021; Retrosi et al., 2022).

Regarding the major clinical sites of the disease, the hands should be emphasized as one of them, since this region of the body is under constant mechanical stress caused by usual activities. Due to chronic inflammation and erosions that result in the development of scars, a number of specific manifestations appear. These patients will be subjected to flexion contractures of the metacarpophalangeal and interphalangeal joints, thus leading to gradual deterioration in hand mobility. Other symptoms include flexion contracture of the thumb, absence of nails, soft tissue atrophy, and pseudosyndactyly (Denyer et al., 2017; Box et al., 2022; Mullett, 1998; Terrill et al., 1992). As a consequence of the development of the disease, an epidermal cocoon may form in the hand; it is referred to as mitten-glove or cocoon hand (Box et al., 2022; Chan et al., 2019; Mullett, 1998; Tuncer et al., 2018). It is not only associated with aesthetic problems but also with the loss of independent movement of fingers and inability to perform thumb-to-index pinch. Therefore, it limits a person's capacity for performing such functions as writing, eating, self-care, grooming, playing, and going to school (Box et al., 2022; Chan et al., 2019; Mullett, 1998; Tuncer et al., 2018).

Beyond the physical abnormality, the condition also has socio-developmental effects. A child may avoid activities such as play, writing, class activities, or interacting with peers because of pain, bulky dressings, the hand abnormality, and fear of injury. Adults may also be prevented from performing self-care tasks, digital interaction, work, and social activities. Caregivers must repeatedly dress and undress the patient, apply splints, transport them to specialized centers, and perform procedures. The connection between mitten-glove management of the hand and the paradigm of Health and Well-being in Interdisciplinary Medical Review is clear since the paradigm stresses the need for autonomy and participation (Retrosi et al., 2022; Denyer et al., 2017; Goldschneider et al., 2014; Box et al., 2022; Chan et al., 2019; Weisman et al., 2021).

The clinical importance of this anomaly is heightened by its high recurrence rate. Both traditional and modern surgical series show the positive effect of surgery on contractures and pseudosyndactyly in terms of gaining function. Yet, considering the chronic and progressive character of EB, the effect achieved is usually only temporary, since the repeated appearance of blisters, inflammation, fibrosis, and scars might result in the subsequent reappearance of deformities (Terrill et al., 1992; Tuncer et al., 2018; Abboud et al., 2022; Lembo et al., 2021; Zhou et al., 2020; Anstadt et al., 2020; Calavul et al., 2025; Ciancio et al., 2026). Therefore, the best outcome of the procedure is not an anatomically perfect or permanent repair of anomalies. Rather, it is a functional recovery as long as possible—primarily of thumb-index pinch and grasping ability—with minimal damage, operative pain, recurrence, and postoperative pain (Box et al., 2022; Terrill et al., 1992; Ladd et al., 1996; Abboud et al., 2022).

Modern approaches to treatment have affected the larger sphere of wound management in RDEB patients. Clinically significant effects in wound healing, pain reduction, or wound durability were achieved in individual cases of DEB or RDEB with topical beremagene geperpavec, birch triterpene gel, and autologous gene-corrected keratinocyte sheets (Guide et al., 2022; Krystal Biotech Inc., 2025; Kern et al., 2023; European Medicines Agency, 2022; So et al., 2022; Tang et al., 2025; US Food and Drug Administration, 2025). However, this approach targets only the wounds and does not treat finger fusion, fixed thumb adduction, and limited joint mobility from severe contractures.

This review presents available scientific data on mitten-glove hand deformities in RDEB for an interdisciplinary audience. The objective is to develop an integrated treatment approach that includes reconstructive surgery, wound management, rehabilitation, and occupational therapy, among others.

2. REVIEW METHODS

Study duration and database/source search: The review covered literature published from 1992 through May 2026. This manuscript included a PubMed/MEDLINE literature review of peer-reviewed publications, whereas guidelines for practice, regulatory literature,

and medication monographs were confirmed by searching specific resources in each category. Search terms reflected the scope defined for this review and included combinations of 'recessive dystrophic epidermolysis bullosa' or 'RDEB' with 'hand', 'pseudosyndactyly', 'mitten hand', 'cocoon hand', 'hand surgery', 'skin graft', 'dermal substitute', 'splint', 'occupational therapy', 'physiotherapy', 'wound care', 'pain', 'pruritus', 'gene therapy', and 'wound healing'.

The sources were selected if they included discussion of any of the following areas: characteristics of RDEB (molecular and/or clinical); natural history of hand deformities, pseudosyndactyly, or mitten/cocoon hands; surgery for EB-related hand deformities, including release and/or reconstruction; wound closure after surgical release; splinting, hand therapy, occupational therapy or physiotherapy after surgery; wound care practices; pain and pruritus treatment; multidisciplinary approach; functioning, independence, and quality of life of patients; and new therapies that could be topical, gene or cell based, addressing the wound burden in RDEB. We prioritized sources specifically related to RDEB/DEB hand deformity, followed by sources providing guidelines for EB patients in general (perioperative/rehabilitative information).

We excluded sources that were irrelevant to EB patients, discussed topics other than skin disorders, had no clinical significance to wound healing or fibrosis, and/or described therapies irrelevant to RDEB wounds and hand function. Sources not available in English were excluded unless an English-language abstract or regulatory summary was available. Opinion-based sources were considered only if they were clinical guidelines.

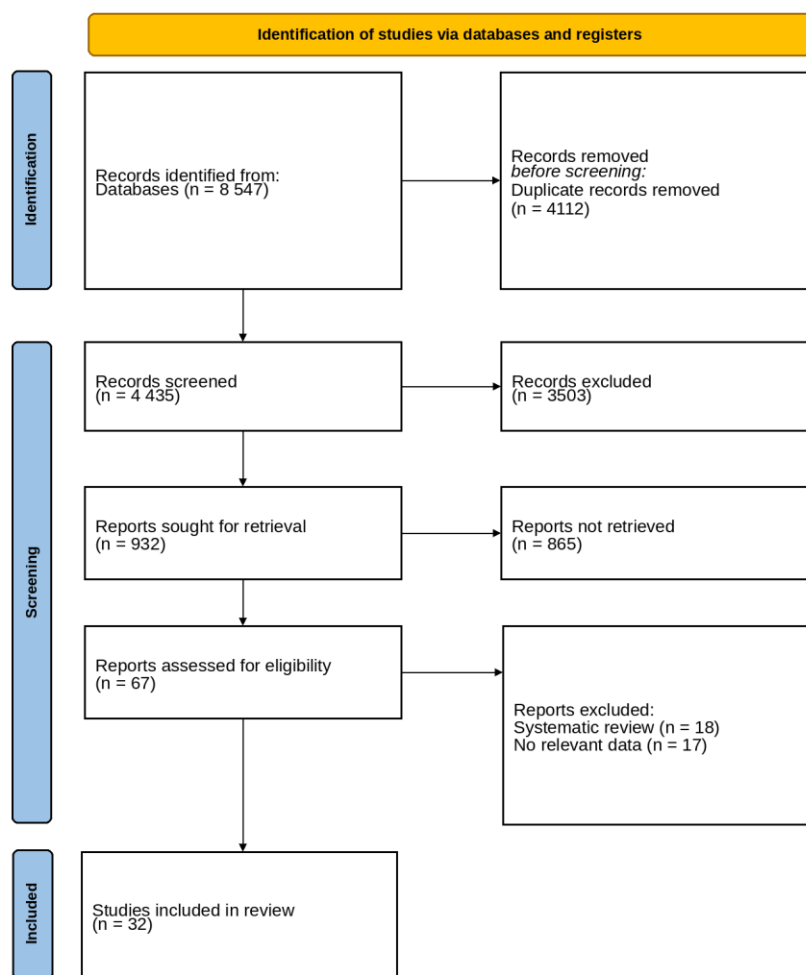


Figure 1. PRISMA-style flow diagram of source identification and selection for the narrative review.

One reviewer screened and extracted data, which is suitable for a narrative review but less reproducible than a systematic review conducted by multiple independent reviewers. For each relevant source, the following data were collected when applicable: design of the study, population, sample size (patients/hands), age group, type of EB, severity of hand deformity, treatment/intervention, surgical

procedure, type of skin cover used, splint/rehabilitation treatment used, follow-up period, functional results, recurrence, wound healing, pain/itch results, complications, limitations, and clinical relevance to the proposed management model.

It was a thematic, not a statistical, synthesis. The results of the analysis were divided into clinically relevant topics: pathophysiology and natural history of the disease; aims and indications for surgery; surgical release and closure; postoperative wound management and pain relief; rehabilitation and occupational and physical therapy; health, well-being, and access to healthcare; new wound-related treatment strategies; and management model. We chose this classification intentionally, given the multidisciplinary approach to RDEB management.

We did not perform a formal risk-of-bias assessment or meta-analysis, which should be considered a limitation of this review. However, a narrative approach allowed us to include a broad range of evidence, which is particularly relevant in a rare condition such as epidermolysis bullosa, where randomized surgical trials are scarce, and treatment decisions often depend on clinical rationale, functional goals, patient tolerance, available resources, and caregiver support. All citations were consistent, and the citation style of the journal in use was the author-date system. The process of selection of articles is presented in Figure 1. The final narrative synthesis and reference list comprise 32 sources.

3. RESULTS AND DISCUSSION

Pathophysiology and natural history of mitten-glove hand in RDEB

In RDEB, blistering occurs due to biallelic causative mutations in COL7A1, which result in absence or structural abnormality of type VII collagen. This type of collagen is produced by basal keratinocytes and dermal fibroblasts; it forms a key component of anchoring fibrils, which connect the lamina densa to the underlying dermal collagen fibers (Shinkuma, 2015; Chung & Uitto, 2010; So et al., 2022). The absence of functional anchoring fibrils makes even the slightest mechanical stress enough to detach the epidermis from the dermis, leading to the development of blisters. Hence, the clinical manifestation of the disease depends on the nature of the mutation itself as well as the amount and intensity of tissue injury. Mitten glove hand formation is best described as the final stage of the fibrotic healing process. Traumas of the hand provoke blistering and erosions with subsequent healing of the wounds due to inflammation, scarring, and stiffness of the tissue. Adhesion of interdigital surfaces, advancement of webs, and pseudo-syndactyly occur. The progressive decrease in mobility is a result of flexion contractures of the proximal interphalangeal joint, distal interphalangeal joint, and metacarpophalangeal joints as well as thumb adduction contracture. As the process develops, the fingers become enveloped by a skin fold and the hand acquires the mitten shape (Box et al., 2022; Mullett, 1998; Terrill et al., 1992; Zhou et al., 2020).

The consideration of recurrence biology after separation should also be made. Studies have confirmed bacterial colonization, proteolysis, release of pro-inflammatory cytokines, activation of the TGF- β pathway, activation of fibroblasts, and wound healing-related fibrosis in patients with RDEB (Nyström et al., 2021; Zhou et al., 2020). While it is possible to perform the procedure, the wound microenvironment is unstable and pro-fibrotic. Therefore, recurrence should be expected in the absence of proper postoperative treatment that minimizes the influence of shearing, inflammation, infection, pain, and wound breakdown.

The natural history also entails extracutaneous variables that affect surgery planning. These include malnutrition, anemia, chronic inflammation, osteoporosis, oral problems, esophageal strictures, pain, and pruritus that would negatively impact wound healing, anesthesia safety, mobility, and cooperation (Bardhan et al., 2020; Shinkuma, 2015; Retrosi et al., 2022; Pope et al., 2012; Goldschneider et al., 2014). Screening for squamous cell carcinoma is necessary in any chronic or unusual wound in adolescent and adult patients with severe RDEB (Bardhan et al., 2020; Retrosi et al., 2022; Pope et al., 2012). No safe and appropriate management of hand deformities is possible without taking into account systemic determinants of healing and functionality.

The natural course of the disease is variable. Nevertheless, according to literature on hand surgery, the disease follows a pattern that consists of webbing with loss of volar skin elasticity and then fixed IP flexion, first web-space adduction contracture, pseudosyndactyly, epidermal cocooning, and finally in severe forms, wrist deformity and joint destruction (Mullett, 1998; Terrill et al., 1992). Early intervention may delay severe joint and tendon changes, while very late intervention may require more complex procedures and may yield less durable functional recovery (Terrill et al., 1992; Ladd et al., 1996).

Goals of treatment and indications for surgery

Treatment should aim for functional reconstruction rather than aesthetic enhancement. The main purpose of surgery is to achieve and maintain the thumb-index pinch, palmar grasp, and proper finger separation to allow the patient to do some basic activities, such as eating, writing, self-dressing, washing, communication through technology, and studying (Box et al., 2022; Chan et al., 2019; Terrill et

al., 1992; Abboud et al., 2022). Normalization of the anatomy is not expected because of the biological nature of the condition. It is very important for the patients and their families to understand that surgery will only help to achieve the interval that allows functional use and is not the end of treatment itself. The indications for surgical procedure include lack of hand functionality, thumb adduction which interferes with pinch strength, pseudosyndactyly, finger contracture, interdigital space constriction, and unsuccessful non-operative maintenance of hand function (Box et al., 2022; Mullett, 1998; Terrill et al., 1992; Ladd et al., 1996; Tuncer et al., 2018; Abboud et al., 2022). Surgery needs to be individualized and planned with consideration of early surgical procedures to prevent secondary tendon and joint alterations. On the contrary, over-surgery can have some negative impact on the patient, such as donor site morbidity and psychological stress (Mullett, 1998; Tuncer et al., 2018). Recurrence of the mild character without functional disability does not require any additional surgery.

Pre-operatively, the assessment has to focus both on the factors specific to the hand and the overall systemic factors. As for the former, it has to include web space width, thumb position, joint range of motion, the degree of pseudosyndactyly, BEBSS hand scar severity score when possible, pain level, skin infection, wound load, dominant functional needs, and patient's concerns (Tuncer et al., 2018; Zhou et al., 2020; Calavul et al., 2025). Preoperative preparation should address the patient's overall medical and nutritional status, including anemia, serum albumin levels, infection risk, and assessment of the airway and oral cavity. Proper pain management, oral cavity and dental care, psychological preparations, and the skills of the family to handle dressing and splinting after the surgery are also crucial aspects of care (Retrosi et al., 2022; Pope et al., 2012; Goldschneider et al., 2014; Zhou et al., 2020).

The process of informed consent should also address the potential for recurrence, the necessity for dressing and splinting, pain management during postoperative care, potential need for re-operation, the drawbacks of new wound-based treatment approaches, and the importance of compliance (Denyer et al., 2017; Box et al., 2022; Mullett, 1998; Ladd et al., 1996). According to current practice in hand surgery, surgical intervention cannot be conducted independently of hand therapy postoperatively due to the necessity for maintenance of the effect (Denyer et al., 2017; Box et al., 2022).

Surgical techniques and wound coverage strategies

The main elements of the surgery have already been determined. First of all, the surgery starts with separating the web spaces that have been fused. Then, the correction of digital flexion contractures is performed. Finally, the surgery releases the thumb adduction contracture and the first web space. The digits are then positioned in an appropriate resting posture, while areas capable of spontaneous epithelialization are protected. (Terrill et al., 1992; Ladd et al., 1996; Tuncer et al., 2018; Abboud et al., 2022; Lembo et al., 2021; Zhou et al., 2020; Anstadt et al., 2020; Calavul et al., 2025). There are a lot of variations in the techniques of wound closure and splinting. In the past, large series combined extensive releases with skin grafts. The most extensive series included 45 patients with 122 hand surgeries involving 80 hands. In this series, finger extension deficit improved from the mean deficit of 139 degrees preoperatively to 60 degrees at one year and to 84 degrees at four years; pseudosyndactyly decreased significantly at one year but returned close to baseline at five years (Terrill et al., 1992).

The experience accumulated in the last two decades confirms the modern principle that hand surgery outcomes should be evaluated based on functional recovery and autonomy rather than appearance. In this series, debridement and release of amorphous epidermolysis bullosa (EB) hand resulted in complete re-epithelialization in 19.2 days with statistically significant improvement in DASH score and VAS pain assessment, with follow-up from 36 months to 10 years (Ciancio et al., 2026). Though this technique does not apply to all techniques described in previous RDEB series, the results confirm the trend toward modern function-based surgery that allows achieving quantitative pain and disability outcomes.

Full-thickness skin grafting is used to prevent contractures in the grafted area and cover critical functional areas, namely, the first commissure and the palm (Ladd et al., 1996; Abboud et al., 2022; Anstadt et al., 2020). Even though technically feasible, full-thickness skin grafting requires a source of healthy skin in patients with fragile skin. Dermal substitutes like Integra or Matriderm can be used to cover digits and commissures after release, usually in combination with grafting. In a series including 18 patients and 30 hands, dermal substitutes allowed obtaining functional gain in the selected group of patients; nevertheless, baseline severity, joint mobility, and postoperative cooperation determined the outcome (Abboud et al., 2022).

Dermal regeneration template glove constitutes another relatively new technique. In Foggia's experience, the outcome of pseudosyndactyly release using a custom Integra glove was compared to the previous Vaseline-gauze protocol. The results showed that the Integra protocol was associated with shorter healing time, shorter hospital stay, less discomfort of dressing changes, and longer recurrence-free period (Lembo et al., 2021). These data suggest that wound closure after surgery may decrease wound burden and

improve tolerance, though prospective or multicenter data are not available. Other approaches like sparing grafts can be used. Secondary intention healing after release eliminates donor-site morbidity and decreases cost but increases the necessity of special wound care and rehabilitation. In a pediatric series of 24 patients, a surgical approach without grafting and dermal substitutes provided an average wound healing time of 4.2 weeks and improvement in 17 of 21 ABILHAND-Kids tasks, though there were recurrences of scars after two years (Calavul et al., 2025).

Another approach includes silicone glove-like dressings, including Mepitel-type adhesive layers, alginate, foam, and silver tulle for separation of webs and draining of exudate (Zhou et al., 2020). An algorithm based on severity is clinically useful. Mild deformity of fingers can be treated with release and secondary healing with use of non-adherent dressings; moderate deformities require autografting of dermis to cover exposed PIP joints; severe deformities require K-wire fixation to maintain extension in addition to dermal grafting or any other covering (Tuncer et al., 2018). The value of this algorithm lies in the fact that different fingers in the same hand may have different severity and therefore a different treatment approach is needed. K-wires and external fixators help to maintain alignment after extensive soft-tissue release but increase the difficulties of wound management and risks of infections or pin-tract problems. They can only be used where the release of soft tissues does not result in functional realignment (Tuncer et al., 2018; Zhou et al., 2020; Calavul et al., 2025). The decision whether to perform surgery on one hand or both should be made according to patient needs. In some centers, unilateral surgery is preferred to retain patient autonomy, while others carry out bilateral surgery in one sitting with two operating teams (Ladd et al., 1996; Tuncer et al., 2018). The main surgical and wound-coverage options are summarized in Table 1.

Table 1. Surgical and wound-coverage options after pseudosyndactyly release

Strategy	Potential advantages	Main limitations
Split-thickness skin grafts (Terrill et al., 1992)	Classical technique with large historical experience; covers broad raw areas.	Donor-site morbidity; contraction; recurrence remains common.
Full-thickness skin grafts (Ladd et al., 1996; Abboud et al., 2022; Anstadt et al., 2020)	May reduce secondary contraction; useful for first commissure and palm.	Limited donor skin; donor wounds; small series.
Dermal substitutes / dermal regeneration template glove (Abboud et al., 2022; Lembo et al., 2021)	May reduce dressing pain, accelerate healing and support pliable coverage.	Cost; availability; evidence mainly retrospective; may still require grafting.
Autologous dermal grafts (Tuncer et al., 2018)	Biological coverage for exposed PIP defects; integrated into severity-based algorithm.	Technical harvesting; donor-site manipulation; single-center evidence.
Secondary healing / silicone-based dressings and graft-sparing approaches (Tuncer et al., 2018; Zhou et al., 2020; Calavul et al., 2025; Ciancio et al., 2026)	Avoids graft donor site; less expensive; can be combined with glove-shaped dressings.	Requires meticulous dressings; prolonged open wound period; recurrence still expected.
Kirschner wire (K-wire) stabilization (Tuncer et al., 2018; Zhou et al., 2020; Calavul et al., 2025)	Maintains extension and thumb position after severe release.	Pin infection risk; requires careful wound care and removal.

Postoperative wound care, pain control and prevention of recurrence

Postoperative wound management is an important determinant of surgical sustainability, not an incidental concern. Guidelines related to wound management in patients suffering from EB call for non-traumatic dressing, use of non-adhesive contact layer, avoiding use of adhesives, proper management of wound exudates, protecting periwound skin, and taking into account the wishes of the patient or their carers (Denyer et al., 2017; Pope et al., 2012). In treating blisters, drainage must be done in a sterile manner, keeping the roof of the blister as a biological dressing where possible (Shinkuma, 2015; Retrosi et al., 2022; Pope et al., 2012). This is especially crucial after hand release surgeries where large open wounds are created intentionally.

Dressing selection should be based on wound size, exudate volume, infection risk, pain, dressing availability, and cost. Clinicians have used silicone contact layers, petrolatum gauze, alginates, polyurethane foams, silver-containing products, and other non-adherent dressings, but no single dressing meets all criteria for all patients. The main goal is to promote epithelialization without causing additional trauma during dressing changes.

Pain and pruritus must be managed proactively. Dressing changes, splinting, management of K-wires, and exercises may cause procedural pain, while chronic wounds and pruritus may disturb sleep, mood, adherence, and engagement in therapy. According to pain management guidelines, individualized treatment should combine pharmacologic therapy with non-pharmacologic measures such as distraction, relaxation, psychological counseling, and environmental modification (Goldschneider et al., 2014). Undertreatment can reduce adherence, while oversedation may interfere with rehabilitation. The strategy should be reassessed as wounds heal and therapy progresses.

Infection and critical colonization require close monitoring. Wounds in RDEB patients are often critically colonized; hence, antibiotic use needs to be used wisely to prevent the development of resistance and sensitization (Shinkuma, 2015; Pope et al., 2012). Changes in wound size, exudate, odor, pain, erythema, edema, as well as any systemic symptoms should be monitored. Any lesion that is atypical, refractory to treatment, and hard to control should put the diagnosis of SCC into consideration, especially in elderly patients with severe RDEB (Bardhan et al., 2020; Retrosi et al., 2022; Pope et al., 2012). The prevention of web space fusion is primarily concerned with minimizing shear forces and maintaining the web spaces separate from each other. This can be accomplished using any supportive intervention that includes night splints, web space retaining gloves, elastic gloves, cotton spacers, silicone casts, thermoplastics, and dynamic splints (Denyer et al., 2017; Box et al., 2022; Chan et al., 2019; Weisman et al., 2021; DEBRA UK, 2024; Mullett, 1998; Ladd et al., 1996; Zhou et al., 2020). It is important to make the splint efficient and comfortable to avoid new blister formation, pressure injury, or scratching, which is more common in patients with nocturnal pruritus (Chan et al., 2019; Mullett, 1998). A good splint is one that can be actually worn by the patient.

Recurrence is expected to happen within the long-term course of the condition. The experience in treating patients with pseudosyndactyly shows that improvement is observed initially, but then there is recurrence after several years (Terrill et al., 1992). Recurrent webbing and contractures have been reported recently even with advancements in dressing technology and treatment approaches (Zhou et al., 2020; Calavul et al., 2025). Hence, recurrence should be assessed based on both anatomical and functional parameters.

Rehabilitation, occupational therapy and functional reintegration

Rehabilitation starts before surgery. The importance of understanding the post-surgical sequence of events, splinting schedule, exercise regimen, dressing changes, activity restrictions, and danger signs for the patient and caregiver cannot be overstated. Occupational therapy should start early and assess web space length, range of motion, hand function, fine motor skills, bilateral coordination, and activities of daily living (Chan et al., 2019). Therapy in children should also consider their developmental level and schooling. After stabilization, the next goal will be to maintain the benefits of surgery, gain safe movement, and incorporate the functions of the hand in the activities of daily living. Rehabilitative procedures may include exercises that involve both active and passive exercise, thumb abduction, metacarpophalangeal joint flexion, tendon glides, and finger abduction/adduction (Denyer et al., 2017; Zhou et al., 2020). It is necessary to be careful and not apply too much force because of the sensitivity of the skin in the interdigital spaces and at joints. The treatment should be individualized, taking into account pain, bulkiness of dressings, injuries, and concerns of the patient. Occupational therapy becomes especially important in this stage. Adaptive equipment, special soft-handled objects, adapted pens, button hooks, modified clothing, education, and appropriate activities will help to decrease shear forces and promote functional independence (Denyer et al., 2017; Chan et al., 2019).

The general goal goes beyond the scope of improving joint flexibility and involves increasing the functional capacity of hands. The principles of physiotherapy for epidermolysis bullosa (EB) are based on this idea. Severe RDEB is associated not only with hand deformity but also with global contractures, reduced mobility, low bone density, pain, deconditioning, and reduced participation (Weisman et al., 2021). Thus, hand rehabilitation needs to be incorporated with whole-body movement, safety of weight-bearing, endurance, development of motor skills, and social participation. A patient who is having problems with overall movement, nutrition, and pain will have difficulty in deriving any benefit from the technically perfect hand surgery. Postsurgical experience suggests that long-term use of night splints and web-retaining gloves may help preserve hand function, provided that patients are able to use them consistently (Ladd et al., 1996). The same principle applies to current conservative management. Any interventions that will lead to

considerable pain, itchiness, embarrassment, or caregiver burden are likely not going to be sustainable over time (Denyer et al., 2017; Chan et al., 2019; Weisman et al., 2021). Due to this, it is important to make decisions about treatments in conjunction with patients and their families, considering the above factors.

Health, well-being, access to care and assistive technology

Consequences of Mitten-Glove Hand are Important for Well-Being. Deformity affects much more than a hand itself. It influences a child's play, learning, writing, using the phone or tablet computer, participation in school activities, and peer relationships. For adults, it influences hygienic procedures, eating, dressing, work, transportation, and social activities. Due to the fact that RDEB is visible, painful, and recurrent, deformity of the hand may affect embarrassment, avoidance, dependence, and reduced confidence despite intact cognitive development (Chan et al., 2019; Weisman et al., 2021; Tuncer et al., 2018).

Caregiver burden can be regarded as a component of the problem as well. After surgical intervention, it is necessary to manage dressing changes, non-adherent dressings, splints, finger spacers, analgesics, observation of infections, transportation to the EB center, and motivation for daily exercises. Technically successful release may become ineffective if the family is unable to implement the postoperative program. The treatment plan should take into consideration time, costs, distance to the medical center, access to dressings, school schedule, and the ability of caregivers (Retrosi et al., 2022; Denyer et al., 2017; Box et al., 2022; Weisman et al., 2021).

Occupational adaptation should be considered an intervention approach rather than only a supportive measure. Devices including softer grips for pens, modified cutlery, button hooks, specially designed toothbrushes, silicone or foamy grips on handles, changes to the touch screen and voice activation software, among others, can decrease shear and increase independence (Denyer et al., 2017; Chan et al., 2019). Simple technology may carry the same weight as more sophisticated treatments because of its cost-effectiveness, repetitive nature, and appropriateness for home use. In a clinical setting, the best form of treatment is often the one that reduces trauma and allows patients to engage in their daily routines. Cautious assessment of digital technology and tele-rehabilitation methods is needed. Tele-wound photography, tele-splint assessment, remote supervised exercises, and telecommunication with experts on EB can ease travel and provide opportunities for individuals with limited knowledge to get consultations with reference centers. Nevertheless, data on tele-rehabilitation after surgery in RDEB patients are scarce, and tele-assistance cannot take the place of physical examination regarding infections, pain, vascular insufficiency, contractures, skin injuries caused by splinting, and squamous cell carcinoma. The possibility of receiving novel treatments is also one of the aspects of patients' well-being.

Although beremagene geperpavec, birch triterpene gel, and prademagene zamikeracel could find their use in alleviating wound burden in certain situations, several aspects, including costs, accessibility, production issues, possibility of being used at home, and need for an expert's involvement, may hinder their use (Krystal Biotech Inc., 2025; Kern et al., 2023; Tang et al., 2025; US Food and Drug Administration, 2025). The ethical dilemma arises because the treatments that best reduce the impact of chronic wounds are often inaccessible to patients in less-developed systems. Therefore, any viable system of management should take into consideration not only treatment but also basic and universal principles – atraumatic dressings, pain control, education, splinting, and adaptation.

The outcome measures should be consistent with this approach. Although range of motion and web-space depth can serve as important criteria, they are not sufficient to evaluate therapeutic success. From a patient-oriented perspective, the set of outcome measures should include pinching, grasping, writing, using assistive devices, personal hygiene, attending school and/or work, tolerance to dressings and splints, pain relief, and caregiver burden. Potential instruments to collect the information include the Birmingham Epidermolysis Bullosa Severity Score (BEBSS), Disability of the Arm, Shoulder and Hand (DASH), ABILHAND-Kids scale, several pain scales, and individual patient functional assessment (Tuncer et al., 2018; Zhou et al., 2020; Calavul et al., 2025; Ciancio et al., 2026).

Adjunctive and emerging wound-directed therapies

There are several treatment modalities currently being considered in the management of RDEB, but their effect on mitten-glove deformity is not fully understood yet. They have the potential to decrease wound burden, promote wound healing, reduce pain, and increase local deposition of type VII collagen. Still, up to now, no modality has been able to reverse pseudosyndactyly, correct thumb adduction contracture, increase the length of shortened tendons, or increase joint mobility. Beremagene geperpavec is a topical non-integrating HSV-1 vector-based COL7A1 gene therapy intended for use in wounds due to DEB. However, in an essential inpatient-controlled study, complete wound healing was observed more in patients given beremagene geperpavec as compared to those who were not (Guide et al., 2022). The drug is given to the patients on a weekly basis for individualized wounds depending on their age,

using either a clinical or a home setting through a health practitioner, the patient themselves, or their caretaker (Krystal Biotech Inc., 2025). This particular approach is based on the up-regulation of COL7A1 gene expression in keratinocytes and fibroblasts. Increased gene expression would lead to more type VII collagen, which allows the creation of anchoring fibrils that link the epidermis and dermis (Krystal Biotech Inc., 2025).

Filsuvez, or Oleogel-S10, is the birch triterpene gel used as the topical treatment for wound healing. In the phase III EASE clinical trial enrolling 223 patients with epidermolysis bullosa (EB), the first efficacy endpoint—fully closed target wounds by day 45—was reached in a higher number of patients receiving Oleogel-S10 than in the control group, with significant results in patients with recessive dystrophic EB (RDEB) (Kern et al., 2023). On the other hand, regarding European regulatory assessment, Filsuvez can be described not as the structural treatment for the existing deformities but as the partial-thickness wound treatment for dystrophic and junctional EB (European Medicines Agency, 2022). The second effect of Oleogel-S10 was achieved at day 90 and demonstrated less prominent results, suggesting that there is an acceleration in wound closure but not a modification in the disease process (Kern et al., 2023).

Prademagene zamikeracel is the autologous keratinocyte sheet therapy modified with COL7A1 and transplanted surgically into large chronic RDEB wounds. Data on long-term phase 1/2a clinical trials demonstrate a steady improvement in wound healing, pain, and itching, with no treatment-related severe adverse effects, on average follow-up of 5.9 years in 7 adult patients (So et al., 2022). The Phase III VIITAL clinical trials reveal that 81% of wounds treated with the drug had reached 50% wound closure after week 24, while only 16% of wounds in the control group showed any such improvement, along with pain relief without the experience of any treatment-related side effects (Tang et al., 2025). These findings are clinically relevant for the treatment of large, chronic wounds in patients with RDEB. However, it is unclear whether the same benefits would be seen in surgically released mitten-glove hands. This difference is also illustrated by the regulatory documents of prademagene zamikeracel, where the drug is meant to treat wounds caused by RDEB but not for the correction of contractures (US Food and Drug Administration, 2025).

The other experimental approaches include protein replacement therapy, fibroblast therapy, mesenchymal stromal cell therapy, gene editing, and repurposing of anti-inflammatory or antifibrotic medications (Bischof et al., 2024; Danescu et al., 2024; Hou et al., 2021). These treatment approaches are especially pertinent for RDEB since they deal not only with the collagen VII deficiency but also with the inflammation and fibrosis mechanisms involved in the development of the disease (Nyström et al., 2021; Bischof et al., 2024; Danescu et al., 2024; Hou et al., 2021). Future perioperative strategy can potentially include the combination of surgical treatment with molecular therapy directly on the wounds, which needs further clinical investigation. The main adjunctive wound-directed therapies and their relevance to mitten-glove hand are summarized in Table 2.

Table 2. Adjuvant wound therapy and applicability for mitten-glove hand

Therapy	Mechanism / type	Evidence summarized	Relevance to mitten-glove hand
Beremagene geperpavec (VYJUVEK) (Guide et al., 2022; Krystal Biotech Inc., 2025)	Topical herpes simplex virus type 1 (HSV-1) vector delivering COL7A1.	Inpatient-controlled trial and official label show improved DEB wound closure.	May support wound healing; does not release fused digits or fixed contractures.
Oleogel-S10 / birch triterpenes (Filsuvez) (Kern et al., 2023; European Medicines Agency, 2022)	Topical triterpene gel supporting keratinocyte migration and wound closure.	EASE trial showed faster closure of partial-thickness EB wounds, especially RDEB subgroup.	Potential wound-care adjunct; not disease-modifying for established hand deformity.
Prademagene zamikeracel / EB-101 / ZEVASKYN (So et al., 2022; Tang et al., 2025; US Food and Drug Administration, 2025)	Autologous COL7A1 gene-corrected keratinocyte sheets.	Long-term phase 1/2a and VIITAL phase 3 data show healing and pain reduction in large chronic RDEB wounds.	Conceptually attractive for postoperative wound beds; direct evidence in mitten release is absent.
Gene editing, protein and cell therapies (Bischof et al., 2024; Danescu et al., 2024; Hou et al., 2021)	Molecular or cellular correction of primary or secondary disease mechanisms.	Mostly early-phase or investigational evidence.	Future adjunctive potential; not current treatment for fixed deformity.

Proposed integrated management framework

Optimal management of mitten-glove deformities involves stages and cycles. Firstly, baseline status of the patient should be optimized through proper confirmation of the diagnosis, education of the caregivers, skin protection, dressing of the involved digits separately, correction of nutritional deficiency and anemia, treatment of infections, management of pain and pruritus, and assessment of function (Retrosi et al., 2022; Denyer et al., 2017; Pope et al., 2012; Goldschneider et al., 2014; Box et al., 2022; Chan et al., 2019; Weisman et al., 2021). Early caregiver education is particularly critical in that home-based care affects the burden of the wound, protection of the web spaces, and tolerability of surgical interventions. Secondly, the hand has to be evaluated at intervals using parameters such as web space depth, thumb placement, joint flexibility, pain, splint tolerance, and functional skills (writing, feeding, personal grooming, dressing, and school activities). Consideration of surgical correction is warranted in cases where there is a continuing functional deficit in spite of the continuation of conservative treatment, especially in cases of the loss of thumb-index pinch or web-space fusion (Box et al., 2022; Mullett, 1998; Tuncer et al., 2018; Abboud et al., 2022). Thirdly, surgery has to be individualized according to the severity of the deformity and local facilities.

In cases where surgery involves simple release and secondary closure, this is enough for the treatment of mild deformities, while dermal grafts and selective coverages of PIP joints are frequently required for moderate deformities (Tuncer et al., 2018; Abboud et al., 2022; Lembo et al., 2021; Zhou et al., 2020; Anstadt et al., 2020; Calavul et al., 2025). It is crucial to focus on the first web space and thumb position since these two factors are essential in maintaining good pinch ability (Mullett, 1998; Terrill et al., 1992; Ladd et al., 1996; Tuncer et al., 2018; Abboud et al., 2022). In addition, postoperative management requires a standardized approach that will still adapt to the patient's requirements.

Preoperative planning has to take care of issues including atraumatic dressing, pain relief, monitoring of infections, exudate management, splinting, instructions for caregivers, and hand therapy. When post-operative care is not available, surgery needs to be deferred or moved to another institution (Denyer et al., 2017; Box et al., 2022). Recurrence of the deformity should be followed up with functional evaluation and not another surgery. Reoperation should only be done in recurrent pseudosyndactyly and contractures that hinder crucial function. However, in mild deformities, recurrent unstable wounds, poor general condition, or inability to manage post-operative care, surgery should be deferred. Improvement in function should be the reason for more surgeries (Mullett, 1998; Tuncer et al., 2018). Fifthly, new wound-directed treatment methods should be considered based on available scientific studies. New treatment approaches will help in reducing wound load, pain, and dressings and can be used perioperatively selectively. However, the mitten-glove deformity continues to be a challenge in reconstruction and rehabilitation.

Discussion

However, in all articles, there is a consistent idea that the mitten-glove hand in RDEB cannot be surgically corrected once. It is a recurrent phenomenon of the systemic genetic disorder, which is accompanied by continuous skin fragility and pathologic wound healing. Hence, surgeries can help and be effective but are temporary. In historical literature, improvements in finger extension and web space separation were described, followed by recurrence (Terrill et al., 1992). Current literature, despite significant improvements in methods of wound management and rehabilitation, describes the same biological mechanism (Abboud et al., 2022; Lembo et al., 2021; Zhou et al., 2020; Anstadt et al., 2020; Calavul et al., 2025).

Thus, surgical success should not be evaluated solely through the criterion of a permanent anatomical correction. If it is the only criterion, recurrence would cause many surgical interventions to become unsuccessful. On the contrary, when success is measured through improvement in pinch, grasping, writing, independence, attending school, and other activities, surgery would remain clinically beneficial even in the case of recurrence. This functional approach is more appropriate from a patient-centered care point of view.

The re-framing of criteria would be particularly useful for interdisciplinary literature. For a surgeon, the issue is whether the web space stays open or not; for a rehabilitation physician, it is about hand function; for a researcher concerned with the health and well-being of patients, it includes independence, attending school and work, and others. Future studies should include not only images and information about recurrence, but also functional scales, pain scales, dressing burden, attending schools/work places, and other parameters (Chan et al., 2019; Weisman et al., 2021; Calavul et al., 2025; Ciancio et al., 2026).

In addition, the literature does not allow making any conclusions regarding a universal method of wound closure. Depending on the indication, split-thickness grafts, full-thickness grafts, dermal substitutes, dermal regeneration templates, autologous dermal grafts, silicone dressings, and secondary intention healing can be used. The choice of the method depends on different factors including size of

the defect, exposed structures, need to keep the first web space open, cost, availability, morbidity of donor site, risk of infection, pain, and rehabilitation capacities (Terrill et al., 1992; Ladd et al., 1996; Tuncer et al., 2018; Abboud et al., 2022; Lembo et al., 2021; Zhou et al., 2020; Anstadt et al., 2020; Calavul et al., 2025). Future comparative studies should include pain scales, dressing burden, cost, and functional outcomes.

Rehabilitation and wound care are not only auxiliary elements in the treatment process, but its essential constituents. Splints and gloves create space, exercise adds mobility, adaptation to work contributes to the functionality of physiological processes, analgesia is needed for cooperation, and atraumatic dressings help to avoid other possible traumas. Evidence for rehabilitation in EB is still poor, and many of the recommendations are largely based on expert opinions. Nevertheless, there are some general guidelines for some aspects of care, which include early assessment, patient-tailored orthoses, physical activities, and individualization of the treatment (Denyer et al., 2017; Chan et al., 2019; Weisman et al., 2021).

Despite that, new therapies are beginning to expand the opportunities for treating RDEB patients. There is no denying that their prospects are favorable; nevertheless, it would be an exaggeration to emphasize their significance in the treatment of hand abnormalities. The following three therapies – beremagene geperpavec, Oleogel-S10, and prademagene zamikeracel – have shown that it is possible to modify local wound biology in RDEB patients (Guide et al., 2022; Krystal Biotech Inc., 2025; Kern et al., 2023; So et al., 2022; Tang et al., 2025). An important unanswered question is whether these therapies could also improve postoperative recovery after surgical hand release. In particular, future studies should determine whether they can reduce wound burden, promote faster epithelialization, lessen pain, or delay the recurrence of deformity. At present, however, no clinical trial has directly evaluated these outcomes. Until such evidence becomes available, these therapies are best regarded as adjuncts for wound management rather than treatments for established mitten-glove deformity.

Caution should also be exercised with regard to technology-based follow-up. Telemedicine and remote follow-up are a convenient approach to the matter since treatment of EBs is usually concentrated in specialized clinics, and thus traveling is a difficult task. However, it should be studied and used alongside traditional examination in case of potential complications. The future approach could involve combining centers for surgery with wound care, telemedicine follow-up, occupational adjustment, and targeted treatment of wounds.

The current review is constrained by the lack of a systematic nature of the review and heterogeneity of evidence. Most studies on hand surgery are retrospective, single-center, small-sized, and include different follow-up times and assessments of function. Older studies were conducted using methods that are not in accordance with contemporary standards, whereas molecular approaches have only been explored in wounds and not in postoperative settings following hand reconstruction surgery. However, consistent results over decades provide some concrete implications: surgery improves function; recurrence is expected; postoperative management is essential; wound healing and pain management influence patient compliance; and multi-disciplinary management is critical.

4. CONCLUSION

Mitten-glove hand deformity in RDEB is best understood as a progressive, recurrent and function-limiting consequence of skin fragility, chronic wounds, inflammation, fibrosis and scarring. The deformity is not isolated from the systemic burden of RDEB, which includes pain, pruritus, anemia, malnutrition, infection risk, osteoporosis, mucosal disease and SCC risk. Surgical release remains the only proven treatment for correcting fixed pseudosyndactyly. The main functional goal is to regain a working thumb-index pinch and grip function, not anatomical normality. Wound coverage is patient-specific and can include skin grafts, dermal substitutes, dermal regeneration templates, autografting of dermis, silicone sheet dressings, and secondary intention. No modality stands out as superior.

Postoperative wound management, analgesia, splinting, hand rehabilitation, adaptation, physiotherapy, and caregiver education are essential for long-term benefit. Recurrence is anticipated and must be addressed with functional strategies. Revision surgery could be performed in case of recurrence of the deformity that limits functional activity. There are wound-directed therapeutic approaches that represent a significant advance in the treatment of RDEB. Topical COL7A1 gene replacement, birch triterpene gel, and autologous keratinocytes genetically modified by COL7A1 represent wound-healing strategies that can be effective in certain situations. However, the use of these interventions in correcting mitten-glove hand deformity is still indirect. The combined strategy, involving surgery, rehabilitation, non-traumatic wound management, analgesia, adaptation, education of caregivers, access to specialized care, and innovative adjuvant treatment, appears to be a most rational way to enhance functional activity, independence, and quality of life in patients with mitten-glove hand deformity as a complication of RDEB. It would be pertinent for future studies to consider not only

recurrence and re-epithelialization but also issues related to patient autonomy, caregiver burden, educational and occupational engagement, and specialized care.

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Data and materials availability

All data associated with this study will be available based on the reasonable request to the corresponding author.

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