Journal of Pediatric Surgery 61 (2026) 162752

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.sciencedirect.com/journal/journal-of-pediatric-surgery

Clinical Research Paper

Congenital diaphragmatic hernia repair: Patches, muscle flaps, and the search for the ideal technique☆

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ARTICLE INFO

Article history:
Received 13 October 2025
Accepted 15 October 2025

Keywords:
Congenital diaphragmatic hernia
Prosthetic patch
Muscle flap

ABSTRACT

There is a variable defect size in both left and right-sided congenital diaphragmatic hernia. The majority can be repaired using primary apposition but in a significant minority this will not be possible. A number of surgical techniques have been developed to overcome this problem but in principle these can be divided into the creation of a muscle flap usually derived from layers of the abdominal wall rotated into the gap or the insertion of a prosthetic patch. The composition of the latter has also been subject to variation and has been largely non-absorbable or absorbable and dependent on surgical preference.

This article summarises the debate at a recent conference symposium by illustrating two forms of prosthetic patch repairs and a muscle flap repair. It concludes with an update on the efforts that have been made to achieve this using various tissue engineering technologies.

1. Introduction

This report summarises a symposium at the British Association of Paediatric Surgeons (BAPS) to discuss current practices, trends, and recent basic science research on aspects of surgical closure of congenital diaphragmatic hernias (CDH). It was driven by shortages and decreased availability of the synthetic patch most commonly used in the UK (GORE-TEX ™). While currently there are no such shortages in the USA, there has been growing pressure from regulatory agencies around the world to limit the use of a number of chemical products such as polyfluoroalkyl substances (PFAS), a common component of most prosthetic patches.

Such developments may force many surgeons around the world to change their practice. While there are market alternatives to the use of simple GORE-TEX ™ patches there is also a growing trend towards the use of muscle flaps in the care of CDHs, particularly in the USA. The following sections illustrate current areas of controversy in the use of surgical prosthetic patches, muscle-flap repairs and novel areas of study for the future.

2. Evolution of the polytetrafluoroethylene (PTFE) Mannheim cone patch

The CDH EURO Consortium has published medical and surgical protocols to try and rationalise management of CDH with its first consensus statement published in 2010 and an update in 2016 [1,2]. Most were medical, concentrating on ventiliation strategies etc. with relatively few on actual surgical repair. These recommendations included: 1. Surgical repair should be performed after clinical stabilization, with certain criteria being defined concerning respiratory and cardiological markers; 2. Routine placement of chest tubes should be avoided; and 3. Repair could be performed during provision of Extra-corporeal Membrane Oxygenation (ECMO) treatment.

Nonetheless, there still exists a great deal of controversial areas within the surgical sphere that were not addressed. So, what is the consensus towards: open *versus* minimally invasive surgery; abdominal approach *versus* thoracic approach; and the nature and type of diaphragmatic substitution in large defects (prosthetic patch *versus* muscle flap), etc. Even the incisions used in the open abdominal open approach could be debated - subcostal, upper transverse or even a median incision.

This article is part of a special issue entitled: BAPS 2025 published in Journal of Pediatric Surgery.

☆ This was presented at the 71ST BAPS Congress, 25TH –27TH June, 2025.

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https://doi.org/10.1016/j.jpedsurg.2025.162752
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The degree of diaphragmatic defect may clearly influence the nature of its repair. In 2013, the CDH Study Group in the USA defined defect as Types A, B, C or D depending on the remaining diaphragm and the portion of the thoracic wall without diaphragmatic attachment. Survival in isolated CDH decreases with larger defect size from ~99 % in defect Type A to ~58 % in Type D [3]. Furthermore, stabilization of the neonate with ECMO is more frequently necessary in children with larger defects due to increasingly severe lung hypoplasia and its associated pulmonary hypertension. Alternative closing techniques may be necessary in some patients with Type B defects and almost always in patients with Types C and D, while a primary repair can always be performed in Type A defects. Minimally invasive techniques are mainly used in smaller defect sizes although some surgeons push the limits applying it also in infants after ECMO-therapy [4] and patients with large defects [5]. The main objection against minimal invasive surgery in CDH is a significantly higher recurrence rate than in open access surgery [6].

The shape of the prosthetic patch has even been debated. It seems to be advantageous to use a patch size that exceeds the defect size to reduce long-term recurrence rates. Since infants with large diaphragmatic hernias also have a hypoplastic abdominal cavity, efforts have been made to enlarge the abdominal cavity and at the same time to reduce redundant thoracic volume by using either dome- or cone-shaped patches [7,8]. The angle at the tip of the cone shaped patch depends on the size of the diaphragmatic defect, allowing the patch to be sutured to the remaining diaphragm and surrounding tissue with an overlapping border (Fig. 1). To secure the patch, pledgeted sutures are used, increases the area of contact between the patch and surrounding tissue to promote adhesions and to reduce the risk of recurrence. Another advantage of this patch configuration and suturing technique is reduced tension on the hypoplastic diaphragm, which may also contribute to the lower risk of recurrence in the long-term [9]. Furthermore, reconstruction of the diaphragm with a more natural contour enables re-positioning of the abdominal content physiologically, incidentally preserving the angle of His (Fig. 2). This may be the reason why there was no advantage of a primary fundoplication during inital CDH repair as was observed in a randomized controlled trial of 79 neonates with left-sided CDH concerning gastroesophageal reflux, neither after follow-up of two years nor after a median follow-up of 10 years [10,11]. The cone-shape patch flattens with growth allowing for thoracic growth without tearing the diaphragmatic remnant. GORETEX® (Gore, AZ, USA) patches seem to stretch, as a diameter of >9 cm can be observed in older children after neonatal CDH repair with a cone-shaped patch.

Structured longitudinal follow-up including radiologic screening at certain intervals showed an overall incidence of either recurrence and/or secondary hiatal hernia in 11.7 % of 326 CDH survivors with a minimum of two years of follow-up. The risk of diaphragmatic complications increased with larger defect size. Within the first year postoperatively only about half of the complications were observed, 17 % occured beyond two years of age, and 9 % beyond four years [9].

Could the principles of such open reconstruction of the diaphragm with a cone-shaped patch be applied in thoracoscopic surgery to reduce the reported higher risk of recurrence? There may be an evolution in attitudes to the minimally invasive approach. For instance, Canadian Congenital Diaphragmatic Hernia Collaborative did not recommend minimal invasive CDH repair in 2018, this has now changed in their most recent update in 2023 [12,13]. In a recent meta-analysis, there was a four-fold overall risk of recurrence in infants undergoing thoracoscopic repair (TR) compared to open repair (OR), both in primary (12.3 % *versus* 0.8 %, $P < 0.0001$) as well as in patch repair (23.6 % *versus* 10.1 % OR; $P = 0.0085$) [6]. On the other hand, the risk of postoperative bowel obstruction was reduced significantly in the thoracoscopic group (5.0 % *versus*. 14.8 %, $P = 0.02$). The authors emphasized the importance of meticulous patient selection for minimal invasive surgery [6]. In our series from Mannheim, recurrence in thoracoscopic repair could be reduced from 20.7 % (12/58 patients) to 5.4 % (2/37 patients; $P = 0.07$) after implementing the following surgical principles: 1) avoiding tension on the hypoplastic diaphragm by a more liberal use of patch implantation in Type B defects; 2) The use of oversize patches being implanted with an overlapping border to promote adhesions to the surrounding tissue and, 3)

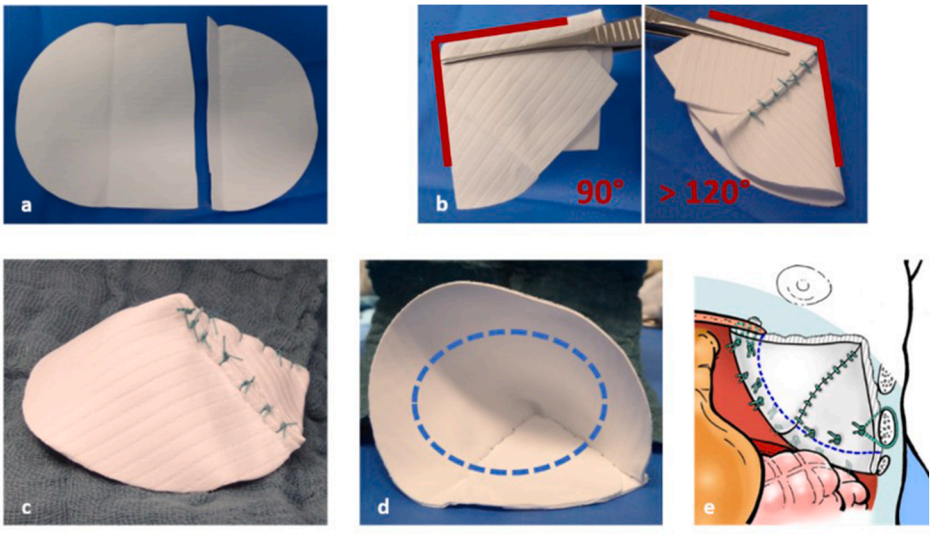

Fig. 1. Construction of a cone-shaped patch for repair of large diaphragmatic hernia. A: Dividing the GoreTex® sheet, the larger part being used for the cone-shaped patch, the smaller part may be used as an abdominal wall patch, if needed. B: The angle at the tip of the cone depends on the size of the defect. C: the shape of the cone-shaped patch is preserved by single stitches after folding. D: appearance from below, the dotted blue line indicates the suture line to the diaphragm and thoracic wall with creation of an overlapping border. E: schematic demonstration after implantation of the cone-shaped patch with diaphragmatic and pericostal sutures on the dotted blue line and additional fixation of the overlapping border to the surrounding tissue. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

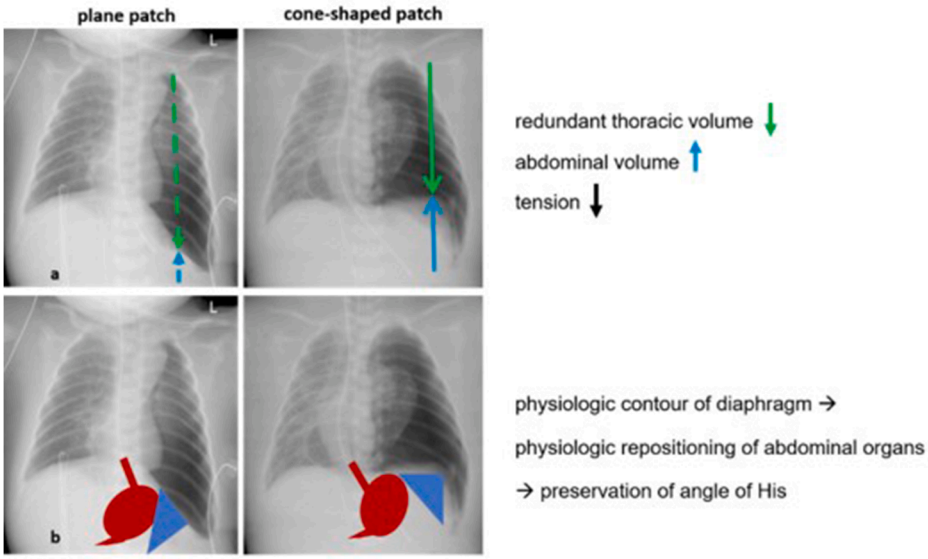

Fig. 2. Advantages of the cone-shaped patch in comparison to implantation of a plane patch in neonatal repair of large congenital diaphragmatic hernia demonstrated on postoperative chest X-rays. A: reduced redundant thoracic volume (green arrows), increased abdominal volume (blue arrows), reduced tension on the diaphragmatic remnant. B: the cone shaped patch mimics a physiologic contour of the reconstructed diaphragm allowing physiologic repositioning of the abdominal content (schematic: stomach in red and spleen in blue), preserving the angle of His. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Careful patient selection with an estimated small defect size and no clinical signs of pulmonary hypertension. Thoracoscopic implantation of a cone-shaped patch was not found to be advantageous as its stiffness makes the procedure more challenging and operating time is longer.

Longitudinal follow-up with serial radiologic screening is essential to identify recurrences early to be able to treat them before they may become life-threatening and cause severe morbidity not only during childhood but also in adolescence and adulthood. There seems to be a substantial risk for women after CDH repair during pregnancy, as they are also at high risk of detrimental effects for both mother and fetus in undiagnosed recurrent CDH [14–16]. Furthermore unspecific signs of recurrent CDH may be misinterpreted by general practitioners less aware of CDH due to its rarity.

3. Prosthetic patches – the filamentous knitted polyester fabric patch

Current dogma suggests that Type C and D diaphragmatic hernias cannot be repaired by direct apposition of diaphragmatic muscle to muscle or muscle to the thoraco-abdominal wall [3,17). Under these circumstances the surgeon is faced with the need to bridge the gap and restrain the abdominal content while allowing necessary pulmonary expansion. Many different artificial materials have been used around the world. A simple GORE-TEX™ polytetrafluoroethylene (PTFE) patch was used in over 60 % of the repairs from a large systematic review published in 2024 [18]. This material, while being inert, does not allow tissue integration and is prone to infection and risk of migration or extrusion. GORE-TEX™ (Livingston, Scotland, UK) is now no longer commercially available in the UK and as such many surgeons will be considering what is available to them to repair large diaphragmatic defects. At Great Ormond Street Hospital in London, the Sauvage™ (Bard, New Jersey, USA) soft tissue patch has been used most recently. This patch (Fig. 3) is constructed of knitted polyester (polyethylene terephthalate PET). The knitted construction resists fraying at the cut edge while maintaining integrity of the patch. Reference markings every 2 cm on the surface of the patch assist in accurate assessment of size and cutting of the patch to match the defect. It is primarily designed for use in cardiovascular procedures as in onlay grafts, but also possesses ideal characteristics for use in bridging large diaphragmatic defects including: 1) Pliability, in order to be able to fit easily into the diaphragmatic defect without pressure effect or local structures; 2) It is easy to suture and maintain tensile strength close to the perimeter; 3) It can be tailored to mimic a dome in the neo-diaphragm; 4) It allows tissue incorporation, thus resisting infection and resultant extrusion, and 5) Its soft nature and pliability of the graft make it ideally suited to thoracoscopic repair as it can be sited in the thorax through the larger working port and manipulates safely without danger to surrounding structures.

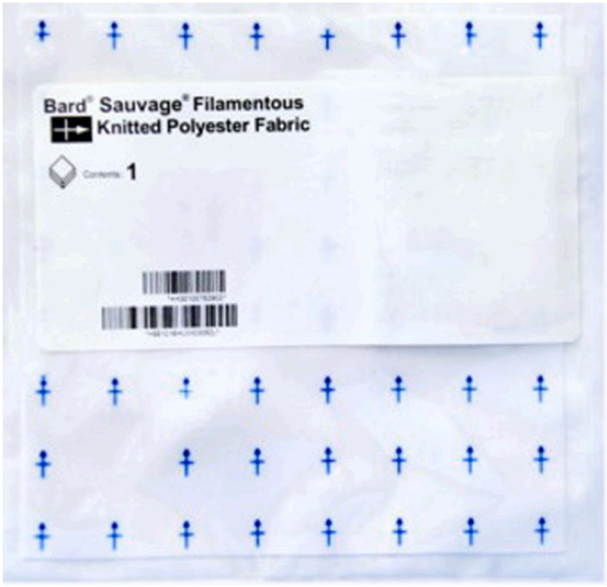

Fig. 3. Sauvage® knitted patch.

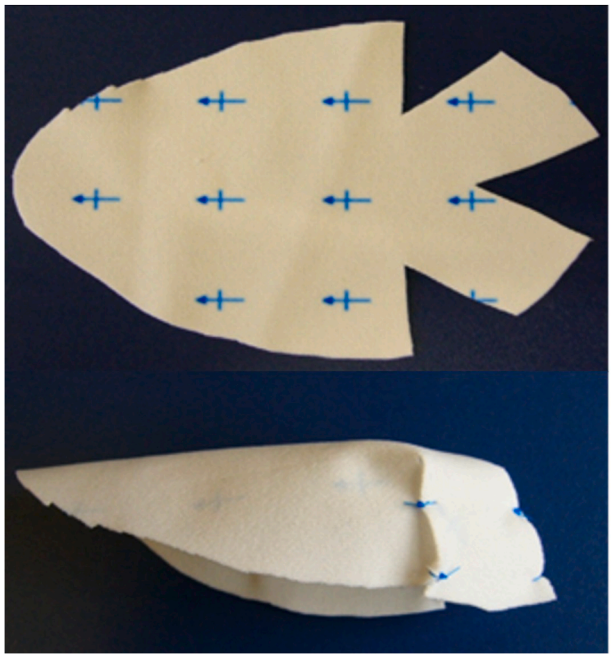

Fig. 4. Template to create a domed structure.

3.1. Surgical technique

A left-sided transverse or subcostal incision is preferred In open surgery. The contents of the hernia are reduced, and the perimeter of the defect is ascertained. Any associated hernia sac would be excised to mitigate against future recurrence. An approximate internal measure of the defect is obtained and the patch then cut to size. The patch can be tailored to create a dome effect. Figure 4 shows the author's (JC) preferred method of creating such a domed effect by cutting out a template and then use non-absorbable sutures to create a 3D domed construction to better accommodate contents back into the abdomen and lessen the thoracic size into which the small ipsilateral lung must expand into.

Monofilament, non-absorbable sutures are used to attach the graft to the perimeter of the defect and where no such rim exists the suture will be placed around a rib. No drain is required to be placed. In minimally invasive surgery the same principles of patch deployment are seen. If a sac is seen, it is not necessary to excise this as the graft will lie superior to the abdominal content. In some circumstances it can be expedient to suture some parts of the graft with continuous suture (Fig. 5).

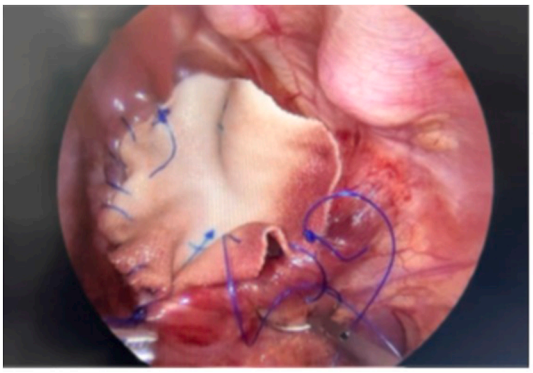

Fig. 5. Patch being sutured into place thoracoscopically.

3.2. Outcomes

A recent meta-analysis shows that patch-repaired patients have a 2.8x higher risk of recurrence with also a significant risk of developing a chylothorax [19]. Most of the studies analyzed showed that the patch material was made either of biological material with an inherent risk of tissue disruption and failure, or PTFE, which is a non-incorporable material and more susceptible to infection. Our unit (GOSH) has analyzed our experience of using the filamentous knitted patch over a 16-year period [20]. Two hundred and three patients were included in the analysis, 107 patients had their diaphragm closed utilizing a patch, the majority being the Sauvage® patch. We compared these to 96 children who had primary repair of their defects. As one would expect there was a higher rate of preoperative ECMO, liver herniation and absence of any significant postero-lateral muscle rim in the patch repair group. We did not observe a statistically significant difference in the incidence of recurrence between patients who were repaired with patch compared to those who were not. No patch had to be removed because of infection. Over the time of this series an increasing number of patients were repaired using patch material, 26 % in the cohort at the start of the study to 80 % in the latter cohort of the study period, to mitigate any tension in the repair. We observed an actual decrease in hernia recurrence being 9.5 % in the first cohort to 3.4 % in the latter. This has led us to conclude that it is better to conduct a repair without tension using this patch material rather than to strive to create a repair primarily without patch.

Near or complete agenesis of the diaphragm, Type D, will always be a challenge and we must accept that no artificial patch will have growth potential [21,22]. We have as yet not combined the use of this patch with an autologous muscle flap technique in the neonatal period but have favored latissimus dorsi flap reconstruction should later recurrence occur. We advocate early and regular follow up clinically and with chest x-rays for all type C and D defects.

4. Evolution of the use of muscle flaps in CDH

From the early to mid-1900s, surgeons have explored a wide variety of methods to treat congenital diaphragmatic hernias (CDH) not amenable to primary repair. Before synthetic materials came along, many body structures such as skin, rib cage, liver, dura, pericardium, and the gastric wall among others, were used to cover the diaphragmatic defect [23–27]. The first reports of CDH repairs using muscle flaps were published in the 1960s and 1970s, but those techniques became somewhat forgotten due to the advent of synthetic patches [28–30] The immediate advantage of synthetic patches was their versatility to be used on CDH defects of any size and shape, and even in cases of diaphragmatic agenesis. Of the different muscle flap techniques, the one that to some degree remained in use was the one published by Simpson et al. in 1971 [28]. In that technique, the internal oblique and the transversus abdominis muscles of the abdominal wall are used to cover the CDH defect. They are divided transversely at the level of the umbilicus, dissected off the external oblique all the way up to their insertion in the costal margin, and divided on the midline from their contralateral counterparts. With this, the flap has a triangle-like shape with a curved base on the anterolateral abdominal wall. The flap is then flipped posteriorly to cover the CDH defect. The transverse edge is sutured to the posterior diaphragmatic rim or posterior abdominal wall, and the vertical edge is sutured to the medial diaphragmatic rim, or the left crus if there is no medial diaphragmatic rim. Of note, if there is an anterolateral diaphragmatic rim, it remains as a hidden edge of tissue above the muscle

flap. The external oblique remains as the only muscle layer of the abdominal wall in the area where the flap was created. As experience with synthetic patches increased, so did the incidence of several complications such as recurrence due to lack of growth and infections due to the presence of foreign material. While the overall incidence was low, several groups begun comparing the outcomes of muscle flaps repair *versus* patch repairs in the 2010s. In 2012, Barnhart et al. published a comparison between 10 patch repairs (5 synthetic patches and 5 human skin-derived biologic patches) versus 23 muscle flap repairs, with an overall follow up of >4 years [31]. They observed a 50 % recurrence rate in the patch repair group versus a 4 % recurrence rate in the muscle flap repair group. In 2019 Dewberry et al. published a comparison between 30 patch repairs (PTFE) *versus* 40 muscle flap repairs (transversus abdominis only) [32]. They observed a 10 % recurrence rate in the patch repair group versus a 3 % recurrence rate in the muscle flap repair group. On a similar trend, Aydin et al. reported in 2020 an 8.8 % recurrence rate in the patch repair group (n = 34) versus a 3.5 % recurrence rate in the muscle flap repair group (n = 57) on 5 years of follow-up [33]. A similar finding was recently published in the largest comparison to date, 80 muscle flap repairs *versus* 15 patch repairs, with recurrence rates of 6.3 % and 46.7 %, respectively, at a median follow up of 5 years [34]. In addition to the perceived higher incidence of recurrence, synthetic patches have an intrinsic risk of infection, which is a complex issue in terms of diagnosis and treatment. Patch infections may manifest with a variety of subtle signs such as digital clubbing, chronic low oxygen saturation, and elevated inflammatory markers. Patch infections can occur decades after the CDH repair [35]. In contrast, muscle flaps carry a near-zero risk of infection.

Using the transversus abdominis and the internal oblique muscle for the CDH repair results in an area of weakness of the abdominal wall on the donor site. This typically presents initially as an abdominal wall bulge, which tends to improve spontaneously in the first years after the repair. Most patients do not need any intervention, and the need for an abdominoplasty has only been reported anecdotally [36–38]. Another potential side effect of CDH repairs is the development of skeletal deformities, which can occur with muscle flaps and with patches. Several studies have shown a low, similar rate of scoliosis after muscle flaps and patch repairs [32,34,38].

A particularly challenging situation is the CDH repair in patients that are on ECMO. The indications and timing for CDH repairs on ECMO are still controversial and certainly beyond the scope of this article. However, even though there are perceived advantages and disadvantages, it is well known that since patients on ECMO are heavily anticoagulated, on-ECMO CDH repairs are associated with a higher blood loss than off-ECMO CDH repairs. The use of a patch typically requires tissue dissection to create edges of tissue to anchor the patch. Additionally, patches require to be sutured along their entire circumference, which means passing needles through tissue multiple times. In contrast, using a muscle flap only requires a tissue rim on the posteromedial side of the defect, since the flap is naturally anchored in the anterolateral side of the abdominal wall. In addition, the plane between the external oblique and the internal oblique muscles is mostly avascular. Several groups have published comparative data between on-ECMO CDH repairs using a patch *versus* using a muscle flap. Brant-Zawadzki et al. compared a small group of seven patch repairs *versus* five muscle flap repairs, all on ECMO [39]. They observed that 2 of the 7 patients in the patch repair group, versus 0 of the 5 patients in the muscle flap repair group required a reoperation for postoperative bleeding. In contrast, Nolan et al. found no significant differences in the bleeding-related reoperation rate or the need for transfusions between a group of 13 patch repairs and a group of 16 muscle flap repairs [40]. Vaughn et al. recently reported a comparison between larger groups: 18 patch repairs versus 34 muscle flap repairs [41]. They observed a significantly higher bleeding-related reoperation rate in the patch repair group than in the muscle flap repair group (23.5 % *versus* 55.6 %, respectively; P = 0.045). Similarly, they observed a higher requirement for transfusion in the first 48 postoperative hours in the patch repair group than in the muscle flap repair group (273.5 mL/kg vs 132 ml/kg; p = 0.006) [41].

For the reasons delineated above, in the last few years many groups in the United States have adopted the muscle flap repair. At the Children's Hospital of Philadelphia, we perform 40–50 CDH repairs/year, about 50 % of which are primary repairs. Up until the year 2020 virtually all non-primary repair CDHs were repaired using a PTFE patch, whereas muscle flaps were used anecdotally mostly for the repair of recurrent CDHs. Since 2020, we have gradually changed our practice, and we currently use muscle flaps in >90 % of CDH repairs not amenable to primary closure (Fig. 6).

5. Tissue engineering of the diaphragm

Prosthetic patches have been widely used for the repair of CDHs and more liberal use achieving a tension-free repair has been associated with improved recurrence rates [9,17]. Furthermore, an evolving population with larger defects due to advances in antenatal therapies require prosthetic patches; >90 % of infants undergoing fetal endoscopic tracheal occlusion (FETO) require prosthetic patch repair [42,43]. However, recurrence remains a major issue. Despite the development of resorbable scaffolds aimed at remodeling the diaphragm as they degrade, recurrence remains at 17 % overall [44]. To address this problem, we must understand the reasons for the failure of diaphragmatic repair. The diaphragm represents a challenging environment for tissue engineering. Firstly, it is a dynamic field; respiratory movements challenge the repair immediately post-implant and rib cage growth represents an ongoing mechanical stressor [45]. The most rapid period of rib cage growth occurs during the first 2 years of life, reflecting the period for most recurrences [9]. Secondly, the defect has to be bridged by the scaffold, therefore unlike on-lay scaffolds, the repair does not benefit from cell migration and neovascularization through direct tissue contact [46]. A vascular network is necessary for cellular migration and scaffold remodeling. Spontaneous vascular network ingrowth into scaffolds from angiogenesis is slow: 5 μm/h [47]. The average human CDH defect is relatively large, at 9 cm^2 [48]. An established vascular network would take 6 months with cellular infiltration from the peripheries of the scaffold. During this time as scaffolds degrade without adequate remodeling, mechanical failure is a risk. Thirdly, the environment the scaffold is implanted into is abnormal. The muscular diaphragmatic defect edges demonstrate an increase in quiescent satellite cells, possibly limiting regeneration [49]. Therefore, scaffolds for CDH repair need to overcome these challenges to result in a durable repair.

Following scaffold implantation, the host response to the implanted biomaterial determines remodeling [50]. Evidence in animal models has suggested scaffolds remodel following infiltration by host cells, collagen production and neovascularization [51]. Failure of native tissue ingrowth into both absorbable and non-absorbable scaffolds results in encapsulation, calcification and re-herniation on histology is widely reported [52]. Translating scaffolds to clinical practice requires robust testing in relevant growing animal models. A recent systematic review reported on 51 translation studies in diaphragmatic hernia models (unpublished data). Less than half (43 %) were in growing animals. The majority in dog, rabbit or rat models tested resorbable scaffolds, primarily

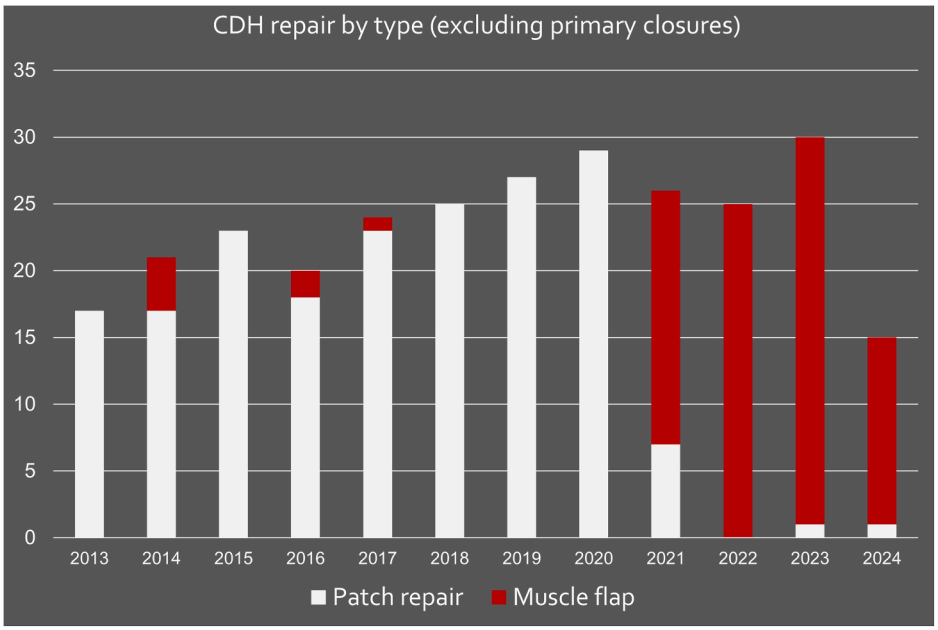

Fig. 6. Type of congenital diaphragmatic hernia repair by year, excluding the primary repairs.

decellularized extracellular matrixes. However, heterogeneity in model creation and in the readouts reported made comparison of scaffolds challenging. Interestingly, the most impressive results were achieved by cellular scaffolds, suggesting the regenerative boast provided by cellular construct beneficial [53–56]. One pre-clinical study investigated a scaffold free 3D printed co-culture of human umbilical vein endothelial cells (HUVEC) and dermal fibroblasts to repair diaphragmatic defect in an immunosuppressed adult rat [53]. This showed muscle, vascular, and neuronal regeneration in diaphragmatic explants suggesting an advantage over clinically used decellularized scaffolds [42]. The feasibility of a scaffold-free 3D printed cell patch to close a larger diaphragmatic defect in an immunocompetent growing animal model has not been tested.

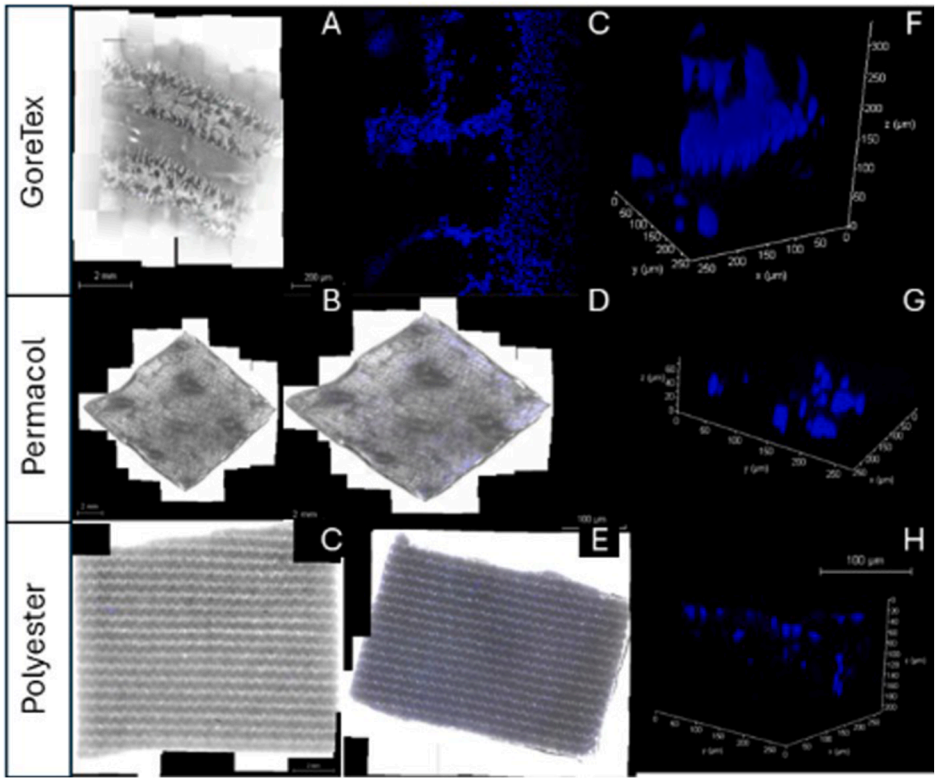

Fig. 7. Confocal imaging of following 48 hs seeding of endothelial colony forming cells on GoreTex (A, C, F), Permacol (B, D, G) and polyester scaffolds (C, E, H); blank scaffolds (A–C), scaffolds + ECFCs (C +D + E) + 3D reconstruction (F, G, H).

Scaffolds have been heavily investigated for orthopaedic tissue engineering. Cell chemotaxis is heavily influenced by the microenvironment [57]. Pore size is closely related to neovascularization and fibrous tissue ingrowth into scaffolds. Endothelial cells are around 60 μm and in biocompatible ceramic materials (i.e. calcium hydroxyapatite), pore sizes smaller than 400 μm have been suggested to limit blood vessel ingrowth and result in fibrosis [58]. Lattices implanted into femurs of growing pigs at 8 weeks showed higher vascularity, greater bone formation and deeper bone ingrowth with larger pore sizes (1100 μm) [59]. Similarly, it has been reported that a pore size of over 89 μm is favorable for myoblast infiltration in collagen sponges [60]. As GORETEX™ (Gore, AZ, USA) is microporous (17–22 μm) it does not permit tissue ingrowth. While optimal pore size for other tissue engineering applications has been extensively studied, the ideal pore size for tissue ingrowth into the diaphragm is not yet known. Permacol™ (Medtronic, MN, USA), a decellularized porcine dermis, has a pore size of 48–100 μm that has been shown to support a range of cell types in survival and growth [61–63]. Polyester scaffolds have large lozenge shaped pores (1000 μm^2) [64]. It is not known which cells are most important in tissue engineering of the diaphragm, however, endothelial cells are vital for neovascularization. Endothelial colony forming cells (ECFCs) are well characterized cells which can be derived from cord blood, peripheral blood, adipose, placenta and lung [65]. They have shown the ability to form microtubules on scaffolds prior to implant [66]. Unlike other progenitor cells, they do not form teratomas, vital for clinical translation. We loaded ECFCS onto 3D printed polymer scaffolds with biomechanical properties favorable to diaphragmatic implant to test cell adherence and survival in vitro [67]. We also loaded ECFCs onto GORETEX™, Permacol™ and polyester scaffolds to test cell survival and adherence at 48 hs (Fig. 7). Preliminary results suggest cell adherence and survival to all three scaffolds, particularly to GORETEX®. Furthermore, bioreactors can modify conditions during seeding, applying tensile forces or flow across scaffolds which may condition cell behavior to the stresses that they will experience in situ. For example, Liao et al., sandwiched scaffolds in an infusion chamber prior to diaphragmatic implant, with media and cells pushed across the scaffold via manually applied hydrostatic pressure [68]. He reported improved donor cell implantation into the scaffold on confocal microscopy. Similarly, Maghin et al., designed a customized bioreactor which applied radial force to tissues to influence cell behavior [69]. They reported a significantly higher percentage of cells in the lower construct side (38.1 %) compared to seeding in static culture (22.1 %) after 7 days.

Alongside adequate elasticity and strength, an ideal scaffold for CDH repair would be gradually remodeled as it is resorbed to maintain strength whilst promoting tissue ingrowth. There are many questions unanswered about the ideal scaffold material, the optimal cell type required for diaphragmatic engineering and how these would be procured for use in a neonate at the time of CDH repair. Rigorous research in standardized animal models using translatable solutions is required to improve tissue engineering in this often-unrepresented population.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors readily acknowledge the valuable contribution made by other contributors to the Symposium and specifically Sean Marven (Sheffield), Gregor Walker (Glasgow), and Kokila Lakhoo (Oxford). Some editorial contributions were suggested by Mark Davenport.

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