International Survey on the Management of Congenital Diaphragmatic Hernia

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Abstract

Aim This study aims to define patterns in the management of congenital diaphragmatic hernia (CDH).

Methods A total of 180 delegates (77% senior surgeons) from 44 (26 European) countries completed a survey at the 2014 European Pediatric Surgeons’ Association meeting.

Results Overall, 34% of the surgeons work in centers that treat < 5 cases of CDH/y, 38% work in centers that treat 5 to 10 cases/y, and 28% work in centers that treat > 10 cases/y. Overall, 62% of the surgeons work in extra corporeal membrane oxygenation (ECMO) centers and 23% in fetal surgery centers. Prenatal work up and delivery: 47% surgeons request prenatal magnetic resonance imaging, 53% offer karyotyping, 22% perform a fetal intervention, 74% monitor head-to-lung ratio, and 55% administer maternal steroids. Delivery is via cesarean section for 47% surgeons, at 36 to 38 weeks for 71% surgeons, and in a tertiary care center for 94% of the surgeons.
Introduction

The management of infants with congenital diaphragmatic hernia (CDH) is complex and far from being standardized. Different strategies have been adopted to improve outcome for this rare condition and overcome single-center experiences by introducing national surveys, international registries, and multicenter studies. In 1995, the Congenital Diaphragmatic Hernia Study Group was established as an international voluntary group of interested participants committed to develop a registry of infants born with CDH.\(^1\) The Canadian Pediatric Surgical Network (CAPSNet) was developed specifically to collect standardized data on every case of CDH evaluated in the 16 referral perinatal centers in Canada.\(^2\) Total 13 pediatric surgical centers in the Scandinavian countries (Denmark, Finland, Norway, and Sweden) joined forces and completed a questionnaire evaluating various aspects of CDH management, such as prenatal diagnosis, intensive care strategies, operative treatment, and long-term follow-up.\(^3\) More recently, a group of European experts funded the CDH EURO Consortium with the aim to produce a consensus statement to achieve standardized treatment across the continent.\(^4\)

Despite all these efforts, many aspects of CDH management are still sources of disputes. There are some evergreen debates on the type of suture material or biological versus synthetic patches and some more recent ones on novelties such as fetal intervention and minimally invasive surgical techniques.\(^5\)

The aim of the present study was to evaluate the current view of pediatric surgeons on controversial issues, and to ascertain the degree of treatment variation among pediatric surgical centers.

Methods

A questionnaire on Bochdalek posterolateral CDH was administered to delegates attending the 15th Congress of the European Pediatric Surgeons Association (EUPSA; June 18–21, 2014; Dublin, Ireland) and collected on the last day of the conference. Respondents were asked to fill in their position (Head of Department/Permanent Staff or Consultant/Trainee), hospital, and country of practice.

The questionnaire focused on the prenatal work up and delivery, postnatal management, surgery, postoperative management, and follow-up of infants with CDH (→ Fig. 1). This survey did not include questions about the management of Morgagni hernia or diaphragmatic eventration.

Overall, 180 delegates, including 12 heads of department, 127 consultants, and 22 trainees, completed the questionnaire. A total of 19 delegates did not disclose their degree. On 164 questionnaires, respondents reported their country of origin: 127 were from 26 European countries (59%) and 37 from 18 non-European countries (41%).

Results

Centre

Overall, 61 (34%) respondents work in centers that treat less than 5 cases of CDH a year, 67 (38%) reported working in a center that treats 5 to 10 CDH cases a year, and 50 (28%) in a center that treats more than 10 CDH cases a year. The majority of the respondents (111, 62%) work in a center that offers extracorporeal membrane oxygenation (ECMO), whereas a minority (41, 23%) work in a center that offers fetal surgical interventions.

Prenatal Work Up

Prenatal imaging consists of ultrasonography alone for 93 (53%) respondents, whereas 83 (47%) request prenatal magnetic resonance imaging. Of the 125 (74%) surgeons who monitor head-to-lung ratio (LHR), only 49% record the observed/expected LHR ratio.

Antenatal karyotyping is routinely offered by 92 (53%) surgeons. Fetal intervention is proposed by 37 (22%), and maternal steroids are administered by 90 (55%) surgeons.

Delivery

The preferred delivery mode for CDH neonates is spontaneous vaginal for 76 (46%) surgeons and elective cesarean section for 69 (42%); 20 (12%) surgeons rate the two delivery modes the same. The majority (104, 71%) of surgeons encourage delivery between 36 and 38 weeks of gestation, 41 (28%) after the 38th week, and only 2 (1%) prefer a delivery earlier than 36 weeks. In 94% of the cases, surgeons want CDH neonates to be delivered in a tertiary center, whereas 6% opt for local hospital delivery.

Postnatal Management

Postnatally, most surgeons report that CDH neonates are electively intubated (128, 76%), and are routinely treated with prophylactic antibiotics preoperatively (110, 65%). Routine administration of surfactant is reported by 75 (45%) respondents. In case of severe refractory hypoxia, 113 (66%) surgeons consider ECMO, even if not present in their center, with a variable course (<, 14 days for 46%, 14–28 days for 8%, and > 28 days for 46%). Parenteral feeding is started preoperatively by 94 (56%) surgeons. Only 22 (13%) surgeons...
Congenital Diaphragmatic Hernia Survey

Head of Department / Permanent Staff or Consultant / Trainee (please circle as appropriate)

Hospital..............................................................................................................Country..............................................................

How many patients with CDH does your Centre treat per year?
☐ <5  ☐ 5-10  ☐ >10

Do you work in an ECMO Centre?
☐ Yes  ☐ No

Do you work in a Fetal surgery Centre?
☐ Yes  ☐ No

Prenatal

Which imaging do you request prenatally?
☐ US alone  ☐ US + MRI

Do you routinely offer karyotyping?
☐ Yes  ☐ No

Do you offer fetal intervention?
☐ Yes  ☐ No

If Yes, which type?

Do you monitor the head-to-lung ratio (LHR)?
☐ Yes  ☐ No

If Yes, which one do you monitor?
☐ LHR  ☐ observed/expected (o/e) LHR

Do you administer maternal steroids?
☐ Yes  ☐ No

Delivery

Mode  ☐ Vaginal  ☐ C-section

Time  ☐ <36w  ☐ 36-38w  ☐ >38w

Place  ☐ Local hospital  ☐ Tertiary centre

Postnatal

In your practice, are all CDH infants intubated electively?
☐ Yes  ☐ No

Do you routinely start antibiotics preoperatively?
☐ Yes  ☐ No

Do you use surfactant in all CDH infants?
☐ Yes  ☐ No

In severe refractory hypoxia do you consider ECMO?
☐ Yes  ☐ No

If on ECMO, what is the maximum course (days)?
☐ <14  ☐ 14-28  ☐ >28

Do you start parenteral feeding preoperatively?
☐ Yes  ☐ No

Do you request a pre-op contrast study looking for malrotation?
☐ Yes  ☐ No

Which prognostic factors do you consider? (tick >1 if necessary)
☐ Defect side  ☐ Liver-up

☐ Stomach-up  ☐ LHR  ☐ o/e LHR  ☐ Oxygenation Index  ☐ Other: ..........................................................

Fig. 1  Questionnaire administered to delegates attending the 15th European Pediatric Surgeons’ Association Congress; June 18–21, 2014; Dublin, Ireland.
<table>
<thead>
<tr>
<th>Surgery</th>
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<tbody>
<tr>
<td>The decision to operate is made by?</td>
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<tr>
<td>Which approach in stable left-sided CDH?</td>
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<td></td>
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<tr>
<td>Which approach in stable right-sided CDH?</td>
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<td></td>
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<tr>
<td>Do you excise the hernial sac, if found?</td>
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<tr>
<td>Which suturing technique do you favour?</td>
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<tr>
<td>In case of large defect, what do you favour?</td>
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<tr>
<td>If patch repair, what is your preference?</td>
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<td>Do you have experience with muscle flaps?</td>
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<tr>
<td>Do you intraoperatively check for malrotation?</td>
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<tr>
<td>If malrotated, do you perform a Ladd’s procedure?</td>
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<tr>
<td>If YES, do you do an appendicectomy?</td>
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<tr>
<td>Do you routinely leave chest drains?</td>
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<tr>
<td>If on ECMO, when do you perform CDH repair?</td>
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<tr>
<td>Postoperative management</td>
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<tr>
<td>Do you electively leave the patient paralysed?</td>
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<tr>
<td>If YES, for how long?</td>
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<tr>
<td>How do you check for compartment syndrome?</td>
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<tr>
<td>When do you start feeding postoperatively (days)?</td>
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<tr>
<td>Which feeding modality do you favour?</td>
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<td>Do you routinely start anti-reflux medications?</td>
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<tr>
<td>Follow-up</td>
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<tr>
<td>How long is your follow-up (years)?</td>
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<tr>
<td>Do you request a chest X-ray at every clinic appointment?</td>
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<td>Do you perform lung function tests?</td>
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<td>Do you request a hearing test?</td>
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<td>Do CDH survivors have a neurodevelopmental follow-up?</td>
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<td>If yes, when?</td>
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<tr>
<td>In case of recurrence</td>
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<tr>
<td>Would you change your operative approach?</td>
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<tr>
<td>Would you do it thoracoscopically?</td>
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<tr>
<td>Would you change the patch material?</td>
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<tr>
<td>Would you remove the old patch?</td>
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</table>
request contrast studies preoperatively to rule out malrotation. The most commonly used prognostic factors for CDH are liver-up position (81%), defect side (66%), oxygenation index (56%), LHR (48%), and stomach in the chest (36%).

Surgical Management
Most respondents (122, 73%) report that the decision to operate is made by surgeons and neonatologists together. If the neonate is on ECMO, 34 (39%) surgeons perform CDH surgical repair while the baby is still on ECMO (20 [23%] during the first days on ECMO and 14 [16%] during the last days of ECMO), whereas 53 (61%) surgeons wait for surgery until the neonate is off ECMO.

Surgeons have different approaches if the diaphragmatic defect is left- or right-sided (Fig. 2). In case of left CDH, 115 (70%) surgeons opt for laparotomy, 38 (23%) for thoracoscopy, 8 (5%) for an open thoracic approach, and only 3 (2%) for laparoscopic repair. In case of right CDH, 100 (61%) surgeons consider laparotomy, 32 (20%) thoracoscopy, 27 (17%) thoracotomy, and 4 (2%) laparoscopy.

The majority of surgeons (83%) excise the hernial sac if present. The favorite suturing technique is interrupted stitches for 90% respondents and running stitches for 10%. In case of large defect, 142 (89%) surgeons prefer to use a patch with the most commonly employed being GoreTex (79%; Gore Medical, Flagstaff, Arizona, United States), followed by Permacol (9%; Covidien, Dublin, Ireland) (Fig. 3); a muscle flap is chosen by the remaining 17 (11%) surgeons. Only 31% of all responders are familiar with the use of muscle flaps.

Intestinal rotation is checked intraoperatively by 113 (70%) surgeons and corrected by 104 (64%); of the surgeons who perform a Ladd procedure in patients with CDH, 69% surgeons perform an appendectomy.

One-third (57, 35%) of surgeons routinely leave a chest drain at the end of the surgery.

Postoperative Management
Following CDH repair, 56% surgeons electively leave the patient paralyzed: 53% for less than 2 days, 34% for 2 to 5 days, and 13% for more than 5 days.

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Follow-Up
The length of follow-up varies among responders: less than 2 years for 10% surgeons, between 2 and 5 years for 33%, between 5 and 10 years for 29%, and more than 10 years for 28%. Chest radiography is requested by 45% surgeons at every clinic appointment. Further follow-up investigations include lung function tests that are requested by 56% surgeons, hearing tests requested by 52%, and neurodevelopmental assessment requested by 75%.

In case of hernia recurrence, 66% surgeons would take the same operative approach of the first repair and 29% would perform a thoracoscopic repair, 71% would remove the old patch and 39% would use a different patch material.

Discussion
The present international survey confirms that many aspects of CDH management are still lacking consensus. The quality of data collected by this questionnaire derives from the seniority of the respondents (86% senior surgeons) and the internationality of their centers (26 European and 18 non-European). Different volume centers were homogeneously represented: one-third small-volume, one-third medium-volume, and one-third high-volume center. ECMO was accessible for two-thirds of the respondents, whereas fetal surgical interventions were less available.

Prenatal imaging is invariably common across the centers. Beyond prenatal ultrasonography, almost half of the respondents routinely use magnetic resonance imaging for the prenatal assessment of fetuses with CDH. The increasing number of centers using this imaging modality confirms its value not just for a better visualization of herniated viscera with the more precise distinction of liver and lung parenchyma and evaluation of lung hypoplasia severity, but also for

Fig. 2 Surgical approaches according to the laterality of the defect. L-CDH, left-sided congenital diaphragmatic hernia; R-CDH, right-sided congenital diaphragmatic hernia.
prediction of survival and the need for neonatal ECMO. The LHR, introduced by Metkus et al in 1996 as a way to estimate the degree of pulmonary hypoplasia and mediastinal shift in fetuses with left-sided CDH, is now used for antenatal treatment patient selection and for prediction of postnatal survival.

To overcome the variability due to the gestational age, Jani et al introduced the observed compared with expected (O/E) LHR, in which the LHR is corrected using the expected normal range lung values provided by the cohort of normal fetuses. The O/E LHR also provides a gestation independent prediction of postnatal outcome, whereby values < 15% predict extreme pulmonary hypoplasia and 0% survival, 15 to 25% severe pulmonary hypoplasia and 20% survival, 26 to 45% moderate pulmonary hypoplasia and 30 to 60% survival, and > 45% mild pulmonary hypoplasia and > 75% survival. However, only half of the responders to our survey seem to have engaged with this most recent and accurate way to measure LHR.

Chromosomal defects, most commonly trisomy 21, 18, and 13, are found in 10 to 30% of fetuses with prenatally diagnosed CDH. According to this survey antenatal karyotyping is routinely offered by half of the surgeons, with no differences attributable to geographical, financial, or cultural differences. Although antenatal administration of steroids remains controversial and for some unlike to offer benefit to most fetuses with CDH, its use is reported by more than half of the responders to our survey.

The mode of delivery for CDH neonates has been a matter of debate. In the Scandinavian survey of practice, following antenatal diagnosis of CDH vaginal delivery was encouraged by 8 out the 13 participating centers. However, in an article from the Congenital Diaphragmatic Hernia Study Group, delivery by cesarean section was associated with a slightly better outcome in terms of a significantly higher survival without the use of ECMO, although there was no significant difference in total survival. In the Canadian study from CAPSNet, the mode of delivery varied widely among institutions with cesarean section rates ranging from 0 to 60%. The present survey shows how much the question is unsolved, as half of the surgeons prefer one modality and the other half the other.

Most surgeons prefer the CDH neonate to be delivered in a tertiary center, and this reflects evidence that location of delivery is a significant predictor of mortality for infants with antenatally diagnosed CDH. Postnatally, most surgeons report that CDH neonates are electively intubated and this reflects the recommendations of the CDH EURO Consortium consensus on the treatment in the delivery room that advice immediate intubation.

Although various studies showed that surfactant does not improve survival rate in preterm infants with CDH routine administration is reported by almost half of respondents.

The use of ECMO has been long debated, differences between centers have been widely addressed and a Cochrane review on its use for severe respiratory failure in infants has failed to demonstrate a clear survival benefit for neonates with CDH. However, two-thirds of surgeons responding to the survey would consider ECMO even if not available in their own centers.

The most commonly used prognostic factor for CDH infants is the liver-up position that in a meta-analysis showed a significant correlation with poor prognosis. A European multicenter study demonstrated that liver position, LHR, and primary repair have predictive value, but the most useful predictor among all is the best oxygenation index on day 1. This index could be used to indicate the need for more intensive medical and surgical care, to characterize the severity of a group of infants with CDH and to enable more appropriate comparison between centers.

It is still controversial whether CDH repair is better done on or off ECMO. Bleeding is a major complication in neonates on ECMO and the rationale behind waiting for the infant to be off ECMO is to prevent surgery-related bleeding complications. In 2012, Keijzer et al reported that infants on ECMO had no greater risk of surgery-related bleeding complications after CDH repair. These findings were in contrast with what reported on the Extracorporeal Life Support Organization registry. The CDH study group reported that 54% of infants with CDH on ECMO underwent surgical repair while on ECMO. Conversely, in the current study, 61% surgeons advocated waiting for surgery until the neonate is off ECMO.

All various surgical approaches to CDH repair carry theoretical advantages and disadvantages, and this is mirrored by the heterogeneity of answers we received on the current survey. Minimally invasive surgery is attempted by a minority of surgeons, regardless of the laterality of the defect.

The majority of responders (83%) excise the hernial sac if present. A hernial sac is present in approximately 20% of CDH patients and it seems to be associated with better fetal lung growth and clinical postoperative outcomes. If present, the sac should be excised to avoid leaving a space-occupying lesion in the chest and to ensure proper healing of the defect. Classically, CDH primary repair is accomplished with interrupted simple sutures of a nonabsorbable material. The vast majority of respondents (90%) follow this technique.

When the patient has a large diaphragmatic defect, almost 90% surgeons prefer to use a patch, whereas the remaining surgeons prefer to use a muscle flap. Muscle flaps as an alternative to a prosthetic repair, was proposed by Bianchi et al in 1983. The main advantage of using, for example, a reversed latissimus dorsi muscle flap was the reliable blood supply coming from the lumbar-perforating blood vessels that allows repair to very large defects and the ability to grow with the child. At present, there is no evidence in the literature to suggest that prosthetic repair is superior to muscle flap repair. A single-center study comparing the anterior abdominal wall muscle flap and prosthetic patch repair concluded that the two approaches provide similar short-term and long-term outcomes.

In the present survey, the majority of responders (87%) favor the use of synthetic, nonabsorbable prosthetic patches, and Gore-Tex (polytetrafluoroethylene) is by far the most popular of all. Conversely, Permacol (porcine dermal collagen) is the most used among the natural absorbable prosthetic patches. The argument of which prosthetic material is associated with the lowest risk of hernia recurrence is a classic.
However, more recently some authors have confuted the hypothesis that patch-repaired diaphragms are more prone to recurrence than primary closures. Tsai et al reported a recurrence rate of 5.4% after patch repair versus 4.3% after a primary repair. Similarly, Garriboli et al reported 8.8% after patch repair versus 5.6% after a primary repair. Most likely, high rates of recurrence in patients who underwent patch repair could be due to technical issues related to the size of the diaphragmatic defect rather than characteristics intrinsic to the patch. If this concept is right, then the search for the best patch material becomes less critical. Alternatively, it is also possible that some of the recurrences after primary repair are due to tension of the diaphragmatic closure, which could be eliminated by more liberal use of patches.

About two-thirds of surgeons reported in the present survey that they check and correct intestinal malrotation in infants with CDH. This is another long-standing controversy of CDH surgery. Most infants with CDH are considered to have a degree of intestinal rotation abnormality, ranging from nonrotation (first stage rotation anomaly) to complete malrotation of the bowel. In a retrospective study, Rescorla et al reported that 2.9% patients with CDH not treated for malrotation presented with midgut volvulus. Interestingly, the presence of intestinal malrotation has been noticed also in the nitrofen rat model of CDH. Some surgeons favor the laparotomy approach as this allows inspection of the bowel looking for rotation anomalies, which if found can be corrected with a Ladd procedure.

Interestingly, one-third of surgeons routinely leave a chest drain at the end of the surgery. It has been reported that the chest drain inserted in the CDH repair could cause undue stretch and distension of the lung contralateral to the diaphragmatic defect. Since pneumothorax due to rapid over-expansion of hypoplastic lungs has been reported as a cause of morbidity and mortality in CDH, many institutions stopped inserting chest drains at CDH repair.

In general, most of the postoperative management, such as feeding regimes, is not evidence-based, but rather come from surgeon preference or institutional practice. The results of the present survey mirror this tendency. Gastroesophageal reflux is a known associated problem for CDH infants and it seems to be proportional to the size of the defect. In the recent years, some centers have proposed preventive antireflux surgery at the time of CDH repair, whereas others have been advocating a tailored approach. According to the results of the present survey, only half of the surgeons routinely start antireflux medications in neonates with repaired CDH, whereas the other half would wait for them to be symptomatic.

Given the significant long-term morbidity noticed in CDH survivors, many centers around the world started having and promoting dedicated multidisciplinary clinics for these patients. In such a follow-up clinic the pediatric surgeon is supported by pulmonologists, gastroenterologists, developmental medicine specialists, nutritionists, and dedicated nurses. However, despite this model, follow-up of CDH survivors is very variable across institutions. This is confirmed by the result of the present survey, where a variation was noticed both in length of follow-up and in the type of investigations requested. Among all long-term tests, particular importance is given to the neurodevelopmental outcomes as reported by three quarters of surgeons. This approach is supported by a growing literature that recognized neurodevelopmental dysfunction as one of the most common comorbidity in CDH survivors.

We acknowledge the limitations of the present survey, some due to the intrinsic nature of surveys, and some related to the difficulty in analyzing a very heterogeneous sample size. In general, the reliability of survey data depends on several factors: answers may not be honest and accurate, responders represent an intrinsic selection bias (nonresponders may answer differently), and answer options may be interpreted differently by different responders. Specific to the present survey is the difficulty of analyzing center-specific questions: in some countries, surgical units are organized in a hierarchical model, whereby the chief of the unit drives most of the management decisions; in other countries, instead, units are run by a group of consultants/attending surgeons, each of them represents an independent group with autonomy regarding clinical decision-making. Therefore, if a group of surgeons from the same institution opts for the same patch material in case of a large diaphragmatic defect, it may be hard to interpret whether this is a choice made by the chief of the unit or whether this represents the unanimity of view among peers.

In conclusion, the current survey shows that many aspects of CDH perinatal, surgical, and postoperative management remain controversial even among highly specialized CDH centers. Management decisions such as early delivery, cesarean section, antenatal use of steroids, chest drain, and correction of intestinal malrotation are made by a high proportion of surgeons, despite the lack of evidence in the literature. Conversely, fetal intervention and minimally invasive surgery are offered by a minority. Guidelines for antenatal and postnatal management of CDH should be developed to support multicenter studies.

Conflict of Interest
None.

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