

Effectiveness and properties of the biological prosthesis Permacol™ in pediatric surgery: A large single center experience



Claudia Filisetti ^{a, b, *}, Sara Costanzo ^a, Federica Marinoni ^a, Claudio Vella ^a, Catherine Klersy ^c, Giovanna Riccipetoni ^a

^a “V. Buzzi” Children Hospital, Milan, Italy

^b Department of Surgery, PhD School of Experimental Medicine, University of Pavia, Italy

^c Servizio di Biometria e Statistica, Direzione Scientifica, IRCCS Policlinico San Matteo Foundation, Pavia, Italy

H I G H L I G H T S

- Use of biological prosthesis is well known for the treatment of complicated abdominal defects in adults surgery but not in pediatric surgery.
- We analyzed the largest case series present in the literature in pediatric surgery.
- Looking at our results the use of Permacol™ seems to be safe and feasible in pediatric complicated abdominal wall closure.

A R T I C L E I N F O

Article history:

Received 8 January 2016

Received in revised form

9 March 2016

Accepted 9 March 2016

Keywords:

Pediatric patients

Biological prosthesis

Permacol

Abdominal wall

A B S T R A C T

Introduction: The use of prosthetic patches of non-absorbable materials represents a valid tool in the treatment of abdominal wall and diaphragmatic defects in pediatric age. In recent years research has developed biological dermal scaffolds made from a sheet of acellular matrix that can provide the desired support and reduce the occurrence of complications from non-absorbable implant. We present our experience and a systematic review to evaluate the use of biologic prosthesis for abdominal wall closure in pediatric patients.

Methods: The study from January 2009 to January 2015 involved 20 patients treated with Permacol™ implant. We observed postoperative complications only in patients treated for abdominal wall closure, which is the major indication for the use of Permacol™. We conducted a systematic review and meta-analysis (according to PRISMA) on PubMed/Medline, Scopus and EMBASE regarding the use of biological prosthesis in pediatric population considering the incidence of complications as the primary outcome.

Results: 3/20 patients experienced complications: 2 patients with skin necrosis healed conservatively and 1 of them developed laparocoele. Thus only 1 patient with incisional hernia had significant surgery complication. In patients who were permanently implanted with Permacol™ it has not determined adverse reactions with optimal functional outcome.

Conclusions: In accordance with the few data (case reports and case series) reported in literature about pediatric patients, our experience in different pathologies and applications has shown the effectiveness of Permacol™, in particular for the non-occurrence of infections, that often affect the use of prosthesis.

© 2016 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Abdominal wall defects (giant omphalocele and gastroschisis) and diaphragmatic hernia repair has historically seen the use of

prosthetic patches of non-absorbable materials (Dacron, Polypropylene, Goretex, Goretex dual mesh with antibiotic) which represented a valid solution. However, they are not integrated in the surrounding tissues and can be a source of infection and complications in the medium–long term [1–3]. In the newborn, particularly in case of abdominal wall defects, the prosthesis is usually covered with very thin skin flaps, with poor representation of the subcutaneous tissue, increasing the risk of skin necrosis,

* Corresponding author. “V. Buzzi” Children Hospital, Milan, Italy.
E-mail address: claudiafilisetti@yahoo.it (C. Filisetti).

infection and recurrence of the defect. The case studies, referring to such rare diseases, are numerically limited and there are no prospective randomized trials that allow a comparative analysis of the results. Research in recent years has developed biological dermal scaffolds made from a sheet of acellular matrix that can provide the desired support and reduce the occurrence of complications from non-absorbable implant (Permacol, Alloderm, Surgisis). Since 2001 Permacol™ Biological Implant has been successfully used in some pediatric and neonatal surgical cases, in particular to repair abdominal wall defects and congenital diaphragmatic hernia [4–7]. It is a sterile acellular sheet derived from porcine dermal collagen, indicated for reconstruction, recontouring and reformation of human soft connective tissue particularly where loss of dermis has occurred, and as a supporting tissue in surgical procedures such as abdominal wall hernias and defects. Permacol™ Biological implant is crosslinked for durability and has a low adhesion profile. The main benefits include strength, biocompatibility and incorporation into the host tissue with associated cell and microvascular ingrowth and with no evidence of sensation, irritation or hypersensitivity reaction [8]. At our Institution Buzzi Children's Hospital we have been using Permacol™ Biological implant from 2009, treating a vast series of patients if compared to the literature published to date. We present our experience on the use of biologic prosthesis for abdominal wall closure in pediatric patients trying to define the safety of biological prosthesis in this population. We also report the results of a systematic review performed to give a meta-analytic pooled estimate of the rate of complications, to assess the safety of the procedure.

2. Methods

The study (from January 2009 to January 2015) involved 20 patients treated with Permacol™. Main characteristics of the population analyzed are reported in Table 1. The patients were affected by the following pathologies: 6 giant omphaloceles (1 after abdominal repair with Goretex mesh); 4 gastroschisis (1 associated with colonic aganglionosis); 1 hypoplastic abdominal wall in congenital diaphragmatic hernia (CDH); 1 abdominal wall defect after multiple laparotomies for necrotising enterocolitis (NEC); 4 CDH: 2 late presentations (1 right, associated with pulmonary sequestration and 1 left + Morgagni-Larrey) and 2 recurrences after Goretex implant; 2 cloacal extrophies; 2 bladder neck incontinence, 1 in cloacal extrophy, and 1 in complex uropathies. 9 patients were males and 11 females. The age ranged between 1 day and 9 years. 10 patients were newborns, 6 infants (1 omphalocele after abdominal repair with Goretex mesh, 1 cloacal extrophy, 1 abdominal wall defect after multiple laparotomies for NEC, 2 late presentation of diaphragmatic hernia, 1 recurrence of left diaphragmatic hernia), 4 children (1 recurrence of left diaphragmatic hernia, 1 cloacal extrophy and 2 continent bladder reservoir). For surgical implant of Permacol™ we used large prosthesis (sizing from 5 × 5 cm to 10 × 15 cm). The thickness chosen was 1 mm for all cases. For abdominal wall closure, in cases of omphalocele, gastroschisis, abdominal hypoplasia, and cloacal extrophy, Permacol™ were fixed on the fascia with monofilament synthetic absorbable interrupted stitches (Glycolide-Trimethylene Carbonate 4/0). Sliding skin flaps were necessary to cover the prosthesis in 5 patients (2 giant

omphaloceles, 2 gastroschisis, 1 abdominoplasty in CDH, and 1 cloacal extrophy). (Fig. 1). One case of omphalocele with a large defect was repaired using two prosthesis of Permacol™ of 10 cm each in parallel. As in the previous cases implants were fixed using single stitches of monofilament synthetic absorbable suture (Glycolide-Trimethylene Carbonate 4/0). The Prosthesis was then covered creating wide skin flaps. For diaphragmatic repair we fixed Permacol™ on the edge of the diaphragmatic defect with monofilament synthetic non-absorbable interrupted stitches (Polypropylene 3–4/0). (Fig. 2). In two patients who required the creation of a continent bladder reservoir Permacol was placed to protect the bladder neck closure. Follow-up ranged from 6 months to 6 years (median follow-up time: 20 months). The systematic review of the literature was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) the search was applied in Medline (considering all years), and in Embase (considering all years). Search terms were as follows: “Abdominal biological prosthesis”; “Congenital abdominal wall defect AND biological prosthesis”; “Abdominal wall closure AND pediatric transplant”; “Permacol AND pediatric”; “Alloderm AND pediatric”; “Surgisis AND pediatric”. The Eligibility criteria for the meta-analysis are shown in the Table 1. Statistical analysis: Pooled estimates of complication rates were computed together with their 95% confidence intervals using a fixed effect model using Stata 14 (Stata Corp, College Station, TX, USA).

3. Results

We did not experienced any intraoperative challenges related with Permacol™ implant, the surgical procedure for the correction of the abdominal defects is standardized and is the same technical procedures applied to the non biological prosthesis. Follow-up, ranging from 6 months to 6 years (median follow-up time: 20 months), showed no infections related to the system of Permacol in any case. Three patients (1 gastroschisis; 1 abdominoplasty in CDH, and 1 cloacal extrophy) presented an ischemic necrosis with partial dehiscence of the skin overlying the implant, resulting in surfacing of the prosthesis (see Table 2). They were conservatively treated; the wound healed by secondary intention and removal of the prosthesis was not necessary. However, the patient with hypoplastic abdominal wall in CDH presented a laparocoele. In patients with diaphragmatic hernia, there were no seromas or pleural effusions. After reaching an adequate development of the abdominal wall, patients with gastroschisis and omphalocele were subjected to removal of the prosthesis, at an age between 4 and 17 months (median 11 months), with good functional and cosmetic results. At the second operation in all patients the prosthesis appeared well integrated in the abdominal wall, not adherent to the viscera with the exception of 2 patients (outcomes of giant omphalocele) in which it was partially adherent to the liver. Histological examination showed prosthetic material coated with vascularized connective tissue and mild chronic inflammatory infiltrate, the presence of fragments of muscle tissue was also highlighted. 2/20 (10%) patients (gastro-esophageal reflux in giant omphalocele and incisional hernia in CDH) required implant of a second smaller prosthesis (≤ 5 cm) to allow the closure of the abdominal wall without affecting hemodynamic and respiratory function. In

Table 1

Summary of the eligibility criteria for the review study.

Types of studies	Clinical trials and/or observational studies including case series and case reports
Types of participants	Pediatric patients who had abdominal wall defects treated with biological prosthesis
Types of outcomes	The main outcome was the incidence of surgical complication: infection; post incisional hernia; reintervention.

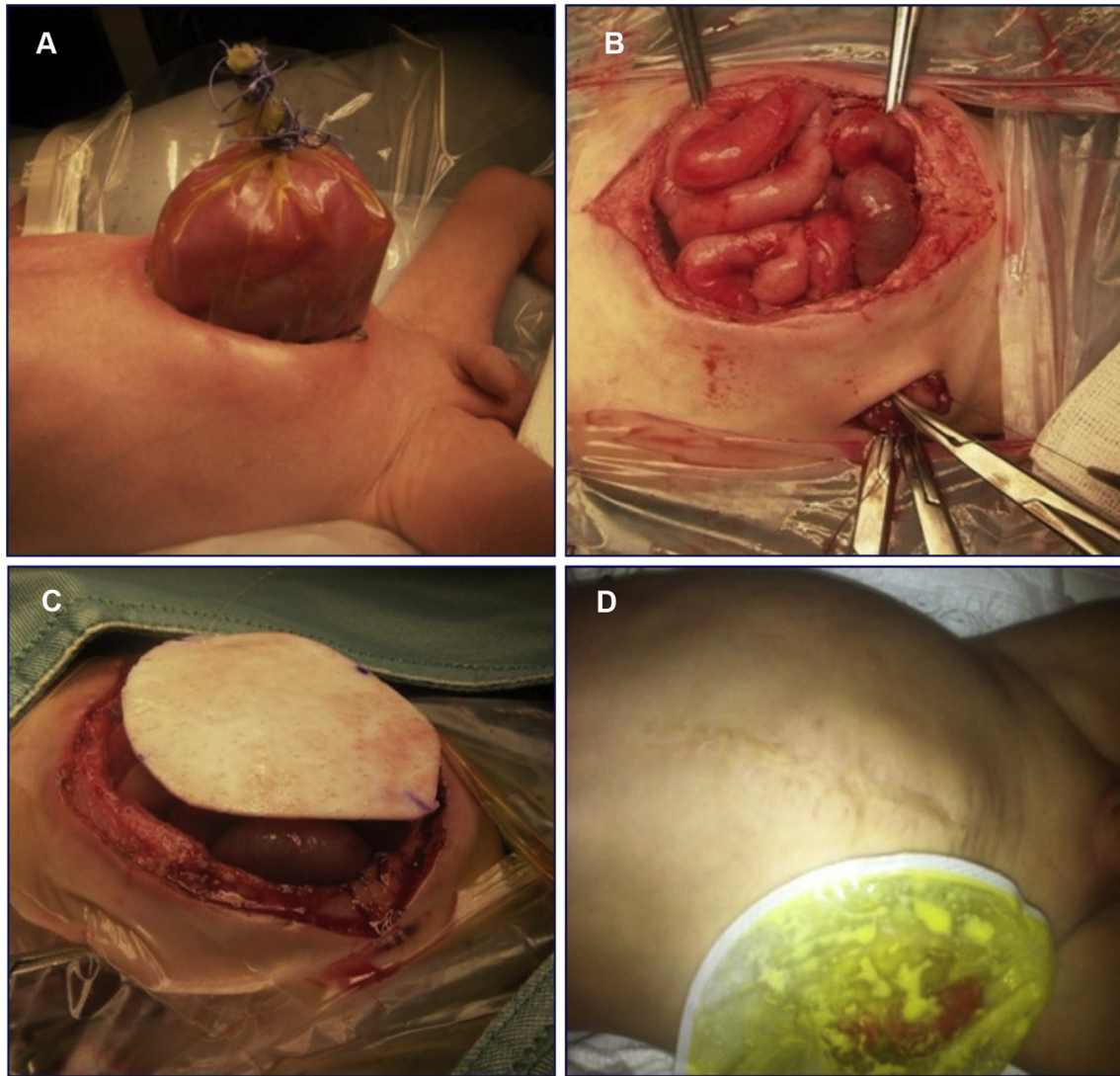


Fig. 1. Use of Permacol™ in the closure of a gastroschisis associated with colonic aganglionosis. A. At birth positioning of silo. B-C) Abdomen closure using Permacol™. D) XI postoperative day.

conclusion 3/20 patients experienced complications: 2 patients with skin necrosis healed conservatively and 1 of them developed laparocele. Thus only 1 patient with incisional hernia had significant surgery complication.

In our review we performed identification and selection following a PRISMA flow diagram (Fig. 3). A total of 114 unique citations were identified in our study. After the application of our inclusion criteria we selected 13 articles. No systematic reviews were found about pediatric population. The overall rate of complications was estimated from the meta-analysis of 13 studies to 27.6% (12.4–42.9). As shown in the Table 3, it ranged from none to 40%, with one exception who reported a rate of 85%. The most frequent types of complications were infection and reintervention, both about 10% (see Fig. 4).

4. Discussion

Many features make Permacol™ a prosthetic implant with high potential: it is biocompatible; immunologically “inert” and does not cause fibrotic encapsulation; sterile; promotes cell growth and revascularization; promotes natural healing of the wound;

maintains strength after implantation; has long life and does not cause viral contamination. Our experience in different pathologies and applications has shown the extreme effectiveness of Permacol™, especially for the non-occurrence of infections that often affect the use of prosthesis. In patients who were permanently implanted with Permacol™ it has not caused adverse reactions with optimal functional outcome. In our patients with abdominal wall defects the prosthesis was removed 4–17 months (mean time 11 months) after the implant, it was well integrated in the abdominal wall, as demonstrated by the histological findings. In the literature, in adult population, grafts perform similarly to synthetic mesh for incisional hernia repair and they are associated with a high salvage rate when infected [9,10]. Authors suggest that cross-linked mesh has the best clinical outcomes in contaminated or infected fields [11–14]. In cases of very complex abdominal wall closure after transplantation, some authors suggest that biological mesh (Permacol, Surgisis, Strattice) allows complete abdominal closure after transplant (liver, intestine, kidney, multivisceral) in children with donor size discrepancy. Biological prosthesis seems to have long term durability with no incisional hernia on short and medium term follow-up [5,15–18]. 3 articles selected in our meta-

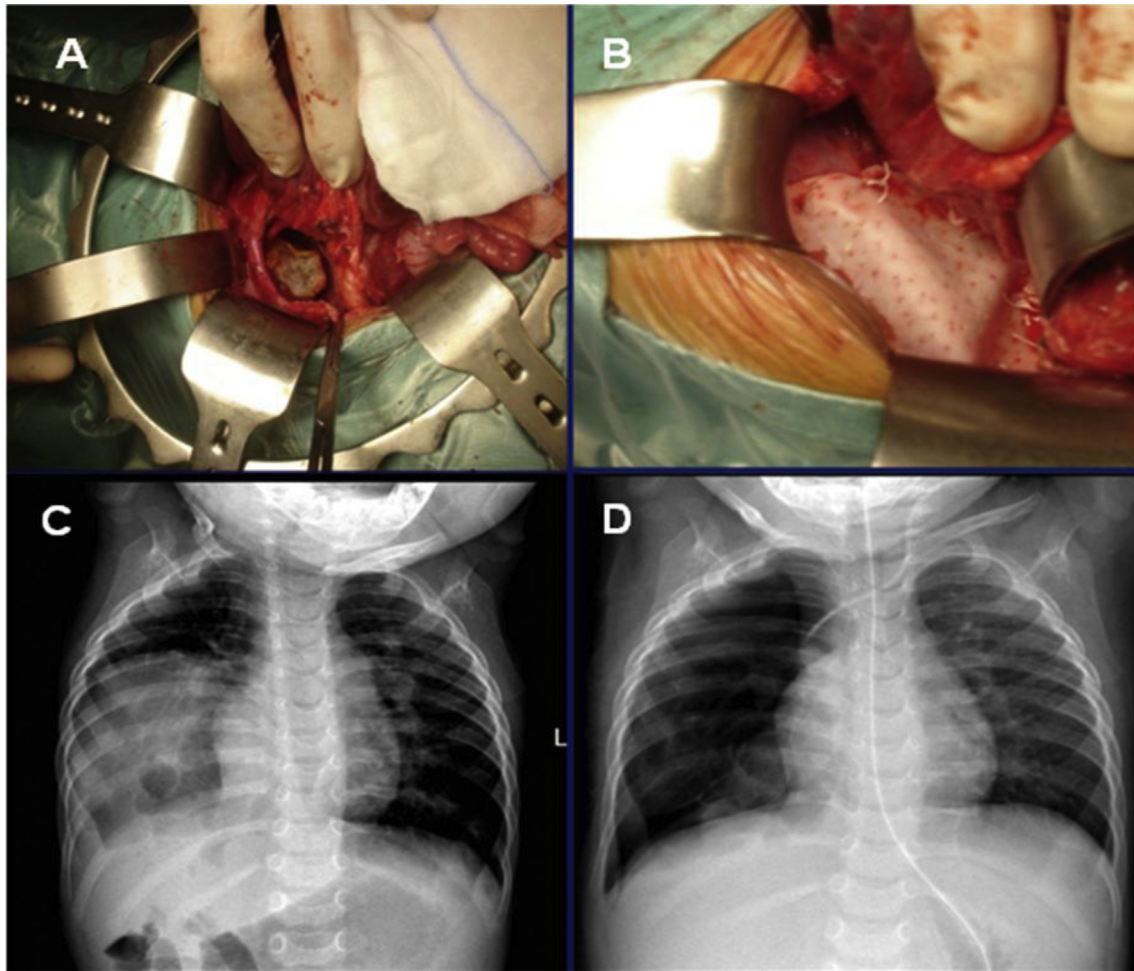


Fig. 2. Right diaphragmatic hernia repair. A) Intraoperative isolation of diaphragmatic defect. B) Closure of the diaphragmatic defect using Permacol™. C-D) Preoperative and postoperative imaging.

analysis assert that Permacol was effective for the reconstruction of the abdominal wall defect in particular cases: multitrauma, conjoined twin, and in assisting abdominal wall closure of pediatric renal transplant recipient [5–7]. Also in the treatment of giant omphalocele biologic mesh was applied as a primary abdominal fascia substitute with good results, no fascial dehiscence or infections were reported [19–24]. The incidence of complications in our case series is in line with the data shown in the meta-analysis. Our systematic review and meta-analysis has revealed that there are few and limited studies published on the application of biologic mesh for pediatric abdominal wall closure (Table 3). There is a relatively high heterogeneity, mainly because they describe different kinds of graft, different patient characteristics and pathologies, different surgical indications and techniques. For this reason a comparison of the data in the literature is really difficult. Low levels of evidence of the case studies presented, lack of randomized studies and of age-related pediatric review only permit to suppose there is a general good outcome using biological prostheses for this kind of disease. With our review and meta-analysis we can conclude that a clear clinical indication for the use of a biological prosthesis rather than a synthetic one still remains a task to deeper investigate. The use of Permacol™ seems to be safe and feasible in pediatric complicated abdominal wall closure. In a contaminated field its use improves the surgical outcome without the need of prosthesis removal even in case of infection. The use of

biological prosthesis allows the abdominal wall closure in patients with congenital abdominal wall defects. The application in case of abdominal wall closure after pediatric abdominal transplantation represents a valid option. In Conclusion we believe that randomized controlled trials might be useful to determine better the specific indication of biological prosthesis application in pediatric abdominal surgery.

Ethical approval

The present clinical study did not require ethical approval.

Sources of funding

We do not have any sources of funding for the present study.

Author contribution

Claudia Filisetti: data collection and writing the paper.
Sara Costanzo: data collection.
Federica Marinoni: data collection and analysis.
Claudio Vella: analysis and interpretation of the data.
Giovanna Riccipetoni: study design and interpretation.

Table 2
Case series summarizing sex, age, pathology, follow-up, and complications.

Case	Sex	Age	Condition	Prosthesis (cm)	Permanent	Removal	Complications
1	M	9 days	Gastroschisis	5 × 10	No	At 8 months	None
2	M	12 days	Gastroschisis	6 × 7	No	Follow-up	Skin necrosis
3	F	1 day	Gastroschisis	5 × 10	No	Follow-up	None
4	M	18 days	Gastroschisis with colonic disganglionosis	4,5 × 6	No	At 17 months	None
5	M	1 day	Giant omphalocele	5 × 6	No	Follow-up	None
6	F	1 day	Giant omphalocele	2	No	Follow-up	None
		11 months		prosthesis 10 × 10			
7	M	1 day	Giant omphalocele	5 × 7	No	Follow-up	None
8	F	1 day	Giant omphalocele	5 × 5	No	At 4 months	None
9	F	1 day	Giant omphalocele	6 × 6,5	No	At 12 months	None
10	M	7 months	Giant omphalocele after Goretex mesh implant	6 × 8	No	Follow-up	None
11	M	12 months	Late presentation of right diaphragmatic hernia associated with pulmonary sequestration	6 × 9	Yes	–	None
12	M	24 months	Late presentation of left + Morgagni Larrey diaphragmatic hernia	7 × 8	Yes	–	None
13	F	28 months	Recurrence of left diaphragmatic hernia	5 × 10	Yes	–	None
14	F	17 months	Recurrence of left diaphragmatic hernia	5 × 7	Yes	–	None
15	M	2 days	Hypoplastic abdominal wall in congenital diaphragmatic hernia	5 × 5,5	No	Follow-up	Laparocele
		17 months		5 × 6			Skin necrosis
16	F	3 months	Abdominal wall defect after multiple laparotomies for NEC	6 × 6	No	Follow-up	Skin necrosis
17	F	2 days	Cloacal extrophy	5 × 10	Yes	–	Skin necrosis
		5 months		7 × 9			
18	F	9 years	Cloacal extrophy	5 × 5	Yes	–	None
19	F	6 years	Urinary incontinence in cloacal extrophy	3 × 4	Yes	–	None
20	F	9 years	Neurogenic bladder in spina bifida	5 × 5	Yes	–	None

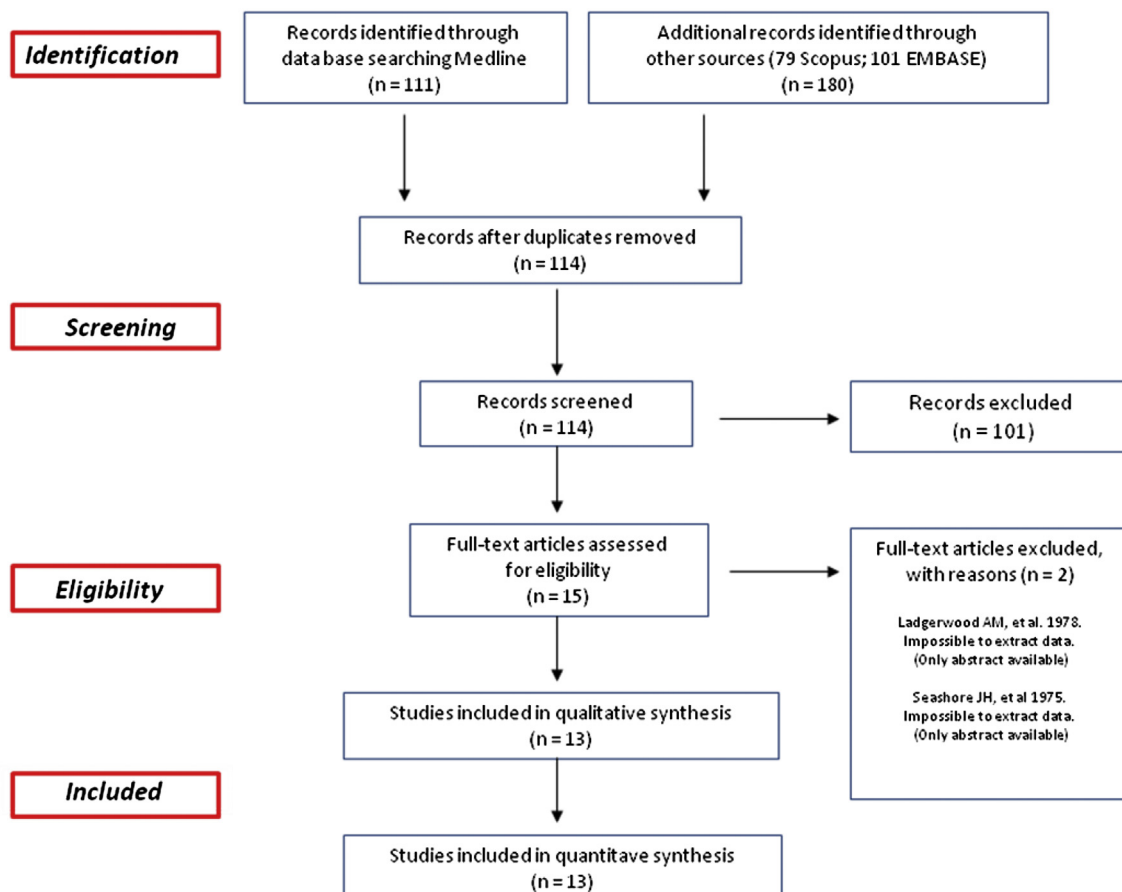


Fig. 3. Search strategy and study selection PRISMA flowchart for the meta-analysis.

Table 3

Meta-analysis of post surgical complication rate. The overall rate of complications was estimated from the metaanalysis of 13 studies to 27.6% (12.4–42.9). It ranged from none to 40%, with one exception who reported a rate of 85%. The most frequent types of complications were infection and reintervention, both about 10%.

Complication	Population (N)	Events (N)	Meta-analytic rate estimate (95%CI)
Any	73	25	27.6% (12.4–42.9)
Infection	73	11	10.7% (0–21.5)
Post-incisional Hernia	73	9	5.5% (0–14.0)
Contaminated Surgical Field	73	6	3.2% (0–11.3)
Reintervention	73	12	9.1% (0–18.8)

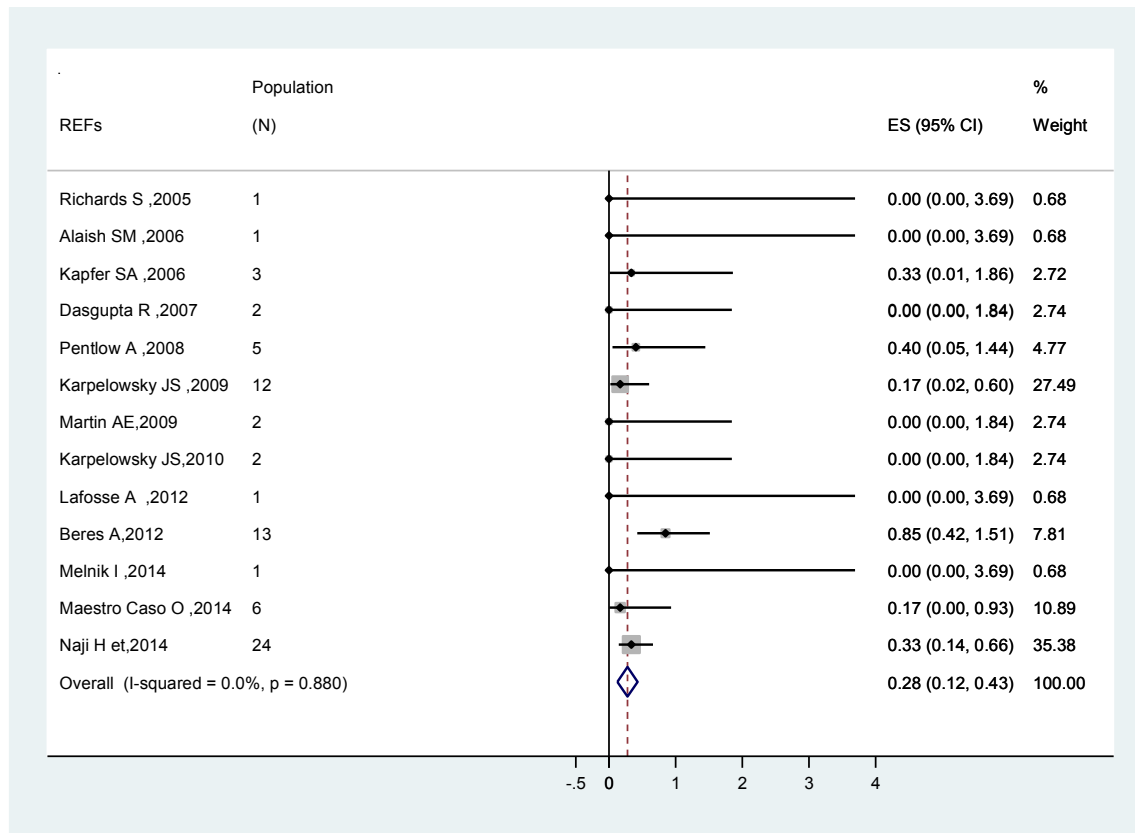


Fig. 4. Meta-analytic estimate of the overall incidence of any complication. Forest plot with the rate of events in each considered study as well as the pooled estimate.

Conflicts of interest

All the authors have no conflicts of interest.

Guarantor

Claudia Filisetti is the guarantor and accept the full responsibility for the present study.

Consent

We obtained the consent for the surgical procedures and for the publication in the present study.

References

- [1] L. Parida, K. Pal, H. Al Buainain, et al., Staged closure of giant omphalocele using synthetic mesh, *APSP J. Case Rep.* 5 (3) (2014 Sep-Dec) 27.
- [2] D. Divkovic, S. Kvolik, M. Sipl, et al., A successful early gore-tex reconstruction of an abdominal wall defect in a neonate with Cantrell pentalogy: a case report and literature review, *Clin. Case Rep.* 3 (1) (2015 Jan) 19–23.
- [3] B. Bekdash, B. Singh, K. Lakhoo, Recurrent late complications following congenital diaphragmatic hernia repair with prosthetic patches: a case series, *J. Med. Case Rep.* 3 (2009) 7237.
- [4] I.C. Mitchell, N.M. Garcia, R. Barber, et al., Permacol: a potential biologic patch alternative in congenital diaphragmatic hernia repair, *J. Pediatr. Surg.* 43 (12) (2008 Dec) 2161–2164.
- [5] A. Pentlow, N.J. Smart, S.K. Richards, et al., The use of porcine dermal collagen implants in assisting abdominal wall closure of pediatric renal transplant recipients with donor size discrepancy, *Pediatr. Transplant.* 12 (2008) 20–23.
- [6] I. Melnik, Y. Mnouskin, E. Verdiger Kurtzbar, et al., Evaluation of a porcine dermal collagen (permacol) implant for abdominal wall reconstruction in a pediatric multitrauma patient, *Case Rep. Emerg. Med.* (2014) 585723.
- [7] J.S. Karpelowsky, A.J. Millar, et al., Porcine dermal collagen (Permacol) for chest and abdominal wall reconstruction in thoraco-omphalopagus conjoined twin separation, *Pediatr. Surg. Int.* 26 (3) (2010 Mar) 315.
- [8] C. Harper, Permacol: clinical experience with a new biomaterial, *Hosp. Med.* 62 (2) (2001 Feb) 90–95.
- [9] C.F. Bellows, A. Smith, J. Malsbury, et al., Repair of incisional hernias with biological prosthesis: a systematic review of current evidence, *Am. J. Surg.* 205 (2013) 85–101.
- [10] N.J. Slater, M. van der Kolk, T. Hendriks, et al., Biologic grafts for ventral hernia repair: a systematic review, *Am. J. Surg.* 205 (2013) 220–230.
- [11] N.J. Smart, N. Bryan, J.A. Hunt, et al., A scientific evidence for the efficacy of biologic implants for soft tissue reconstruction, *Assoc. Coloproctology G. B. Irel.* 14 (Suppl. 3) (2012) 1–6.
- [12] N.J. Smart, M. Marshall, I.R. Daniels, et al., Biological meshes: a review of their use in abdominal wall hernia repairs, *Surgeon* 10 (2012) 159–171.

- [13] E.W. Beale, The role of biologic mesh in abdominal wall reconstruction: a systematic review of the current literature, *Am. J. Surg.* 204 (2012) 510–517.
- [14] W.B. Jawaid, E. Quasem, M.O. Jones, et al., Outcomes following prosthetic patch repair in newborns with congenital diaphragmatic hernia, *Brit. J. Surg.* 100 (2013) 1833–1837.
- [15] S.K. Richards, E. Quasem, M.O. Jones, et al., Porcine dermal collagen graft in pediatric renal transplantation, *Pediatr. Transplant.* 9 (2005) 627–629.
- [16] J.S. Karpelowsky, G. Thomas, A. Shun, et al., Definitive abdominal wall closure using a porcine intestinal submucosa biodegradable membrane in pediatric transplantation, *Pediatr. Transplant.* 13 (2009) 285–289.
- [17] A. Lafosse, C. de Magnee, A. Brunati, et al., Combination of tissue expansion and porcine mesh for secondary abdominal wall closure after pediatric liver transplantation, *Pediatr. Transplant.* 16 (2012) E150–E152.
- [18] O. Caso Maestro, M. Abradelo de Usera, I. Justo Alonso, et al., Porcine acellular dermal matrix for delayed abdominal wall closure after pediatric liver transplantation, *Pediatr. Transplant.* 18 (2014) 594–598.
- [19] A.E. Martin, The use of intraabdominal tissue expanders as a primary strategy for closure of giant omphaloceles, *J. Ped. Surg.* 44 (1) (2009 Jan) 178–182.
- [20] S.M. Alaish, E.D. Strauch, The use of Alloderm in the closure of a giant omphalocele, *J. Ped. Surg.* 41 (3) (2006 Mar) e37–e39.
- [21] S.A. Kapfer, T.H. Kesen, The use of human acellular dermis in the operative management of giant omphalocele, *J. Ped. Surg.* 41 (1) (2006 Jan) 216–220.
- [22] H. Naji, J. Foley, H. Ehren, et al., Use of Surgisis for abdominal wall reconstruction in children with abdominal wall defects, *Eur. J. Ped. Surg.* 24 (1) (2014 Feb) 94–96.
- [23] A. Beres, E.R. Christinson-Lagay, R.L. Romano, et al., Evaluation of Surgisis for patch repair of abdominal wall defects in children, *J. Ped. Surg.* 47 (5) (2012 May) 917–919.
- [24] R. Dasgupta, P.W. Wales, R.M. Zuker, et al., The use of Surgisis for abdominal wall reconstruction in the separation of omphalopagus conjoined twins, *Pediatr. Surg. Int.* 23 (9) (2007 Sep) 923–926.