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GLOSSARY OF ABBREVIATIONS

CWR: chest wall reconstruction
PCWT: primary chest wall tumor
SCWT: secondary chest wall tumor
PMCWT: primary malignant chest wall tumor
LD: latissimus dorsi
PM: pectoral major
ICU: intensive care unit
VATS: video-assisted thoracic surgery
PTFE: polytetrafluoroethylene
BM: biological meshes
PACLIDEM: porcine-derived acellular cross-linked dermal matrix
RT: radiation therapy

CENTRAL MESSAGE

Biological mesh represents a valuable option in chest wall reconstruction, especially in infected or high-risk of infection surgical sites.

PERSPECTIVE STATEMENT

Chest wall reconstruction is still a challenge for surgeons. We report a large multicenter experience in using porcine-derived acellular cross-linked dermal matrix for chest wall reconstruction. Biological mesh showed excellent results in terms of stability, wound healing and no complications related to its use have been reported, suggesting that this material is a safe and valuable option in chest wall reconstruction.
Central Picture

Anterior chest wall reconstruction with cross-linked porcine dermal acellular collagen mesh.

Abstract

Objectives

Aim of the study is to evaluate clinical applications, safety and effectiveness of a porcine-derived acellular cross-linked dermal matrix biological mesh in chest wall reconstruction.

Methods

We retrospectively analyzed a prospective multicenter database of chest wall reconstructions using a biological mesh in adult patients operated between October 2013 - December 2020. We evaluated preoperative data, type of resection and reconstruction, hospitalization, 30-day morbidity and mortality and overall survival.

Results

A total of 105 patients (36 females/34.2%, mean age 57.0 ± 16.1, range 18-90) were included, they have admitted for: primary chest wall tumor n=52 (49.5%), secondary chest wall tumor n=29 (27.6%), lung hernia n=12 (11.4%), trauma n=10 (9.6%) and infections n=2 (1.9%). The surgical sites were pre-operatively defined as at high risk of infection in n=28 patients (26.7%) or as infected in n=16 (15.2%) patients. 30-days morbidity was 30.5% (n=32 patients); 14 patients (13.3%) had postoperative complications directly related to chest wall surgical resection and/or reconstruction. We experienced no 30-day mortality; 1-year and 2-year mortality was 8.4% and 16.8% respectively.

Conclusions

Biological mesh represents a valuable option in chest wall reconstruction even when surgical sites are infected or at high-risk of infections. This mesh shows low early and late postoperative complication rates and excellent long-term stability.
INTRODUCTION

Despite the wide range of prosthetic materials available, the ideal method for chest wall reconstruction (CWR) is still a matter of debate, even if this surgical procedure clearly improves postoperative ventilation, shortens overall hospital stay and aids postoperative pulmonary physiology and mechanics [1-5]. The primary challenge for surgeons is the difficulty in predicting the nature and extension of chest wall defect, because the excision can result in partial- or full-thickness thoracic wall defects [6-8]. Currently there are two ways to cover chest wall defects: prosthetic or biologic mesh and/or soft tissue flaps [9-12]. The introduction of biological prosthetic materials represents an innovation in CWR. Initially used in the 1990’s, extracellular biological meshes provide the extracellular scaffold necessary for tissue healing. Biological meshes (BM) can either derive from human (allograft; derived from dermis, intestinal mucosa or pericardium) or animal (xenograft; usually porcine or bovine) tissues. Most published studies on BM are case series, and their use is limited to contaminated or infected fields for abdominal wall reconstruction where a synthetic mesh is considered strongly contraindicated [7-9].

OBJECTIVES

Here, we show a large multicentric retrospective series reporting the use of the porcine-derived acellular cross-linked dermal matrix (PACLIDEM) for CWR, either alone or in combination with rigid reconstruction. The purpose is to confirm clinical applications, to assess safety and performance, and to evaluate short term and long-term patient outcomes following the use of biological mesh in CWR.
MATERIALS AND METHODS

Retrospectively, we analyzed a prospective multicentre database of chest wall reconstruction using the PACLIDEM mesh 1.5 mm thick named Permacol™ (Covidien, Mansfield, Massachusetts, United States;) in the following Italian university hospitals: Firenze, Pisa, Roma-Umberto I, L’Aquila-Teramo, Chieti.

We evaluated the data in the database from the first case involved in October 2013 through 31st December 2020. The use of the biological tissue matrix was approved by the clinical directorates of the involved Institutes.

Indications for using biological mesh and including patients in the database were: CWR in oncological patients; CWR after trauma; CWR in lung hernia; CWR after resections for infectious disease.

When its potential use was considered in the preoperative planning, patients were advised, and informed consents were obtained; all patients provided also an informed consent for the publication of their study data. Patients <18 years old were excluded. Muslim patients were warned of the porcine origin and biochemical characteristics including the decellularization of the dermis and therefore the absence of genetic material (i.e. DNA). The study was approved first by the University Hospital Careggi (Florence) Institutional Review Board (ID:09, April 2020) and then by the other involved Institutes.

Surgical policy followed in the series

Primary or Secondary Tumours

Our surgical policy in the treatment of chest wall tumours was, in general, as it follows: skin incision included the site of the previous biopsy (in case present) and the invaded skin or previously irradiated tissues; wide resection of a lateral tumour included the affected ribs with at least 3-cm free margin proximally and distally to the tumour and the adjacent portions of one normal rib above and below
the lesion; the extent of surgery in sternal primary tumours (partial subtotal or complete sternectomy) depended on the dimension and the location of the tumour and, in all cases, resection included the adjacent sternocostal cartilages on each side; tumour extension into the chest cavity was evaluated and any other structure involved in the tumour was also excised. Resection and reconstruction were performed as a one-stage procedure in all cases. Every effort was made to wean patients rapidly from the ventilator. The need to perform induction chemotherapy or postoperative chemotherapy and radiotherapy in the case of high-grade sarcomas was discussed and planned with the medical oncologist and the radiotherapist in an oncological multidisciplinary group.

Trauma, lung hernia and infections

In case of benign disease, the reconstruction first aimed to restore chest wall stability, removing, in case of trauma, bone fragments from the pleural cavity and reducing rib and sternal fractures as much as possible. In case of infection, the resection was limited to the compromised bones. Lung herniation usually results from the loss of the intercostal muscle (sometimes of two adjacent intercostal spaces); therefore, primary closure cannot be an option. Indication to surgical correction of lung hernia was the presence of parenchymal herniation, with paradoxical movement of the lung outside the chest, which led lung trauma documented by CT scan and/or by symptoms like hemoptysis or recurrent pneumonia [13]. Even if direct closure has been previously described, based on the anatomy of the defect and the available tissues, we felt more confident by using a mesh repair [14]. The clinical and radiological absence of lung herniation during the follow-up period was considered as measure of success.

Drainages

Pleural drainages were placed whenever the pleural cavity was opened during surgery; policy for their removal was: no air leak in the last 24 hours and fluid production <3ml/kg/24h. As a rule, a Redon
soft tissue drainage was always positioned, mainly in case of an associated muscle flap associated;
policy for their removal was: liquid production of serous quality <50ml/24h.

Data collected in the clinical database

We evaluated preoperative data such as demographics, gender, comorbidities, BMI, chest wall
disease, indication for surgery. Type of resection and reconstruction were considered including the
use of rigid reconstruction or not and soft tissue coverage with muscular or muscular-cutaneous
flap. We also considered the postoperative results evaluating short and mid-term complications
(including post-surgery complications and prosthesis complications), the presence of paradoxical
respiration movements clinically and/or radiologically observed (i.e. lung hernia), hospitalization
time, 30 days and overall survival. Complications were defined as any deviation from the standard
postoperative course [15] and recorded according to the Clavien–Dindo classification [16].

Based on their preoperative characteristics (Figure 1), the surgical sites were classified as it follows:

1. Normal site

2. High risk of postoperative infection:
   a. the surgical site has undergone previous local treatments (i.e. surgery or radiotherapy)
   b. cancer infiltration of soft tissues, without skin involvement.
   c. Giant tumours in which a large amount of prosthetic material is planned for CWR.

3. Infected
   a. cancer with skin ulceration (i.e., local relapse from breast cancer)
   b. trauma with loss of soft tissues and exposed lesions

In case of oncological surgery, resection margins were classified following the Enneking
classification [17], adapted to chest wall surgery, as it follows: wide, marginal, intralesional. The
categories wide and marginal correspond to R0 resection. The Enneking category “radical”
corresponds to limb amputation and cannot be used in chest wall resections. In case of intralesional
resection, the further subdivision in R1 (microscopic infiltration) and R2 (macroscopic infiltration) was used too.

Follow-up consisted in radiological examination (Chest X-Ray and/or CT scan), outpatient visit or phone interview (depending on the disease and the interval from treatment).

Data will be presented with median and interquartile range for continuous variables and percentage for discreet variables.

RESULTS

Between October 2013 and December 2020, 105 patients (36 females/34.2%, mean age 57.0 ± 16.1, range 18-90) had a porcine-derived acellular cross-linked dermal matrix implanted and were registered in the prospective database by the involved institutes. The indications for using biological mesh implant in chest wall repair / reconstruction were: primary chest wall tumor (PCWT) n = 52 (49.5%), secondary chest wall tumor (SCWT) n = 29 (27.6%), lung hernia n = 12 (11.4%), trauma n = 10 (9.6%) and infections n = 2 (1.9%).

Forty-eight (45.7%) patients received the device alone, whereas in n=60 (57.1%) patients biological mesh was associated with titanium bars; n=61 (58.1%) patients underwent also a myo-cutaneous flap and n=26 (24.8%) a simple muscular flap.

Pre-operative classification of surgical site was: Infected n=16/15.2%, High risk of infection n=28/26.7%, Normal n=61/58.1%

Chest wall defect was located as it follows: Anterior or Antero-lateral n = 52 (49.5%), Lateral n = 39 (37.1%), Posterior n = 14 (13.4%). R0 resection was achieved in n = 79 out of n = 81 tumor resections (97.5%).

Mean follow-up was 30.4±20.1 (range 01-84). One patient (0.95%) was lost at follow-up after 22 months. 30-days morbidity was 30.5% (n = 32 patients) as it follows: Clavien-Dindo Grade I n=17; grade II n=12; grade III n=2, Grade IV n=1.
The most represented adverse events were: complications anatomically related to the chest wall surgical resection and/or reconstruction site \( n = 14 \) (13.3%); anemia requiring transfusion \( n = 8 \) (7.6%); atrial fibrillation \( n = 5 \) (4.8%); fever \( n = 2 \) (1.9%); broncho-pleural fistula in a lobectomy \( n = 1 \) (0.9%); other \( n = 2 \) (1.9%).

The surgical complications \( (n = 14 / 13.3\%) \) were: myo-cutaneous flap ischemia/necrosis \( n = 2 \) (1.9%); bleeding with hemothorax (treated conservatively) \( n = 3 \) (2.9%); wound hematoma or seroma \( n = 8 \) (7.6%); respiratory failure linked to impairment of chest wall movement \( n = 1 \) (0.9%).

In one case of lung hernia repair, the wound hematoma required a surgical revision so that the prosthesis was removed and then repositioned once the hemostasis was achieved.

Regarding the PACLIDEM implant, we experienced no prosthesis infection, no patient required prosthesis removal because of its detachment or rupture; and no patient had paradoxical respiration movement impairing respiratory function. No 30-day mortality was observed. The analysis of survival rates and curves depends on the underlying disease and this kind of study is beyond our intention and will not be evaluated. Figure 2, 3, 4 and Video 1 illustrate different cases of chest wall resection and reconstruction from this series.

Due to the heterogeneity of the indications, the patients have been divided into 4 homogeneous groups and each group has been separately analyzed: group 1 - chest wall tumors, group 2- trauma; group 3- lung hernia; group 4 - infectious disease.
**Group 1 - Chest Wall Tumors**

This is the largest group with 81 patients: PMCWTs $n = 48$ (59.2%); SCWTs $n = 29$ (35.8%), Benign lesions: $n = 4$ (4.9%). Main results were summarized in Table 1.

**Primary Malignant Chest Wall Tumors**

We performed 22 antero-lateral (45.8%), 19 lateral (39.6%) and 7 posterior (14.6%) resections, with a mean number of 2.9 ribs removed (range 1-8). Rigid reconstruction with titanium bars was necessary in $n = 28$ (56.3%) cases, and muscular flap was associated in 37 patients (77.1%): Latissimus Dorsi (LD) $n = 15$ (31.3%), Pectoralis Major (PM) $n = 13$ (27.1%), other $n = 9$ (18.7%).

Histological types are depicted in Table 2/A.

Forty-six patients (96%) were extubated at the end of surgery; two patients (one complete sternectomy and one subtotal sternectomy) were extubated in the intensive care unit within the first 24 h. One patient, after a total anterior chest wall demolition (total sternectomy extended to both clavicles and antero-lateral ribs), needed prolonged mechanical ventilation, tracheostomy, and discharge with home ventilatory assistance for 3 months. There was no perioperative mortality. Neither major septic complications nor flap-related complications occurred: four patients (8.3%) developed a seroma ($n = 1$: subtotal sternectomy; $n = 3$: lateral chest-wall non-rigid reconstruction) and were treated conservatively without consequences. No prosthesis infection nor other complications directly related to the PACLIDEM were registered. Postoperative Intensive Care Unit (ICU) and hospital stay averaged $2.3\pm9.1$ and $10.8\pm9.9$ days (range 0-63 and 4-63 days) respectively.

A partial paradoxical movement occurred in 1 case (2.1%) in a patient with non-rigid reconstruction, but without respiratory complications linked to chest-wall instability. No mortality was seen through 30-days postoperative. The mean follow-up was $33.9\pm21.0$ months and overall survival was 77%.

Histological examination showed wide resection margins in $n = 44$ patients (91.6%), $n = 2$ patients (4.2%) had marginal resection (both Grade I chondrosarcoma), while $n = 2$ patients (4.2%) showed an intralesional R1 resection and underwent a redo-surgery to enlarge the resection margins where required. We had a local recurrence in two patients (4.2%) 15 months and 18 months after surgery,
performed for a desmoid tumor and a Grade II chondrosarcoma, respectively. Both patients underwent a new radical resection. Interestingly, the histological examination of the surgical specimen in the patient with local recurrence from Grade II chondrosarcoma includes the area where the PACLIDEM mesh was implanted at the time of first resection (18 months prior). In this specimen there was an absence of the classic “foreign body reaction” as it would have been observed in case of a synthetic mesh.

Primary Benign Chest Wall Tumors

Our series includes 4 patients with benign chest wall tumors, treated with radical resection and reconstruction (2 males, median age 42.5 years old, range 24-55 years). Histology was as it follows: aneurysmatic osseous cyst n = 3; fibrous dysplasia n = 1. In n = 2 patients (50%) a rigid reconstruction was associated with biological mesh implant. No perioperative complications were registered. At a mean follow up of 52 months morbidity was 0%.

Secondary Chest Wall Tumors

Twenty-nine patients underwent surgery because of a chest wall secondary lesion (mean age 66.8±9.6, male n = 19/65.5%). The histological types are depicted in Table 2/B. A previous chemo- and/or radiation therapy (RT) was performed in n = 25 patients (86.2%). Preoperative RT on the surgical site was performed in n = 7 breast cancer recurrences and n = 1 lymphoma. A rigid reconstruction with titanium bars was performed in n = 18 (62.1%) patients while a muscular flap was associated in all cases (LD n = 11, PM n = 17, transverse rectus abdominis n = 1). All patients were extubated after surgery. In n = 4 cases (13.8%) we had a seroma at the prosthesis and muscular-flap receiving area, always conservatively treated without infection and/or the need for invasive treatment or prosthesis removal. No case of respiratory failure was registered. Mean hospital stay was 13.5±10.9 days (1.2±0.9 ICU stay). The histological examination showed wide resection margins in n = 27 patients (93.1%); n = 2 patients (6.9%) had marginal resection (both local recurrences from breast cancers). No 30-day mortality was registered. Patients had a mean follow-up of 26.7±20.65
months (range 1-71) and survival was 37.9%. No complications other than seromas and flap ischemia (as described above) were identified.

**Group 2 - Trauma**

Chest trauma was the indication for CWR with PACLIDEM in \( n = 10 \) (9.5%) patients of the series (male \( n = 6 \) / 60%, mean age 70.9±14.9 years, range 40-90). More than one comorbidity was present in \( n = 8 \) patients (80%): diabetes \( n = 4 \) (40%), renal failure \( n = 1 \) (10%), cerebrovascular disease \( n = 2 \) (20%). In all cases chest wall stabilization and prosthetic reconstruction was necessary because of the chest wall destruction and the loss of soft tissues and bones (always >3 ribs with displaced fractures). In \( n = 3 \) (30%) patients a sternal displaced fracture was associated; bone fragments were dislocated into the lung or into the mediastinum in \( n = 4 \) cases (40%); a compound fracture of the clavicle was present in \( n = 2 \) patients (20%). The chest wall defect was always > 5cm at the major diameter and the dimension of the biological mesh used was 15x20cm \( n = 6 \) (60%), 5x10 cm \( n = 3 \) (30%); 20x30cm \( n = 1 \) (10%). A rigid reconstruction with titanium bars was always necessary (\( n = 10, 100\% \)) and muscular flap was used to cover the reconstructed area in \( n = 7 \) patients (70%).

We experienced 1 case (10%) of dehiscence on soft tissue at the site of the sternal wound; this case had no prosthesis infection despite the abundant foreign body materials (PACLIDEM 20x30 cm plus titanium bars) under the soft tissues (a bilateral PM flap) and was treated conservatively (using the vacuum assisted closure system) healing in one month by secondary intention. Mean hospitalization was 28.4±26.8 (range 8 - 97) days (17.7±23.8 in ICU, range 0-75); chest and soft tissues drainages were removed after 7.8±4.2 and 5.9±3.5 days respectively. Overall survival at 30 days was 100%.

**Group 3 - Lung Hernia**

We had \( n = 12 \) cases (11.4% in the series, males \( n = 9 \), mean age 58.1±9.9 years) of lung hernia, all but one following anterior mini-thoracotomy for mitral valve surgery (\( n = 11, 91.7\% \)); in \( n = 1 \) case (8.3%) lung hernia involved the anterior port after a Video Assisted Thoracic Surgery (VATS)
lobectomy. The chest wall defect was always repaired with a PACLIDEM 10x15cm (Video 2). In all cases the homolateral PM was mobilized to cover the defect and the prosthesis. One case (8.3%) of complication was registered consisting in a postoperative bleeding with prosthesis displacement due to the chest wall hematoma; surgical revision was necessary with repositioning of the mesh without any other inconvenience. Mean hospitalization was 5.5±2.6 days; chest and soft tissues drainages were removed after 2.5±1.3 and 3.9±2.6 days respectively. No 30-day morbidity and mortality were registered. At a mean follow up of 29.1±21.5 months (range 2-67) we had no complications and no relapses.

Group 4 - Infectious Disease

In two patients (1.9%) chest wall resection and reconstruction were indicated because of an infectious disease: n = 1 abdominothoracic fistula due to complicated Crohn disease; n = 1 septic arthritis of the sterno-clavicular joint with bones erosion and compression on the cervical esophagus and subclavian vessels. Both patients were treated with chest wall resection and reconstruction using PACLIDEM 10x15cm. In the last case, osteomyelitis evolved and extended to the anterior chest wall after failure of conservative treatment; resection of the left sterno-clavicular joint was extended also to the manubrium, first and second sterno-costal cartilages and the involved soft tissues, creating a large defect needing reconstruction. Debridement of infected tissues in this region uncovered the subclavian vessels until the origin of the innominate artery so that a mesh was placed to protect big vessels and separate them from titanium bars used to reconstruct the bones. In both cases a LD myocutaneous flap was used to cover the prosthetic materials. Hospital stays were 18 and 24 days (ICU 2 and 6 days) respectively; chest drainage lasted 2 and 6 days while soft tissue drainage stayed for 17 and 9 days respectively. Patients had no 30-day morbidity and mortality, and both are free from relapse after 17 and 15 months from surgery.
DISCUSSION

The goals of CWR are several: to maintain the respiratory function, to restore the chest wall rigidity avoiding its contraction, to reestablish the chest wall integrity in order to protect the contents of the thorax from trauma and infection, to prevent lung herniation and paradoxical chest wall motion, to ensure shoulders stability, to avoid the trapping of the scapula and last but not least, and whenever it’s possible, to provide an acceptable cosmetic result. In case of extended resections and depending on the location of disease, a composite reconstruction is necessary (rigid and not rigid materials) to replace bones-cartilages and soft tissues. Meshes in these situations are needed to replace parietal pleura and intercostal muscles or to protect and separate the mediastinum (in case of antero-laternal resections or sternectomies), since, unfortunately, rigid materials allow lung or visceral herniation between their structure. Muscle flaps are needed to replace superficial soft tissues, to separate prosthetic materials from the skin and to put over the defect and the meshes a well vascularized tissue for a safe healing (Video 1 and 3).

For these reasons, chest wall resection often needs a complex series of steps during reconstruction which are not always able to recreate the pre-operatory physiological condition. As shown in previous literature, complication rate after chest wall surgery can be very high, varying from 38% to 69% [1-4, 11-12]. For example, in 2006, Weyant et al. showed that within 30 days complication rates were 38% for rigid methylmethacrylate sandwich techniques and a 4.5% 90-day prosthesis removal rate was observed; for PTFE or polypropylene mesh, the 30-day mortality was 27% and the 90-day prosthesis removal rate was 4.1%. We are far from the ideal prosthetic material such as it was defined in 1983 by LeRoux and Shama: rigid, malleable, radiolucent, durable inexpensive, easily incorporated by the body, physically and chemically inert, resistant to infection and strain, unable to elicit inflammatory or foreign body reaction, non-carcinogenic hypoallergenic, and sterilizable [18]. Although synthetic tissue materials (meshes and titanium) provide strong tissue reinforcement, they remain a source of a foreign body reaction, which can result in serious complications. This was also...
our historically experience, with several cases of synthetic meshes infection needing redo-surgery with their removal. The introduction of biological prosthesis in thoracic surgery is a new challenge. Extracellular biological mesh provides the extracellular scaffold needed for a physiologic tissue healing; they are either derived from human (allograft; derived from dermis, intestinal mucosa or pericardium) or animal (xenograft; usually porcine or bovine) tissues.

PACLIDEM is a collagen matrix patch derived from porcine dermis in which cells, cell debris, DNA, and RNA have been removed through a decellularization process. The resulting acellular matrix together with its constituent collagen fibers is cross-linked with hexamethylene diisocyanate for giving the mesh additional stability and reduction of collagenase degradation. The biomechanical characteristics of PACLIDEM have been tested and compared with other collagen materials in experimental settings; in a porcine model of ventral incisional hernia repair, PACLIDEM demonstrated excellent biomechanical characteristics and histologic remodeling compared to other biological meshes. The tensile strengths of sites repaired with biologic mesh were not impacted by very high de novo tensile strength/stiffness or mesh-specific variables [19,20]. Crosslinking resulted in an increased tensile strength of the tissue before a strong, mature wound has formed; this is crucial not only in abdominal hernia repair, but also in CWR [21], where mechanical stresses are high. These characteristics made PACLIDEM our choice for CWR.

In cases of chest wall tumors, the main objective of surgery is to achieve disease-free margins (R0) [21]. R0 can only be accomplished by an aggressive bone and soft tissues resection; depending on the extent of resection, distortion and malfunction of chest wall dynamics may ensue. Failure of the postoperative chest wall musculoskeletal system, including the area of reconstruction, to provide adequate physiological respiratory function may result in acute and potentially chronic restrictive respiratory failure. A favorable chest wall reconstruction method promotes early extubation and potentially reduces the risk of mortality [4,22,23]. Respiratory failure has been reported in up to 26% of patients with large chest wall resection utilizing non-rigid reconstruction [24,25]; however in this series an R0 resection was achieved in >90%, with only one case (1.2% of oncological series) of
respiratory failure after surgery, with the need of prolonged postoperative mechanical ventilatory support (3 months) in a patient undergoing an extended anterior chest wall resection with total sternal titanium replacement.

Regarding infections of the sternoclavicular joint, several authors report successful treatment by debridement and closure with muscle flaps, with or without bony stabilization and no mesh [26]. In our case, the mesh was needed to protect blood vessels from the titanium bars used to recreate chest wall stability, since the chest wall resection involved the whole manubrium and a large quantity of soft tissues.

The addition of rigid prosthetic material to non-rigid biologic reconstruction systems increases the strength of the reconstruction but also raises the risk of infection [1-4, 24]. Reconstruction using the PACLIDEM alone was successful in n = 48 patients, whereas in the remaining 57 the repair was achieved by adding a rigid titanium system. In n = 61 (58.1%) patients, a myo-cutaneous flap was also added. Further, anterior chest wall defects all required additional rigid fixation at least from an aesthetic point of view. Despite this extensive use of prosthetic materials and myo-cutaneous flaps, complications related to the chest wall resection and reconstruction occurred in 14 patients (13.3%) which is acceptable.

In cases of surgical site infection, treatment should include the removal of synthetic materials. Recent evidence suggests that the resorbable features of the biological patches do not require their removal even if infected [27,28]. In our series we did not experience prosthesis infection, despite the surgical site being already infected (n=16 patients - 15.2%) or at high risk of infection (n=28 patients - 26.7%). None in the group of n = 9 patients with wound hematoma and/or seroma developed an infection. No patient needed prosthesis removal due to infection or for any reason. Reconstruction with prosthetic materials after radiotherapy also is considered a high-risk scenario; we safely used biological meshes in n = 2 radio-induced sarcomas among primary tumours and n = 7 breast cancer recurrences and n = 1 lymphoma among the secondary tumours group.
PACLIDEM withstands high tensile forces, resulting in a strong biological scaffold incorporated into the repair with the necessary properties to facilitate soft tissue healing. We therefore utilized this feature to reconstruct the chest wall in non-malignant diseases. The device was effectively implanted on its own in n = 12 lung hernia patients and in n = 10 trauma patients without postoperative complications or further herniation. This experience in benign patients confirms previous results in repairing secondary incisional herniations [13,14,28,29].

CONCLUSIONS

The conclusions of this study can be summarized as follows:

1. PACLIDEM represents a valuable option in CWR, especially in case of high-risk patients or infected surgical sites. PACLIDEM showed excellent results on a large series with a long follow-up.

2. Excellent wound healing and long-term stability are achieved even in large defects by using biological meshes, and PACLIDEM confirms these results.

3. The use of PACLIDEM was not associated with any infections; early and late postoperative complications are acceptable.

The main limits of this study are:

1. There’s no comparison group. A retrospective match analysis would be not feasible, since the low number of cases and the need to involve a long period series, including different reconstruction techniques (with a lower technological quality of prosthetic materials).

2. This is not a randomized trial, although a future randomized trial could be support based on the data from this study.
**Figure Legend**

**Figure 1.**
Surgical site classification. Sites with high risk of infection, A: previous radiotherapy; B: giant tumors in which a large amount of prosthetic material is planned for chest wall reconstruction; C: redo-chest wall surgery. Infected sites, D: extensive soft tissue infiltration with ischemia; E: external cancer vegetation; F: cancer ulceration.

**Figure 2.**
Figure 2 reports the case of a sternal tumour with a wide skin infiltration. A: pre-operative view; B: muscular and cutaneous flap; C: intraoperative result and D: late cosmetic result.

**Figure 3.**
Figure 3 reports the case of a breast cancer recurrence infiltrating the skin. A: pre-operative view; B: muscular and cutaneous omolateral flap; C: the flap covers the defect.

**Figure 4.**
Figure 4 shows the case of a re-redosurgery for a local relapsed chest wall sarcoma. A: pre-operative view; the lesion is ulcerated on the skin. B: chest wall resection and reconstruction with biological mesh. C: muscolo-cutaneous perforator flap prepared. D, E,F: final result.

**Video Legend**

**Video 1.** Video 1 shows a case of subtotal sternectomy, with both clavicles resected without reconstruction. The sternal defect has been reconstructed with biological mesh, titanium and muscle flap to cover the prosthetic material. The post-operative result was excellent from a cosmetic and functional point of view (no deformities, neither paradoxical movement). Both arms move normally even if clavicles were not reconstructed.

**Video 2.** Video 2 shows the chest wall defect after anterior mini-thoracotomy

**Video 3.** Video 3 shows a case of total sternectomy and reconstruction with biological mesh and 3-D customized titanium implant.
References


<table>
<thead>
<tr>
<th></th>
<th>Primary Malignant Chest Wall Tumors (PMCWT)</th>
<th>Secondary Chest Wall Tumors (SCWT)</th>
<th>Benign lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N (%)</strong></td>
<td>48 (59,2%)</td>
<td>29 (35,8%)</td>
<td>4 (4,9%)</td>
</tr>
<tr>
<td><strong>Age (mean, years)</strong></td>
<td>49,2±15,9</td>
<td>66,8±9,6</td>
<td>39,5±3,0</td>
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<tr>
<td><strong>Comorbidity</strong></td>
<td>25(52%)</td>
<td>20 (70%)</td>
<td></td>
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<tr>
<td><strong>Resection</strong></td>
<td></td>
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<td></td>
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<tr>
<td>- mean ribs removed</td>
<td>2,9 (range 1-8)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>- partial sternectomy</td>
<td>2 (4,2%)</td>
<td>6 (20,7%)</td>
<td></td>
</tr>
<tr>
<td>- clavicular resection</td>
<td>16 (33%)</td>
<td>1 (3,4%)</td>
<td></td>
</tr>
<tr>
<td>- extended to other organs</td>
<td>1 (3,4%)</td>
<td>21 (72%)</td>
<td></td>
</tr>
<tr>
<td><strong>Dimension of the biological mesh</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 15x20 in n=26 (54,2%)</td>
<td>20x30 cm n=6 (12,5%)</td>
<td>15x20 cm n=11 (37,9%)</td>
<td>15x20 cm n=1 (25%)</td>
</tr>
<tr>
<td>- 20x30 cm n=11 (22,9%)</td>
<td>10x15 cm n=1 (2,1%)</td>
<td>10x15 cm n=1 (25%)</td>
<td></td>
</tr>
<tr>
<td>- 10x10cm n=1 (2,1%)</td>
<td>10x5 cm n=3 (6,3&amp; 15x20 cm n=1 (2,1%)</td>
<td>10x10 cm n=1 (25%)</td>
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<td>- 10x10cm n=1 (2,1%)</td>
<td>10x5 cm n=3 (6,3&amp; 15x20 cm n=1 (2,1%)</td>
<td>10x10 cm n=1 (25%)</td>
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<tr>
<td>- 15x20 cm n=1 (25%)</td>
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<tr>
<td><strong>Reconstruction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- biological mesh with</td>
<td>28 (56,3%)</td>
<td>18 (62%)</td>
<td>2 (50%)</td>
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<tr>
<td>- rigid reconstruction</td>
<td>37 (77,1%)</td>
<td>29 (100%)</td>
<td></td>
</tr>
<tr>
<td>- muscular flap</td>
<td></td>
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<tr>
<td>**Peri-operative major</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>complications</td>
<td></td>
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<tr>
<td><strong>Mean hospitalisation</strong></td>
<td>10.8 ± 9.9</td>
<td>13.5±10.9</td>
<td>5± 1.1</td>
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<tr>
<td>(days)</td>
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<tr>
<td><strong>30-day mortality</strong></td>
<td>0 %</td>
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<tr>
<td><strong>Overall survival</strong></td>
<td>77% (33,9±1.21)</td>
<td>37,9% (26,7±20,65)</td>
<td>100% (52)</td>
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<tr>
<td>(mean follow-up, months)</td>
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Table 2

A: Histopathological findings in Primary Malignant Chest Wall Tumours (number, percentage)

<table>
<thead>
<tr>
<th>Histological type</th>
<th>n.</th>
<th>%</th>
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<tbody>
<tr>
<td>Chondrosarcoma</td>
<td>31</td>
<td>64.6</td>
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<tr>
<td>- Grade I</td>
<td>21</td>
<td>(67.7)</td>
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<tr>
<td>- Grade II</td>
<td>9</td>
<td>(29.0)</td>
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<tr>
<td>- Grade III</td>
<td>1</td>
<td>(3.2)</td>
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<tr>
<td>Osteosarcoma</td>
<td>2</td>
<td>4.2</td>
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<tr>
<td>Ewing sarcoma</td>
<td>3</td>
<td>6.3</td>
</tr>
<tr>
<td>Radio-induced sarcoma</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Solitary plasmacytoma</td>
<td>2</td>
<td>4.2</td>
</tr>
<tr>
<td>Desmoid tumour</td>
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<td>4.2</td>
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<tr>
<td>Other sarcomas</td>
<td>6</td>
<td>12.5</td>
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B: Histopathological findings in Secondary Malignant Chest Wall Tumours (number, percentage)

<table>
<thead>
<tr>
<th>Histological type</th>
<th>n.</th>
<th>%</th>
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<tbody>
<tr>
<td>Non-small cell lung cancer</td>
<td>12</td>
<td>41.4</td>
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<tr>
<td>Mesothelioma</td>
<td>3</td>
<td>10.3</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>7</td>
<td>24.1</td>
</tr>
<tr>
<td>Colonic cancer</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td>Renal cancer</td>
<td>2</td>
<td>6.9</td>
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<tr>
<td>Thyroid cancer</td>
<td>1</td>
<td>3.4</td>
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<tr>
<td>Hepatocellular carcinoma</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td>Thymic carcinoma</td>
<td>1</td>
<td>3.4</td>
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repair with biological mesh