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Reconstruction of diaphragm with cadaveric fascia lata during extended surgery for pleural mesothelioma: A single-center experience

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ABSTRACT

Introduction: Synthetic materials have traditionally been used to reconstruct the diaphragm during extensive surgery for pleural mesothelioma. However, new biomaterials have shown promising results in various surgical fields. This study describes our experience using homologous fascia lata for diaphragm reconstruction in patients undergoing surgery with radical intent for pleural mesothelioma.

Material and methods: Data from patients who underwent extensive surgery for pleural mesothelioma requiring diaphragm reconstruction from January 2021 to December 2023 were extracted and analyzed. Patients were divided in two groups based on the type of material used for diaphragm reconstruction: expanded polytetrafluoroethylene (ePTFE) and cadaveric homologous fascia lata.

Results: Forty-three consecutive patients were included in the analysis. Of these, 22 patients (51 %) underwent diaphragm reconstruction with expanded ePTFE prostheses, while 21 patients (49 %) had reconstruction using homologous fascia lata. No significant differences were found between the two groups in terms of in-hospital stay (14.5 vs 17 days, $p = 0.865$) and early post-operative complications (19 % vs 18 %, $p = 0.943$). Concerning long-term complications, a lower rate was found in the group treated with fascia lata (5 % vs 23 %, $p = 0.09$).

Conclusions: Diaphragm reconstruction using cadaveric homologous fascia lata after extended surgery for pleural mesothelioma is feasible and results in satisfactory post-operative outcomes. Although the trend suggests fewer long-term complications with fascia lata, further research is needed to confirm these findings and determine the ideal prosthetic material for diaphragm reconstruction.

1. Introduction

The aim of radical surgery, as a part of a multimodal treatment, for pleural mesothelioma (PM) is to achieve macroscopic complete resection (MCR). MCR can be accomplished through either extrapleural pneumonectomy (EPP) or pleurectomy decortication (PD). EPP involves the removal of the entire lung along with parietal and visceral pleura, diaphragm, and pericardium. In contrast, PD spares the lung but may include diaphragm and pericardium removal in its extended form (EPD) [1].

In both surgical techniques, resecting the ipsilateral diaphragm necessitates reconstruction to prevent complications [2]. Currently, there is a lack of clear evidence or guidelines for determining the optimal material for diaphragm reconstruction. Consequently, surgeons often rely on their personal preferences and habits when making this decision.

Autologous materials, including muscle flaps from the great oblique, transverse abdomen, great dorsal, or fascia lata, can be used for diaphragmatic reconstruction [3,4]. While these materials may reduce the risk of infections, they require a longer operative times and may involve potential complications related to the harvesting procedure.

Synthetic prostheses, such as Dacron mesh, polypropylene, and expanded polytetrafluoroethylene (ePTFE) in the double-mesh formulation, are commonly used in thoracic surgery for diaphragmatic reconstruction due to their high tensile strength and effectiveness [5]. The microporous structure of ePTFE allows for tissue growth, promoting its incorporation into the surrounding soft tissues of the host. However,

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the use of alloplastic synthetics carries potential risks such as infection, mesh extrusion, and adhesion formation, which often require a reintervention for removal, especially in contaminated surgical environments [6].

Homologous prosthesis are biologically derived materials, often sourced from humans or animals, which are engineered to eliminate the immunogenic properties of allografts. These materials have gained increasing attention for their ability to integrate with host tissues and resist infections. Various materials, including human fascia lata, amniotic membrane, dura mater, acellular human dermis, and bovine pericardium, have been used in different surgical specialties with mixed results [7].

Concerning the utilization of fascia lata to replace diaphragm after radical surgery for pleural mesothelioma some studies have explore the use of autologous fascia lata, sourced from patient's own body [4]. However, the use of homologous (cadaveric) fascia lata for this purpose has not been previously reported in literature.

Here, we present our initial experience using homologous fascia lata for diaphragm reconstruction during radical surgery for mesothelioma, also comparing short- and long-term outcomes to patients who underwent reconstruction with synthetic prosthesis.

2. Materials and methods

2.1. Data collection

Starting from our thoracic surgery institutional prospectively maintained database, we analyzed all the patients who underwent to radical surgery (EPD or EPP) for pleural mesothelioma at the Thoracic Surgery Unit of the University Hospital of Padova (Italy) between January 2021 and December 2023. For diaphragm reconstruction, ePTFE was utilized in all patients operated on between January 2021 and December 2022, while fascia lata was used for the remaining period. The information collected included patients' demographics, intra-operative details of surgical procedures, hospital and intensive care unit (ICU) length of stay, early post-operative complications (defined as those arising during hospitalization), late post-operative complications (after discharge), and follow-up information.

Descriptive statistics were reported as median (I-III quartiles) for continuous variables and absolute numbers (percentages) for categorical variables. Their distributions between the two groups were compared using a chi-squared test for categorical variables while a Wilcoxon rank-sum test for continuous variables. Analysis was conducted with the statistical software Jamovi [The jamovi project (2022). Jamovi. (Version 2.3) Computer Software retrieved from https://www.jamovi.org].

The study was approved by the local ethical committee (5966/AO/24).

2.2. Operative technique

2.2.1. Surgical procedure

In all patients, the surgical procedure (EPP or EPD) was performed through a postero-lateral thoracothomy in the fifth intercostal space. This approach could also involve the removal of the sixth rib or a counter incision in a lower intercostal space, depending on the surgeon's preferences and distribution of the disease. The decision to remove and replace pericardium was based on the presence of evident macroscopic disease at this site.

2.2.2. Retrieval processing and cryopreservation of fascia lata

Fascia lata allografts were collected, processed and cryopreserved by Fondazione Banca dei Tessuti del Veneto (FBTV) ETS in accordance with requirements approved by the National Transplant Center and European directives. Donor selections included serological tests for detecting hepatitis B and C viruses, HIV, cytomegalovirus, human T-cell lymphotropic virus, and the syphilis pathogen, along with polymerase chain reaction for detecting HIV and hepatitis B and C viruses. All tissues were decontaminated two times with a validated antibiotic cocktail consisting of gentamicin, vancomycin and meropenem.

To ensure the safety and quality of the tissues, microbiological tests were performed following FBTV procedures at different steps. During the processing of fascia lata, adipose tissue and muscle tissue were removed. According to EDQM - *Guide to the quality and safety of tissues and cells for human application* 5th *Edition* [8], for fascia lata, decellularization is not foreseen and therefore we do not apply any specific immunosuppression protocol.

Before cryopreservation, fascia lata was transferred in low temperature–resistant ethylene vinyl acetate bags with a solution composed of BASE medium (Alchimia srl, Italy), 10 % dimethyl sulfoxyde DMSO (WAK-chemie Medical GmbH, Germany) and 10 % human serum albumin (Alburex 20 %, CSL Behring GmbH, Germany). Cryopreservation was achieved using a programmable cryogenic freezer (Planer KryoSave Integra, 750–30), which triggers a controlled cooling rate. Tissues were stored at −140 °C in the nitrogen vapor phase even if currently there are no standardized methods for fascia lata preservation. Each tissue bank independently validates appropriate storage conditions in compliance with safety, quality and microbiological tests, as required by the National Competent Authority. Finally, fascia lata is thawed before use which tipically requires approximately 30–40 minutes.

The expiration date is 5 years from the retrieval if the tissue is kept in the nitrogen vapor phase.

2.2.3. Diaphragm reconstruction

The diaphragm reconstruction technique, using both with ePTFE (Fig. 1) and fascia lata (Fig. 2), involved the direct suturing of the patch into the defect with interrupted nonabsorbable stitches. These anchored the patch to the residual muscular diaphragmatic tissue and around the ribs.

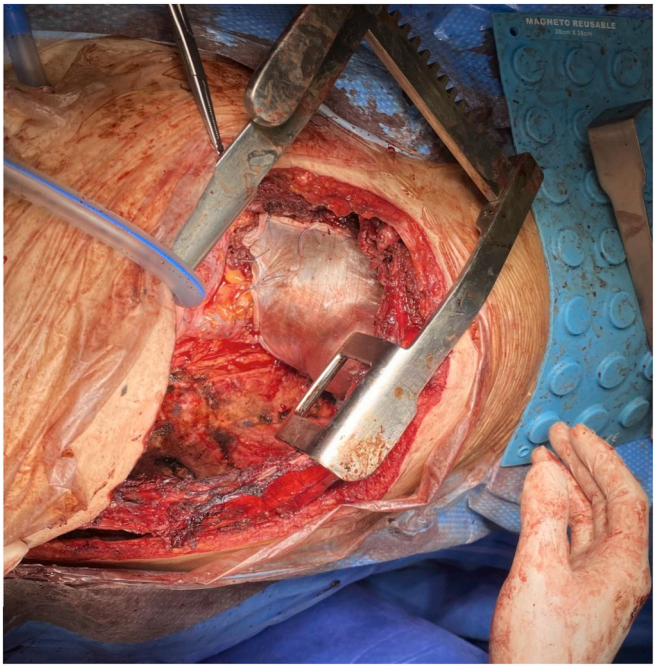

Fig. 1. Diaphragm reconstruction with fascia lata after extrapleural pneumonectomy (EPP).

Fig. 2. Diaphragm reconstruction with expanded polytetrafluoroethylene (ePTFE) in the double-mesh formulation after EPP.

3. Results

3.1. Patients' characteristics

Forty-three consecutive patients were enrolled, including 34 (79 %) males and 9 (21 %) females with a median age of 65 years [IQR 48–79]. All patients underwent induction chemotherapy before surgery. EPD was performed on 40 (93 %) patients while EPP was required in 3 cases (7 %). Twenty-eight patients (65 %) received adjuvant treatment: 13 radiotherapy, 2 chemotherapy while 13 were enrolled in a randomized clinical trial based on immunotherapy versus placebo. Histological examination of the surgical specimens revealed epithelioid mesothelioma in 31 patients (72 %) and biphasic in 12 patients (28 %). The patient's characteristics are summarized in Table 1.

Table 1
Patients' characteristics.

Variable	N = 43
Sex	
Male	34 (79 %)
Female	9 (21 %)
Age (y)	65 [IQR 48–79]
NeoAdjuvant treatment	
Chemotherapy	43 (100 %)
Type of surgery	
EPD	40 (93 %)
EPP	3 (7 %)
Adjuvant treatment	
Radiotherapy	28 (65 %)
	13
Chemotherapy	2
Clinical trial	13
Histology	
Epithelioid	31 (72 %)
Biphasic	12 (28 %)

EPD: extended pleurectomy decortication; EPP: extrapleural pneumonectomy; y:years.

3.2. Post-operative outcomes according to the diaphragm reconstruction

Diaphragm reconstruction was performed with homologous fascia lata in 21 (49 %) patients (group 1) and with ePTFE patch (Gore-Tex® DualMesh Biomaterial) in 22 (51 %) patients (group 2).

The median length of ICU stay was 2 days in both groups (p = 0.849) and the in-hospital stay was 17 and 15 days, respectively (p = 0.865). No intra-operative or in-hospital deaths were reported.

Early post-operative complications did not differ between the two groups (18 % vs 19 %, p = 0.943). In the fascia lata group, three patients experienced hemothorax requiring surgical reintervention, and one had liver herniation due to diaphragmatic patch dehiscence. In ePTFE group, two patients experienced prosthesis dehiscence with liver herniation, one patient had hemothorax and another developed persistent chylothorax which required reoperation for thoracic duct closure.

Late post-operative complications were higher in group 2 than group 1 (23 % vs 5 %, p = 0.09) although this difference was not statistically significant. In group 1, only one patient was readmitted to the hospital due to a persistent pneumothorax caused by surgical wound dehiscence, which necessitated surgical revision. In group 2, late complications were reported in five patients: one experienced a pleural effusion without microbiological isolation which required chest drainage, and four patients developed empyema. One of these required a surgical procedure involving the removal of the synthetic prosthesis and transposition of the omentum.

A direct comparison between the outcomes of the two groups is reported in Table 2.

4. Discussion

This study reports our first surgical experience using cadaveric homologous banked fascia lata for diaphragm replacement during extensive radical surgery for pleural mesothelioma.

The use of autologous fascia lata for diaphragm reconstruction has already been reported, garnering significant attention due to its unique properties, such as high tensile strength and resistance to infection.

An experimental study performed on dogs [9] found that autologous fascia lata for diaphragm reconstruction is a feasible and viable option for its high tensile strength, though it requires a femoral incision for harvest. Similarly, Yamashita et al. [4] presented a successful case of diaphragm reconstruction using autologous fascia lata in a patient undergoing surgery for a recurrent pleural solitary fibrous tumor, demonstrating its long-term efficacy and resistance to infection.

With the increasing popularity of tissue banking, cadaveric homologous fascia lata can be harvested from multi-organ donors and stored for future use, avoiding donor site morbidity. The use of this biobanked material has been described in various settings, including gynecologic and urological surgery [10,11], ophthalmology [12,13] and more recently, skull base reconstruction [14,15]. However, there is limited

Table 2
Post-operative outcomes.

Variable	Group 1 (N = 21)	Group 2 (N = 22)	P Value
ICU stay (d)	2	2	.849
In Hospital stay (d)	17	15	.865
Early post-operative Complications	4 (18 %)	4 (19 %)	.943
Hemothorax	3	1	
Liver Herniation	1	2	
Chylothorax	0	1	
Late post-operative Complications	1 (5 %)	5 (23 %)	.09
Persistent Pneumothorax	1	0	
Pleural Effusion	0	1	
Empyema	0	4	

d: days.

evidence on the use of cryopreserved fascia lata for diaphragmatic reconstruction. Vereczkei et al. [16] conducted an experimental study on animals to reinforce hiatal hernia closure, finding that the patches integrated well with the surrounding tissues over time, showing fibrosis and neovascularization without inflammation or significant adhesions. In clinical settings, its use has been tested to repair congenital diaphragmatic hernias in pediatric patients [7,17].

Based on this evidence, we explore for the first time the possibility of using cadaveric fascia lata for diaphragm replacement in radical mesothelioma surgery. Our preliminary results confirm that this homologous tissue can be safely utilized in this type of surgery, with similar peri and postoperative outcomes in both groups. The complication rates were comparable between the two groups with one patch dehiscence in the fascia lata group and two in the synthetic group. Notably, all the dehiscences occurred on the right side, and the patient with fascia lata prosthesis dehiscence was obese.

Regarding infectious complications, a higher rate was found in the PTFE group, with four cases of empyema. While we cannot conclude that the empyemas were directly due to the synthetic materials, the only case of prosthetic infection requiring removal was reported in this group, with no reported infections in the chest cavity in the fascia lata group. This suggests that biological materials are less prone to infection compared to synthetic ones.

Another important consideration is cost analysis: based on our hospital's fee schedule, cadaveric fascia lata is slightly cheaper than ePTFE for the same dimensions (1016 euros vs 1302,84 euros).

The small sample size and the limited follow-up period are the main limitations of this study. We began using cadaveric fascia lata for diaphragm reconstruction in mesothelioma surgery at our center at the beginning of 2023, so we cannot draw meaningful conclusions on the long-term outcomes comparing the two groups.

Despite these limitations, we conclude that cadaveric fascia lata is a safe and effective alternative to other materials for diaphragm reconstruction during extended surgery in patients with pleural mesothelioma. Future research should focus on long-term outcomes and larger patient populations to validate these findings and establish guidelines for best material selection in diaphragmatic reconstruction.

CRediT authorship contribution statement

Eleonora Faccioli: Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft, Writing – review & editing, Supervision. **Giovanni Zambello:** Investigation, Writing – original draft. **Diletta Trojan:** Methodology, Resources. **Gianluca Canu:** Investigation, Writing – original draft. **Viola Sambataro:** Investigation, Writing – original draft. **Chiara Giraudo:** Validation, Methodology. **Marco Schiavon:** Writing – review & editing, Supervision. **Andrea Dell'Amore:** Writing – review & editing, Supervision. **Federico Rea:** Writing – review & editing, Supervision.

Declaration of competing 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.

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