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***Retrospective Cohort Study***

**Effectiveness and versatility of biological prosthesis in transplanted patients**

Vennarecci G *et al*. Prothesis in liver transplant

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**Abstract**

***AIM***

To emphasize their effectiveness and versatility and the good tolerance by the patients.

***METHODS***

From December 2001 to February 2016, 270 liver transplantations were performed at San Camillo hospital. IH occurred in 78 patients (28.8%). Incisional hernias usually appeared early within the first year post-orthotopic liver transplantation. In the first era, fascial defect was repaired by primary closure for defects smaller than 2.5 cm or with synthetic mesh for greater defects. Recently, we started using biological mesh (Permacol™, Covidien). We present a series of five transplanted patients submitted to surgery for abdominal wall defect correction repaired with biological mesh (Permacol™, Covidien).

***RESULTS***

In our cases the use of biological prosthesis (Permacol™, Covidien) have proven to be effective and versatile repairing hernia defects of different kind; patients did not suffered infections of the prosthesis and no recurrence was observed. Furthermore the prosthesis remains intact even in the years after surgery.

***CONCLUSION***

The cases that we presented show that the use of biological mesh (Permacol™, Covidien) in transplanted patients may be safe and effective being careful to the management of perioperative immunosuppression, renal and graft function although the cost of the product itself has been the main limiting factor and need of prospective studies for further evaluations.

**Key words:** Incisional hernia; Liver transplantation; Heart transplantation; Biological mesh; Surgery; Morbidity; Risk factors; Immunosuppression; Infection; Recurrence

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**Core tip:** Incisional hernias (IH) following abdominal organ transplantation have a high rate and evenmore in immunosuppressed patients. Several factors have been described to be associated with IH in transplant patients. Herein, we present our preliminary experience with porcine dermal collagen mesh.

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**INTRODUCTION**

Incisional hernias (IH) following abdominal organ transplantation have a high rate. Every year thousands of transplant procedure are performed worldwide. Equally, the number of IH in this population is growing every year. This postoperative complication rate is estimated to be for kidney transplant, liver transplant and pancreas transplant; from 1.6% to 18%[1,2], from 1.7% to 32.4%[3,4] and 13% to 34.8%[5,6], respectively.

Different cause has been proposed to increase IH risk. Of them, pretransplant malnutrition, presence of abundant ascites for liver candidates, type of incision and type of wall closure, and co-morbidities as diabetes, obesity, multiple surgery, and male gender.

The compromised wound healing processes is major in patients with an immunsuppressive regiment. Nontheless, this therapy increase the infections rate.

The European Hernia Society recommend to use a porcine dermal collagen (PDC) mesh in this cases. In spite of this no proven benefit versus synthetic mesh (SM) has been described.

Recent studies have shown that biological prosthesis have a greater ability to integrate into tissues, resist bacterial colonization, reduce cytotoxic or allergic reactions, and provide similar functional results, compared with SM[7,8]. This article shows the experience of our surgical division in the use of PDC mesh (Permacol™, Covidien) in transplanted patients, emphasizing their effectiveness and versatility and the good tolerance by the patients.

**MATERIAL AND METHODS**

From December 2001 to February 2016, 270 liver transplantations were performed at San Camillo hospital. The transplant procedures were performed with the piggy-back technique without venous-venous bypass. Surgical access was obtained by a bilateral subcostal laparotomy with a cranial midline extension or a J-shaped (Makuuchi) laparotomy. Closure of the abdomen was performed with a slowly absorbable two-layer running sling suture. All patients receive a triple immunosoppressive therapy with steroid, tacrolimus and mycophenolate. Everolimus has been used since 2010 in patients with renal dysfunction and/or associated hepatocellular carcinoma (HCC). IH occurred in 78 patients (28.8%). IH usually appeared early within the first year post-orthotopic liver transplantation (OLT). The elective surgical repair of the abdominal defect was delayed until patient recovered good general conditions. On average repair was performed at a median of 29 mo (range: 22-45) after OLT. IH were diagnosed by phys­ical examination. In the first era the fascial defect was repaired by primary closure for defects smaller than 2.5 cm or with synthetic mesh for greater defects. Whenever possible, the sublay technique with implanta­tion of the mesh between the closed posterior fascia and the muscle in the majority of patients was used. Otherwise a dual-mesh prosthesis was implanted intraperitoneally. Recently, we started using PDC mesh (Permacol™, Covidien). The patient’s management included everolimus withdrawal before surgery, early nasogastric tube removal to facilitate oral feeding, administration of immunosuppressive therapy, peri-operative antibiotic administration, monitoring “graft function”, monitoring patient for local or chest infections, e.v. fluid administration to avoid dehydration and renal dysfunction. In our practice we used a third generation of cephalosporin until the tube-drain removal. Herein, we present a case series of OLT patients submitted to surgery for abdominal wall defect correction repaired with PDC mesh (Permacol™, Covidien): 1 case of subcostal/epigastric IH, 1 case of paraombelical IH, 1 case of reconstruction of the diaphragm in a patient with HCC recurrence infiltrating the diaphragm, 1 case of large-for-size liver graft mismatch and 1 case of epigastric IH in a heart transplant (HT) patient (Table 1).

**RESULTS**

A 52 years old male was admitted to the hospital with a giant IH in the epigastrium region ~~4~~ years after OLT. A PDC (10 cm × 15 cm) mesh (Permacol™, Covidien) was positioned without tension to the edges of the fascia defect, and fixed with 2-0 interrupted polypropylene sutures. We used a Jackson-Pratt drain (Cardinal Health™) above the mesh construct. Skin was closed with interrupted sutures. Prophylactic antibiotics were given until postoperative day 5. The patient continued immunosuppressive therapy without any changes. Drain was removed and the patient was discharged on postoperative day (POD) 5 without complications. No hernia recurrence was observed at 2-year follow-up after surgery.

A 58 years old male was admitted with a subxiphoid-epigastric IH 5 years after a heart transplant. The surgical access was a sternotomy with a subxiphoid exstension. The abdominal IH occurred within 1 year from HT. He was on a immunosuppressive regimen with steroids, once-a-day tacrolimus and everolimus. Everolimus was stopped 2 mo before surgery. Physical examination showed that the defect was about 20 cm of diameter. The operative procedure started with incision xypho-supraumbilical. The hernia sac was prepared and isolated by adhesions with cutaneous scar to the back-end of the rectus abdominis without opening the sac. The dissection was continued with the preparation of the rear end of the rectum to the lateral margin, the fascia was sutured on midline obtaining the reduction of the hernia sac in subfascial position. Permacol™ mesh (molded with diameter 15 cm × 13 cm) was implanted using the sublay technique and sutured with 0 interrupted polypropylene sutures. We placed 1 drain in the subfascial over the prosthesis and then suture of the front fascia of the rectus abdominis. Everolimus was restarted 2 wk after surgery. Drain was removed and the patient was discharged on POD 5 without complications. No hernia recurrence was observed at 3-year follow-up after surgery (Figure 1).

A 55 years old male received a liver transplant 6 years earlier for a liver cirrhosis autoimmune related. At the time of transplant procedure his giant umbilical hernia (10 cm × 8 cm) was not repaired. The hernia sac was opened carefully, no adhesions were found. The PDC mesh (Permacol™, Covidien) was fixed with not-absorbable sutures at the muscle-aponeurotic plane, bridging the defect without primary fascial apposition. A drain was placed in the subcutaneous plain. Subcutaneous tissue and skin were closed with interrupted sutures. Antibiotics were given until postoperative day 6. The patient continued immunosuppressive therapy without any changes including steroids at 7.5 mg a day. Drain was removed and the patient was discharged on POD 6 without complications. At 5 year after surgery no hernia recurrence was observed.

A 58 years old female received a liver transplant in the November 2015 for a primary biliary cirrhosis. The surgical access was a bilateral subcostal laparotomy with a cranial midline extension. Due to large-for-size liver graft mismatch, with a graft-to-recipient-weight-ratio of 3.3%, and presence of bowel edema, abdominal wall closure was not possible at the end of procedure. In order to prevent the onset of a compartment syndrome, a temporary wound closure with Bogota Bag was performed. After three days, a PDC mesh (Permacol™, Covidien) was molded 28 cm × 18 cm and sutured at the muscle-aponeurotic plane with 0 interrupted polypropylene sutures (Figure 2A). We placed 1 drain in the subcutaneous plain and the skin was closed with continuous sutures above the mesh (Figure 2B). Postoperative course was characterized by a respiratory distress (classified as Dindo-Clavien Grade II) resolved in post-operative day 3. She was discharged on POD 5 and followed as out-patient. Three months after LT, a CT scan showed the complete integrity of the biological prostheses, and the patient had an excellent functional result (Figure 2C) and a normally perfusioned graft.

Four years after OLT for HCC, a 70 years old male was admitted to the hospital with a recurrence of HCC infiltrating the peritoneum pericardium and diaphragm. The abdominal exploration showed a neoplasm of left lobe liver graft with infiltration of the diaphragm which extended to the pleura and pericardium. The operative procedure included a left lobectomy of the graft with resection of the diaphragm “*en bloc*” with adjacent portion of right pleura and pericardium. The resection created a wide pleura-pericardial wall defect (Figure 3A). The wall defect was sheltered by apposition of a PDC mesh (Permacol™, Covidien) sutured to diaphragm with 2-0 continues polypropylene sutures. At the end of procedure the subcostal wall defect was repaired by apposition of the same prosthesis used before. Everolimus therapy was discontinued seven days before IH repair until postoperative day 7. A mild pleural effusion (Figure 3B) was observed as postoperative complication.

**DISCUSSION**

The rate of IH after OLT estimates ranging from 1.7% to 32.4%[10]. In OLT patients several risk factors have been defined including male gender, elevated Body Mass Index, wound infection, hematoma, ascites, repeat interventions, immunosuppressive drugs, low platelets count, abdominal wall closure technique, diabetes mellitus, and smoking history[11,12]. Different techniques are disposable to repair the IH: Open techniques with primary fascia closure, open or laparoscopic repair with synthetic or biological mesh[13]. Although permanent mesh prosthesis are considered the best treatment for minimizing IH recurrence, they have been associated with a high risk of complications due to their non-absorbable characteristics such as erosion into the abdominal viscera, protrusion, extrusion, adhesion, infection, and bowel fistulae that can lead to more complex and costly surgery[14]. Biological mesh was introduced as an alternative to synthetic mesh in the 1990s[15]. The bioprosthetic materials are taken from several different species (bovine, porcine and equine) and from different organs (pericardium, skin and bowel submucosal)[14]. Biological mesh prosthesis allow neo-vascularization and regeneration due to infiltration of native fibroblasts and they are incorporated into the surrounding tissue. During incorporation, they generate active neofascia to withstand the mechanical forces of the abdominal wall[16]. Recent studies have shown that biological prosthesis have a greater ability to integrate into tissues being colonized by host cells and blood vessels, resist bacterial colonization minimizing the risk of infection, reduce cytotoxic or allergic reactions, and provide similar functional results, compared with synthetic prosthesis. Porcine dermis is the closest to human dermis and it is not cytotoxic, hemolytic, pyrogenic, or allergenic, and it does not elicit a foreign body response[17]. It is soft and flexible, and it has bilateral smooth surfaces with high tensile strength[17]. It is sold in sheets, allowing it to be cut to shape, and provides the largest grafts available (maximum size, 28 cm × 40 cm)[16,17]. In animal studies, a porcine dermal collagen implant produced a substantially weaker inflammatory response and less extensive, less dense adhesions[17,18].

To date, no prospective studies have been performed for witch surgical technique in abdominal closure in IH, neither in indications about use of PDC mesh (Permacol™, Covidien). Some retrospective studies show that the use of biological prosthesis may improve clinical outcome[[19]](http://www.sciencedirect.com/science/article/pii/S1743919115010079#bib4).

Schaffellner *et al*[20] reported an experience of 3 cases of ventral IH after OLT. They do not observed wound healing disorders or signs of postoperative infections.

Our experience is limited to the use of PDC mesh (Permacol™, Covidien) in patients who underwent liver and heart transplantation. In our series, biological mesh have been also used to bridge fascial defects, defined as placement of the PDC between edges of the rectus sheath where primary closure was not feasible, although the data reported in the literature do not militate in favor of the use of biological prostheses in bridge repairing[21,22]: Of the two cases examined, one (case 5) has a follow up too short to consider a recurrence of incisional hernia, the other (case 2) showed a good outcome, with no hernia recurrence at 3-year follow-up after surgery.

A grading system to stratify patients according to their risk factors for adverse surgical site occurrences has been proposed by the Ventral Hernia Working Group (VHWG)[23]. In this grading, the immusuppressed transplanted patients are classify as grade 2. Which suggest that a PDC mesh may improve the outcome[23].

An Italian study described as the use of the dermis was proven useful and found a lower rate of infection and recurrence in transplanted patients[24]. Nontheless, the use of banked fascia lata allografts seem to provide a biocompatible, safe, and effective alternative to other biological meshes[15].

Biological prosthesis is related with decrease number of infections, recurrence and mesh removal comparing to SM. The cases that we have presented show that the use of PDC mesh (Permacol™, Covidien) in transplanted patients may be safe and effective being careful to the management of perioperative immunosuppression, renal and graft function although the cost of the product itself has been the main limitating factor and need of RCTs for further evaluations. Our experience with PDC has been successful for several reasons: The prosthesis have proven to be effective and versatile repairing hernia defects of different kind; moreover, in our series, patients did not suffered infections of the prosthesis and no recurrence was observed, even in cases in which they were used to bridge fascial defects. Furthermore the prosthesis remains intact even in the years after surgery.

**COMMENTS**

***Background***

Incisional hernias are a common complication after organ transplant. Think of the immunosuppressed status, transplanted patients may have an increased risk of postoperative morbidity.

***Research frontiers***

The use of biological mesh (Permacol™, Covidien) in transplanted patients, emphasizing their effectiveness and versatility and the good tolerance by the immunosuppressed patients.

***Innovations and breakthroughs***

To date, no prospective studies have been performed for witch surgical technique in abdominal closure in incisional hernias (IH), neither in indications about use of porcine dermal collagen mesh.

***Applications***

IH following abdominal organ transplantation have a high rate and due to the immunosuppressive status. Each year thousands of new transplantation are performed and in the same way the number of IH in these patients.

***Terminology***

A porcine dermal collagen mesh prosthesis have a greater ability to integrate into tissues, resist bacterial colonization, reduce cytotoxic or allergic reactions, and provide similar functional results.

***Peer-review***

It is a well-written paper.

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**Figure 1 Computed tomography scan at 6 mo after abdominal wall repair.** Arrow: Biological prosthesis.



**Figure 2 In order to prevent the onset of a compartment syndrome, a temporary wound closure with Bogota Bag was performed.** A: Implantation of Permacol™ mesh; B: Skin closure after Permacol™ mesh implantation; C: Computed tomography scan at 3 mo after abdominal wall repair (arrow: Biological prosthesis).



**Figure 3 The abdominal exploration showed a neoplasm of left lobe liver graft with infiltration of the diaphragm which extended to the pleura and pericardium.** A: Left liver lobectomy of the graft with resection of the diaphragm “*en bloc*” with adjacent portion of right pleura and pericardium; B: Computed tomography scan at 6 mo after abdominal wall repair (arrow: Biological prosthesis).

**Table 1 Patients characteristics**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Case No.** | **Age/gender** | **Type of transplant** | **Immunosoppressive therapy** | **Hernia size (cm)** | **Time from transplantation to repair** | **Recurrence** | **Follow-up** |
| 1 | 52/male | Liver | Tacrolimus + Everolimus | 10 × 8 | 8 mo | None | 2 yr |
| 2 | 58/male | Heart | Steroids + Tacrolimus | 10 × 10 | 5 yr | None | 3 yr |
| 3 | 55/male | Liver | Steroids + Tacrolimus + Everolimus | 8 × 8 | 6 mo | None | 5 yr |
| 4 | 58/female | Liver | Steroids + Tacrolimus + Everolimus | 20 × 15 | 3 d | None | 3 mo |
| 5 | 70/male | Liver | Tacrolimus | 6 × 7 | 4 yr | None | 6 mo |