Definitive abdominal wall closure using a porcine intestinal submucosa biodegradable membrane in pediatric transplantation

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Abstract: Abdominal closure in children less than 10 kg following liver or kidney transplantation can be challenging. Excessive pressure attained from a tight closure can result in abdominal compartment syndrome, graft compromise and loss. Concerns over using prosthetic patches are that of infection and dehiscence. We report a series of definitive abdominal wall closure using a biodegradable membrane from porcine intestinal submucosa (Surgisis®; Cook Biotech Incorporated, West Lafayette, IN, USA). A prospective collection and follow up of liver and kidney transplant patients weighing less than 10 kg who required abdominal wall augmentation with Surgisis® in order to achieve satisfactory closure. There were 10 liver and two renal transplant patients. The average weight of the liver transplant patients was 6.6 kg (5.4–8.5 kg) and the renal 9.8 kg. The average area of Surgisis® used was 71.2 cm^2 (25–160 cm^2) and length of follow up was 15.3 months (1–27 months). Concomitant measures to aid abdominal closure included bilateral recipient nephrectomy for the renal patients and reduction by 33% of the lateral segmental grafts in two liver transplant patients. Delayed closure occurred in all patients except one and the average days to closure from the first surgery was 3.75 days (0–6 days). Following liver transplantation one patient died from multiple organ failure at one month secondary to hemophagocytosis from underlying combined immune deficiency syndrome and one patient with hepatic artery thrombosis was salvaged at re-exploration. There were two wound complications, one patient developed two small sinuses and some skin dehiscence which healed over four months and the second developed a skin sinus following trans-patch liver biopsy which healed in three wk. Both had positive microbial cultures but neither necessitated removal of the graft. There were no incisional hernias. Surgisis® is a safe method for facilitating abdominal closure in pediatric transplant patients. It appears to have long-term durability with no incisional hernias on short- and medium-term follow up, and is fairly resistant to infection.

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Children less than five yr of age, representing 46% of children listed for liver transplantation have the highest mortality rate on the waiting list compared with other age groups (1). This has mandated the utilization of a variety of grafts, including split, reduced segment, and living related grafts to overcome the organ shortage (2). In renal transplantation deceased donation grafts from donors less than age five yr had significantly inferior long-term outcomes compared with all other donor age groups (3, 4). Thus, adult deceased donation grafts and living-related grafts are preferable in children (5). Renal transplantation in children of less than 10 kg has been found to be an independent variable for increased risk of graft loss (6). Several technical

factors contribute to this one of which is the safe closure of the abdominal wall in the presence of a large adult graft (7). Excessive pressure used to attain closure can result in abdominal compartment syndrome, graft compromise, and loss (8). Concerns over using prosthetic patches are that of infection and dehiscence. We report a series of definitive abdominal wall closure using a bio-degradable membrane from porcine intestinal submucosa (Surgisis®; Cook Biotech Incorporated, West Lafayette, IN, USA).

Methods

A prospective collection and follow up of liver and kidney transplant patients weighing less than 10 kg who required abdominal wall augmentation with a biodegradable membrane from porcine intestinal submucosa in order to achieve safe closure. Indications for its use were graft congestion, compromise, or abdominal compartment syndrome during attempts at delayed definitive closure. The analysis and reporting of data received institutional review board approval.

Results

There were 10 liver and two renal transplant patients over a 30-month period whose abdominal wall closure was assisted by using porcine intestinal submucosa implants.

The liver transplant patients had an average age of 8.5 months (5–15 months) and weight of 6.6 kg (5.2–8.5 kg). The average donor to recipient weight ratio was 10.1:1 (7.6–12.5:1). All patients received left lateral segment grafts, nine of which were *in situ* deceased donation splits. None of the patients had definitive abdominal closure at the primary surgery and were closed at 3.8 days post-operatively (2–6 days). Three patients had a further 33% back table reduction of their graft to improve the patient graft size mismatch and one patient required a prosthetic to optimize the graft position to prevent outflow obstruction. None of the patients developed large graft for size syndrome.

The average size of porcine intestinal submucosa implant used to augment sheath closure was 71.3 cm^2 (25–162 cm^2), which was placed in a central wound position in eight cases and in a right subcostal position in two cases. The implant was secured to the full thickness of the muscle edge with 2/0 polydioxanone sutures (Fig. 1). Skin coverage was then achieved in all cases by subcutaneous flap mobilization. No subcutaneous drains were used.

All patients received standard immunosuppression of methylprednisolone and tacrolimus. In addition, liver patients received azothioprine and renal patients basiliximab and mycophenolate.

Fig. 1. Surgisis® sutured into the wound replacing the sheath.

In relation to the liver transplant patients, there were four systemic complications and one mortality. The systemic complications were one hepatic artery thrombosis prior to abdominal closure and was recognized and thrombectomized on day three with long-term patency. One patient developed a transection margin hematoma. One patient a bile duct leak that was oversewn prior to definitive closure and one patient developed cholangitis. The mortality was in a child transplanted for veno-occlusive disease secondary to combined immune deficiency syndrome. He developed multi-organ failure and sepsis with hemophagocytosis and subsequently died one month post transplant. One wk prior to his demise, the graft was working well and at death the wound was intact.

The remaining patients were followed for an average of 15.3 months (4–24 months). There were no incisional hernias. There were two wound complications. In the first a core liver biopsy through the porcine intestinal submucosa implant resulted in a sinus from which yeast was cultured. It however healed spontaneously by six wk without active treatment. The second was that of skin dehiscence over a length of 2 cm with partial extrusion of the porcine intestinal submucosa implants. The extruded portion was trimmed sequentially and healed by four months post transplant. The exposed Surgisis was dressed daily with Chloromycetin ointment.

The two renal transplant patients were 18- and 36-month-old with weights of 9.8 and 9.85 kg, respectively. Both received adult living-related grafts, which were placed intra-abdominally via a midline transperitoneal approach onto the aorta and inferior vena cava. One patient had a delayed closure. Both had native nephrectomies

in order to create space for the graft. The sizes of the intestinal submucosa implants placed were 105 and 60 cm^2; both were placed in a central position. Once again skin closure was achieved by subcutaneous flap mobilization. There were no systemic or wound complications. Follow up was at four and 14 months, respectively.

Discussion

We describe the use of biodegradable membrane from porcine intestinal submucosa (Surgisis®). Porcine-derived small intestinal submucosa is a biomaterial consisting of a laminar matrix of freeze-dried collagen. Its function depends on the correct balance between the rate of degradation and the rate of host remodeling and tissue in growth within the small intestinal submucosa matrix graft (9). Endothelial cell proliferation and neovascular in growth form an essential role in this remodeling process (10).

The use of a temporary abdominal dressing with subsequent staged reduction in size until definitive closure has been used. This technique, however, is likely to place the patient at greater risk of acquiring an iatrogenic infection as the timing of the closure would not be predictable. Abdominal wall augmentation is a better planned procedure achievable in a shorter period of time. This series would show that porcine intestinal submucosa (Surgisis®) can be safely left *in situ* to achieve this goal.

One has to be cautious with the use of prosthetic material for abdominal wall closure as it has been associated with a significant risk of complications, including intra-abdominal adhesions, chronic inflammation, seroma formation, infection, shrinkage, migration, and fistula formation (11, 12). Absorbable synthetic materials, such as polyglycolic acid, have been used in this situation, but formation of a recurrent hernia defect is nearly inevitable (13, 14). Porcine-derived small intestinal submucosa has been well studied for use in adult inguinal hernia patients in both immune competent (15, 16) and immune depressed patients (17). Its use in ventral wall hernia repair has been shown to be safe and effective (16, 18) and its use in abdominal wall reconstruction in the pediatric literature has also been documented (19). This is, however, the first reported series of immune suppressed pediatric patients to have abdominal wall reconstruction with porcine-derived small intestinal submucosa.

Alternative biodegradable scaffold meshes have been reported in renal transplant patients using a porcine dermal collagen graft Permacol®

(Tissue Sciences Laboratories plc, Aldershot, UK) (8). The article, however, only describes five renal transplant patients who were all significantly larger than our own series with ages 2–15 yr and weights 12–46 kg. They do, however, show the successful application of a biodegradable prosthesis in transplant recipients. Few clinical comparative studies have been made between dermal collagen graft Permacol® and porcine intestinal submucosa Surgisis®. Aybi et al. (20), however, using a rat model found Surgisis® to be superior for ventral hernia repair than Permacol®.

It would appear from both the literature and our own experience that porcine intestinal submucosa is relatively resistant to infection. Badylak et al. (9) deliberately challenged small intestinal submucosa infra-renal aortic grafts with *Staphylococcus aureus*. After a 30-day follow-up period, none of the small intestinal submucosa grafts were infected as determined by clinical observation, clinical pathology, bacterial culture, and histopathology this in contrast to an expanded polytetrafluoroethylene group which all became infected. The authors surmized that the apparent infection resistance of small intestinal submucosa in this vascular graft study might have been caused by rapid capillary penetration of the small intestinal submucosa (2–4 days) and delivery of body defenses to the local site early in the healing process (9). The use of small intestinal submucosa in contaminated fields have demonstrated a similar resistance to infection (21). Our own clinical experience would support both of these findings. Two patients developed wound complications, which had pathogenic bacteria and fungi growing from wounds in direct contact with the implant. Both resolved and neither required removal of the implant.

The potential concern with the use of foreign material in a heavily immune suppressed patient has tended to encourage some centers to achieve abdominal closure with autologous tissue despite an increased intra-abdominal pressure. Raised intra-abdominal pressure post-liver transplantation has been noted frequently and may be associated with a complicated post-operative course (22) and post-operative renal failure (23). Reductions in hepatic arterial blood flow and portal blood flow have been documented during early abdominal closure (24, 25). This effect was found to more significant in children (24) and may result in increased vascular thrombosis. Similar reductions in blood flow have been documented in renal transplant patients (26). The safe application of small intestinal submucosa for

abdominal wall reconstruction can thus avoid unnecessary tension in closing the abdominal wall incision.

The long-term durability of anterior abdominal wall repair using Surgisis® has not been well established. It has been well documented that porcine intestinal submucosa becomes well integrated into the patients abdominal wall with deposition of collagen, neovascularization (27). The process is one of incorporation, where a reproduction of a site-specific tissue identical to the original host tissue is created. This reconstructed tissue, from a histologic point of view as well as a functional one, is alleged to resemble the original tissue it is replacing (15). While our follow up was limited to a mean of 15.3 months some patients were seen after two yr, and none had developed incisional hernias. Thus medium-term follow up shows it to be effective.

The delay in definitive abdominal wound closure this study was in the hope of doing a delayed primary closure after the early post-operative edema has settled. With the safety of porcine intestinal submucosa, Surgisis® may be a viable alternative to use in primary closure and hence negate the need for a second procedure. This notwithstanding, the authors have not had any major infective complications from doing delayed primary closures.

The product appears as a thin opaque material (Fig. 2), comprising four layers of porcine intestinal submucosa. It requires rehydration in saline or ringers lactate solution for 10 min prior to use. Surgisis® comes in a variety of sizes and thicknesses from 0.6×7 to 7×20 cm and four or eight layer thick. In our study, a four layer graft usually of a preformed size 7×10 cm cut to size was used. The cost for the four layer 7×10 cm

Fig. 2. Piece of four ply Surgisis®.

Surgisis® product was approximately 890 Australian Dollars.

In conclusion, Surgisis® is safe in pediatric immune compromised hosts, appears resistant to infection and in medium-term follow up appears to be durable without evidence of hernia development. The series shows it to be an effective option for ventral abdominal wall closure, with a low rate of complications.

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