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Clinical outcomes of a fully resorbable biosynthetic mesh (Poly-4-hydroxybutyrate) for abdominal wall hernia repair: our experience in India

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Abstract :

Introduction: In past decade, poly–4-hydroxybutyrate (P4HB) a biosynthetic fully resorbable mesh which can serve as a potential alternative to biologic and traditional synthetic meshes in abdominal wall hernia repair, circumventing issues associated with both has been introduced. Present study aims to assess assessing the clinical outcomes associated with P4HB in abdominal wall hernia repair in Indian population.

Patients and methods: A total of 25 patients at our center who underwent abdominal wall hernia repair with P4HB mesh was retrospectively reviewed to assess the postoperative outcomes associated with this mesh. The primary endpoints include the rate of recurrence and the rate of surgical site occurrence.

Results: 25 patients were included (16 women, 9 men) with an average age of 49 years and average BMI of 28.9 kg/m2. High risk comorbidities included were obesity (12%), hypertension (48%), diabetes mellitus (20%), asthma (4%), hypothyroidism (20%), coronary artery disease (8%) and malignancy (4%).

Hernia types included were umbilical (40%), infraumbilical (20%), epigastric (8%), Incisional (20%), right lumbar (4%) and inguinal (8%).

Mean defect area was 24.96 cm2. Hernias were repaired by open onlay approach in 8 patients, laparoscopic intraperitoneal onlay mesh in 15 patients and laparoscopic totally extraperitoneal in the 2 inguinal hernia patients.

At an average follow up of 18 months, only one patient developed a hernia recurrence, two patients developed surgical site infection managed conservatively and one patient complained of heaviness at the site of mesh. No patient developed a seroma/ hematoma/mesh infection/enterocutaneous fistula/need for reoperation.

Conclusion: Study data demonstrates that P4HB mesh for abdominal wall hernia repair has a favorable outcome, acceptable recurrence rate and low rate of complications. This study supports P4HB mesh as an effective and safe biomaterial for abdominal wall hernia repair.

Statement of Declaration: 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. There were no financial interests/personal relationships which may be considered as potential competing interests**.**

IndexTerms **- Abdominal hernia, resorbable biosynthetic mesh, mesh infection.**

INTRODUCTION

An abnormal protrusion of the abdominal contents through a weakening or defect in the abdominal wall is known as an abdominal wall hernia. They are among the most prevalent issues that general surgeons deal with. They can be either primary or acquired. Primary hernias can be midline such as epigastric and umbilical, or lateral such as spigelian and lumbar. Acquired hernias typically occur after surgical incisions and are therefore termed incisional hernias estimated to occur in 10-20% of laparotomy incisions and significantly higher percentages occurring in high-risk groups [1] Individuals with symptomatic hernias or those who are at risk of complications are often advised to have surgery if the operating risk is acceptable. Hernia repair options include initial simple suture

repair, installation of synthetic or biologic mesh, or repair using relaxing incisions and component separation. In comparison to primary suture repair, synthetic mesh repair has been proven in numerous investigations to result in much fewer recurrences [2-4]. The current gold standard for a successful abdominal wall hernia repair is mesh reinforcement. Repair can be carried out using biological (porcine dermis and, bovine pericardium) or synthetic (polypropylene, polyester, polytetrafluoroethylene [PTFE] and composite) materials. Despite these advancements, long-term permanent mesh implantation carries considerable hazards, such as chronic discomfort, mesh infection, mesh erosion, and reoperation [5-7]. While permanent synthetic mesh has been demonstrated to provide long term biomechanical support and reliably reduce the risk of hernia recurrence [8,9], yet with a reported infection rate of about 5%, synthetic meshes are more prone to infection than biological materials [10].

Biological meshes are typically only used in contaminated or infected fields because of their lower strength of repair compared to synthetic mesh. It is hypothesized that biological meshes have a higher ability to resist infection, cause more orderly collagen deposition and have a milder inflammatory response than permanent synthetic meshes [11-13]. However, the huge downside to biologic meshes is their high cost. Given the significant cost burden and inadequate repair strength, surgeons have been led to search for alternative biomaterials [14]. Recently, biosynthetic meshes have been proposed as a novel class of materials. They combine the greatest qualities of synthetic and biologic mesh by offering short-term mechanical support and clearing bacterial burden, respectively. They are made from absorbable synthetic material such as polyglycolide, polylactide, trimethylene carbonate, and poly–4-hydroxybutyrate (P4HB) which gets incorporated into native tissue and show the ability to resist infections [15].

Poly–4-hydroxybutyrate is a macroporous, fully absorbable synthetic mesh that consists of co-knitted absorbable P4HB while its composite form is a P4HB mesh with additional sodium hyaluronate, carboxymethylcellulose and polyethylene glycol-based hydrogel on the visceral surface for intraperitoneal positioning [16-17].

The P4HB mesh has been used in several clinical studies for hernia repair with medium (18-24 months) to long term (36 + months) [18-20]. It provides a long-term resorption profile of 12-18 months, thereby providing a mechanical support to the defect thus preventing early hernia recurrence [21,22]. Early evidence suggests that bioresorbable mesh may provide a clinical advantage over synthetic mesh and a cost advantage over biologic mesh in ventral hernia repair [23, 24].

The purpose of this study is to describe our experience of using P4HB mesh for abdominal wall hernia repair to add evidence to support the choice of new generation biosynthetic prosthesis.

PATIENTS AND METHODS

In present report electronic medical records of the 25 abdominal wall hernia repair patients operated by us those were implanted with PHASIX® (extraperitoneal positioning)/PHASIX ST® (intraperitoneal positioning) mesh (manufactured by Beckton Dickinson India Private Ltd. Size 10 cm x 20 cm) between Jan 2020 and July 2022 and were reviewed. A follow up was performed with an outpatient visit for physical examination at the first postoperative month and via telephonic conversation for the following months (predefined at 1, 3, 6, 9, and 18 months with 24 months follow-up ongoing). A preset questionnaire was prepared for everyone.

All operative reports, clinic notes and imaging reports were reviewed. If there was a suspicion of relapse or complication, the telephonic follow-up was arranged by an outpatient visit and if required, an imaging examination (ultrasound, CT scan) would be performed.

We collected data on multiple parameters, including site of hernia, area of defect, type of repair, type of mesh used, patient comorbidities, recurrence, and complications. The primary endpoints were hernia recurrence and surgical site occurrence (SSO). A recurrent hernia was defined as any hernia identified by the investigator within 5 cm of the repair. If found, hernia recurrence would be confirmed by MRI or CT scan. The SSO was defined as chronic pain, hematoma, seroma, surgical site infection and wound dehiscence, mesh migration, mesh infection, requiring any type of medical or surgical intervention.

RESULTS

A total of 25 patients underwent abdominal wall hernia repair with PHASIX® and PHASIX ST® mesh, with an average post operative follow up of 18 months (3-30 months).

Preoperative data:

Average age of included patients was 49 years (33-74 years), more commonly reported in women (n=16, 64%) than in men (n=9, 36%) with an average BMI of 28.9 kg/m^2.

The most commonly reported comorbidity among study patients was hypertension (48%), followed by diabetes mellitus (20%), hypothyroidism (20%), obesity (12%), coronary artery disease (8%), asthma (4%), malignancy (4%), and dyslipidemia (4%). Hernia types included were umbilical (n=10, 40%), infraumbilical (n=5, 20%), epigastric (n=2, 8%), incisional (n=5, 20%), right lumbar (n=1, 4%), inguinal (n=2, 8%).

Table 1 Demographic and clinical characteristics:

Demographic and clinical variables	
Total no of patients	n=25
Sex	16 (64%) women
	9 (36%) men
Average age, mean (min-max) years	49 (33-74) years

Average body mass index (BMI)	28.9 Kg/m2
Comorbid conditions (n, %)	Obesity (n=3, 12%)
	Hypertension (n=12, 48%)
	Diabetes (n=5, 20%)
	Hypothyroidism (n=5, 20%)
	Coronary Artery Disease (n=2, 8%)
	Asthma (n=1, 4%)
	Dyslipidemia (n=1, 4%)
	Malignancy (n=1, 4%)
Type of Hernia (n, %)	Umbilical (n=10, 40%)
	Infraumbilical (n=5, 20%)
	Epigastric (n=2, 8%)
	Incisional (n=5, 20%)
	Lumbar (n=1, 4%)
	Inguinal (n=2, 8%)

Operative data:
The mean defect area of hernia was 24.96 cm^2. Hernias were repaired using open onlay approach in 8 patients, laparoscopic IPOM in 15 patients and laparoscopic TEPP in 2 patients. The type of mesh used was PHASIX® in 10 patients and PHASIX ST® in 15 patients.

Table 2 Operative data:

Operative data	
Mean defect(cm^2)	24.96 cm^2
Surgical Approach	Open onlay (n=8)
	Laparoscopic intraperitoneal onlay mesh (n=15)
	Laparoscopic totally extraperitoneal (n=2)
Type of mesh	PHASIX® (n=10)
	PHASIX ST® (n=15)

Postoperative outcomes:
The recurrence was noted in 1 patient with an average follow-up of 18 months. It was reported that 2 patients had surgical site infections which was managed by conservative treatment, 1 patient complained of heaviness at the site of mesh. No patient reported any event of hematoma/seroma/mesh infection/mesh migration/enterocutaneous fistula/intestinal obstruction or required reoperation.

DISCUSSION.
Our study is a single-center study conducted at an Indian tertiary care centre. It evaluates the safety, performance, and clinical results of P4HB mesh in abdominal wall hernia repair. There have been no clinical studies from India on the clinical results of P4HB mesh reported to date. To fill this void, we set out to investigate the long-term clinical results of P4HB mesh in hernia repair.

Synthetic meshes have been universally acknowledged as the gold standard for incisional hernia repair [2], with mesh patients having a lower recurrence rate than suture patients. Despite its advantages, long-term problems with synthetic meshes such as infection, migration, erosion, and adhesions outweigh the advantages of decreased hernia recurrence [9]. Although improvements in surgical techniques and emergence of mesh reinforcement have enhanced outcomes in ventral hernia repair, advancements in biomaterials can potentially further improve results for patients. Biological mesh has been advocated by some authors as an alternative to synthetic mesh due to its resorbable nature in patients with higher risk of wound complications. However, there is a significant increase in cost compared to synthetic mesh with substantial variability in long term clinical outcomes.

An idea mesh, should be biodegradable, does not promote seroma formation, allow placement in contaminated/infected field, promotes tissue ingrowth and is durable enough to offload the fascial repair until the wound strength reaches plateau (approximately 6 months). Our experience demonstrated that P4HB mesh meets many of these criteria. The P4HB is a new and increasingly utilized surgical scaffold in ventral hernia repair. It is a biosynthetic graft that slowly reabsorbs and was created as a possible replacement for its more conventional biologic and synthetic counterparts. It is a naturally occurring monofilament framework made up of butyrate monomers, a short chain fatty acid, which has been shown to possess antibacterial properties [25]. Although it has not been proved in humans, animal models have shown that butyrate can protect them against sepsis. Inflammation in the presence of infection is anticipated to hasten the enzymatic breakdown of the biologic mesh [26], weakening the scaffold and predisposing to recurrence. Unlike the biologic mesh, the P4HB degrades by a hydrolytic process into carbon dioxide and water which may reduce the inflammatory response [21]. This is a potential mechanism by which the P4HB protects against recurrence in the setting of surgical site infection (SSI), but further research is needed to validate this information.

The P4HB achieves full resorption by 12-18 months [22]. The byproducts carbon-dioxide and water are rapidly metabolized with minimal effect on local wound pH. This allows the mesh to offload the repair for the 6-month time period required to achieve maximum wound strength prior to its degradation. Histologically, this material presented with excellent biocompatibility with minimal inflammation or tissue reactivity after 64 weeks in vivo [27]. Furthermore, preclinical models had demonstrated increased

resistance to bacterial contamination with P4HB compared to polypropylene mesh and P4HB's ability to induce noncytotoxic effects and increase the expression of antimicrobial peptides (cramp and B-defensin-4) [28,29].

Though human data are lacking, in a porcine hernia model, mesh repair with P4HB demonstrates greater burst strength than even the native abdominal tissue at 52 weeks despite significant resorption of the material [21]. Synthetic scaffolds produce a M1 macrophage response whereas biologic scaffolds produce a M2 macrophage response. A persistent, proinflammatory (M1-like) macrophage phenotype is typically associated with fibrosis and scarring. In contrast, an early transition to a regulatory, remodeling (M2-like) macrophage phenotype is predictive of organized, site appropriate connective tissue deposition. The P4HB is naturally derived polymer which favors a M2 like macrophage response. Uncoated polypropylene mesh elicits a dominant M1 response at the mesh fiber surface.[30]

Our study was conducted on CDC class-1 (clean wounds) patients where we placed mesh in both primary and incisional hernias. Majority of patients underwent laparoscopic hernia repair. None of these patients were lost to follow-up with a mean follow-up period of 18 months which was comparable to previous studies (18-24 months) performed on P4HB mesh [18, 20]. The P4HB mesh was used safely in all our patients with recurrence in only one patient after mean follow up of 18 months. Although in previous studies 9% and 5.7% recurrence was reported, we observed a recurrence of 4%; that highlights the efficacy of this mesh. In our study, postoperative SSI was reported in 2 patients (8%) both of which were managed conservatively with antibiotics, and no patient required mesh removal. It is known that all postoperative infections are not preventable, the use of an absorbable mesh for patients at higher risk of SSI could be part of a strategy to reduce costs associated with mesh infection. In our study none of the patients reported of seroma/hematoma/mesh erosion/enterocutaneous fistula/intestinal obstruction, thus not requiring any reintervention. These complications are very common with permanent synthetic meshes.

Our initial experience with P4HB mesh seems promising. The initial results with the use of this mesh favors this mesh as a reliable alternative to prosthetic/biological meshes circumventing issues associated with both. Our findings warrant further investigations into the specific role that P4HB mesh plays in hernia repair. Further study with more sample size with a longer term follow up is necessary to better establish the clinical benefits of P4HB mesh over traditional meshes.

CONCLUSION

In conclusion, according to clinical outcomes results the P4HB mesh are acceptable and may serve as an effective and safe alternative to the traditional synthetic and biologic mesh in abdominal wall hernia repair with acceptable surgical site occurrence rates. It remains to be studied whether hernia repair with P4HB mesh causes lower recurrence and is more cost effective than biologic or synthetic mesh, for which further follow up is required. This study is currently ongoing through 24 month follow up.

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