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A Prospective Randomized Controlled Trial Comparing Clinical Equivalence of PD Synth® and PDS® Slowly Absorbed Polydioxanone Sutures in Elective/Emergency Midline Laparotomy

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Abstract

Introduction:

Incisional hernia is a common complication of midline laparotomy that may develop even after several years of surgery. Abdominal fascia closure with ideal suture material reduces the incidence of incisional hernia. This study compared clinical equivalence of PD Synth® and PDS® slowly absorbed polydioxanone suture with respect to occurrence of incisional hernia, following elective/emergency midline laparotomy.

Methods:

Eighty-eight subjects undergoing elective/emergency midline laparotomy were randomized to PD Synth® (n=45) and PDS® (n=43) groups of this prospective, multicenter, randomized (1:1), single-blind, two-arm, parallel-group study (December 2020-May 2023). Primary endpoint was incidence of incisional hernia, occurring within 6 and 12 months of surgery. Secondary endpoints included incidence of fascial dehiscence, SSI, suture sinus, seroma, hematoma, scar tenderness and re-suturing, and evaluation of operative data, hospital stay, intraoperative suture handling, pain, time to return to normal day to day activities and work, overall patient satisfaction score, and adverse events.

Results:

One subject in both PD Synth® and PDS® groups ($p>0.05$) developed incisional hernia at umbilicus 12 months post-laparotomy. In PDS® group, one subject each had incidence of SSI on Day 2, Day 7 and Month 1, two subjects developed seroma on Day 7 and one subject had a readmission on Month 1; two subjects in PD Synth® group developed superficial SSI (Month 1). Findings of other secondary endpoints were comparable between the groups.

Conclusion:

Primary and secondary outcomes manifested that PD Synth® and PDS® slowly absorbed polydioxanone sutures are clinically equivalent, and can be used for abdominal fascial closure following midline laparotomy.

Categories: Emergency Medicine, General Surgery, Oncology
Keywords: polydioxanone suture, midline laparotomy, incisional hernia, fascial dehiscence, absorbable suture

Introduction

Quick and easy abdominal access prevailed midline laparotomy as the most frequently used technique in the field of emergency/elective surgery [1]. Patients presenting life-threatening clinical condition undergo laparotomy only after provisional diagnosis [2]. According to the Centers for Disease Control (CDC), approximately 4-5 million laparotomies are performed per year in the Unites States alone [3]. However, post-laparotomy development of incisional hernia is common (9.9%), especially after midline abdominal incision, which further causes 2-20% surgical morbidity [4]. Although incisional hernia may develop several years

after surgery, but 50% cases are diagnosed within one year [5]. Rate of incidence may vary from 5-20% depending upon follow-up duration, techniques used for closure of the incision, and biological factors, associated with patients healing, which may increase up to 40% in high risk patients [6]. This affects patient's quality of life, and around 30% of the hernias needs to be repaired, adding financial burden [3, 7].

Wound dehiscence is another post-laparotomy complication; 0.2-5% results from elective laparotomy and up to 45% are associated with emergency laparotomy, leading to 30% incidence of mortality and morbidity [8]. Ideal closure of midline laparotomy incision is crucial to minimize the occurrence of incisional hernia and wound dehiscence, along with other frequently occurring post-operative complications like wound pain and surgical site infection (SSI) [9]. Investigation of best technique (interrupted vs. continuous suture) for wound closure that may result in lesser complications is controversial since long time. The best technique must be simple and convenient that can provide tensile strength throughout the process of healing and good approximation of the tissue, with lesser chances of wound infection [10]. The guidelines from the European and American hernia societies, developed using GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation) has suggested the use of slowly absorbable suture with continuous suture technique for closure of incision in elective midline laparotomy [11]. Use of absorbable suture reported to reduce wound pain and risk of sinus formation when compared to non-absorbable suture [12, 13]. Monofilament suture material lowers the incidence of SSI [12]. Previous studies have compared monofilament absorbable polydioxanone with non-absorbable polypropylene [14] or polyamide nylon [15] suture for abdominal wound closure, and reported comparatively lower wound complication rate with the former. However, comparative study on two commonly used brands of slowly absorbed polydioxanone sutures for fascia closure in a single layer is not available. Therefore, this study was designed to compare clinical equivalence of PD Synth® and PDS® slowly absorbed polydioxanone sutures, for abdominal fascial closure following elective/emergency midline laparotomy.

Materials And Methods

Study Design

A multicenter, prospective, two-arm, parallel-group, randomized (1:1), single-blind 12 months follow-up study was conducted between September 2020 and May 2023. The primary objective was to compare the rate of incisional hernia with PD Synth® and PDS® polydioxanone sutures, at 6 months and 12 months post-abdominal fascial closure. Secondary objectives included assessment of SSI, fascial dehiscence, suture sinus, overall intraoperative handling, tissue reaction and material problems, post-operative discomfort, pain, overall patient satisfaction score, and other adverse events.

Ethical Approval

The study was registered in the Clinical Trial Registry of India and carried out in compliance with the declaration of Helsinki. Ethical approval was granted by the Ethics Committees of participating sites. The study complied with ICH-GCP E6(R2), EN-ISO 14155:2020, Medical Device Rules India 2017, Medical Devices Regulation (EU) 2017/745, New Drugs and Clinical Trials Rules, 2019 and Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Study Participants

Female or male adults (18 to 60 years) with good systemic/mental health (as per opinion of the investigator) and CDC surgical wound classification class I/II/III, requiring elective/emergency midline laparotomy were included in this study. Written informed consent was obtained from all participants.

Participants with body mass index (BMI) of <18.5 and ≥30 Kg/m2, American Society of Anesthesiologists (ASA) class V, undergoing elective/emergency laparoscopic abdominal surgeries, requiring an early (within 30 days) reintervention after index surgery, or prophylactic mesh augmentation after midline laparotomy were excluded from the study. Participants with history of midline laparotomy, or allergy to polydioxanone or similar products, or abdominal hernia, or systemic diseases (chronic obstructive pulmonary disease, tuberculosis and bleeding disorders), or who were pregnant or planning pregnancy in next one year were excluded. Participants having life expectancy of <1 year, or active infection at/around skin incision site, or abdominal hernia or wall metastases, or experimental drug or medical device within 30 days prior to the planned start of procedure were also excluded. Other exclusion criteria were habit of drug abuse, participation in another trial, unlikely to comply with current surgical procedure or complete the study follow-ups (in the opinion of investigator), direct involvement in the proposed study or other studies under the direction of that investigator or study center (employees of the investigator or study center) and other indication-based exclusion.

Study Setting

Surgical departments in four tertiary care centers across India were involved in this study.

Intervention

PD Synth® suture (Healthium Medtech Limited) and PDS® II (Ethicon, Johnson & Johnson) both are sterile, absorbable, synthetic, monofilament, polydioxanone surgical suture, intended for use in approximation of the general soft tissue, including pediatric cardiovascular tissue in micro and ophthalmic surgery. Both sutures are particularly useful where the combination of an absorbable suture with extended wound support for up to 6 weeks is desirable.

Study Procedure

The primary cause for midline laparotomy was corrected, and abdominal fascia was closed in a single layer with wide bites through the rectus sheath (minimum 1 cm from the incision edge) using either of the sutures. For both sutures, a similar strength of material was used and suture to laparotomy wound length ratio was kept at least 4:1. The skin was closed with surgical staples and the surgeon reconfirmed proper closure, leaving little room for surgical error. The primary dressing was removed after 24-48 hours, and further wound care was done as per the Institutional protocol. The wound was inspected for signs of infection and dehiscence before each dressing, and subjects having infection were put on antibiotics according to the Institutional protocol and culture and sensitivity report. Skin staples were removed in conventional way in 1-3 weeks, based on Investigator discretion.

Subjects were screened (Month -3 to Day -1) and enrolled to undergo elective/emergency midline laparotomy (Day 0, baseline visit). Six post-operative visits were conducted on Day 3, Day 7, Month 1, Month 3, Month 6 and Month 12, to record the outcomes.

Demographics and Other Relevant Characteristics

At screening, subject’s age, gender, ethnicity, occupation, weight, height, BMI, occupation, and history of alcohol consumption and smoking were recorded. Vital signs including respiratory rate, pulse rate, and systolic and diastolic blood pressure were also measured. In addition, radiation therapy (if done), medical/surgical history, and physical examination for any abnormality (central nervous system, respiratory system, gastrointestinal system, skin, joints and extremities, ear, nose and throat, general appearance, edema and lymph nodes) were noted. Pre-surgery pain at screening visit using visual analog scale (VAS) was evaluated.

Study Outcomes

Primary Endpoint

Incidence of incisional hernia, occurring within 6 and 12 months of the primary surgery in both groups was assessed clinically. Ultrasound examination was performed at Investigators' discretion to confirm the presence of an incisional hernia and for its complete evaluation.

Secondary Endpoints

Secondary endpoints were incidence of fascial dehiscence, SSI, suture sinus, seroma, hematoma and scar tenderness. In addition, intraoperative suture handling parameters (ease of passage through tissue, first-throw knot holding, knot tie-down smoothness, knot security, surgical handling, suture fraying were rated on a five-point scale, 1 poor; 2 fair; 3 good; 4 very good; and 5 excellent), operative data, requirement of re-suturing, and length of hospital stay were assessed. Operative data included length of surgery (time from skin incision to completion of skin closure), suture size, needle-tip geometry and diameter, suture length and wound length ratio, length of the incision, method of suturing, duration of surgery, blood loss, number of sutures used, antibiotic and thrombosis prophylaxis, drain, use of epidural catheter and suture-related challenges. Time to return to normal day to day activities and work were also recorded.

Pain was measured using VAS (0-100 scores), self-completed by the respondent. No pain was designated as 0-4, mild pain as 5-44, moderate pain as 45-74 and severe pain as 75- 100. Median patient satisfaction score for overall discomfort and EuroQoL five-dimensional three-level (EQ-5D-3L) questionnaire for overall well-being of the subject were evaluated. Five dimensions of subject’s health state viz., mobility, self-care, usual activities, pain/discomfort and anxiety/depression were estimated on three levels: no problems, some problems, and extreme problems. EuroQol-visual analogue scales (EQ-VAS), part of EQ-5D was used for global assessment of subject’s health on a vertical VAS (100, best imaginable health and 0, worst imaginable health).

Clinical sign, injury or disease, not reported as study endpoint was noted as adverse event (AE). Side effect related to the standard care for index disease, or a condition requiring a pre-planned procedure (unless the condition worsened since screening), or a pre-existing condition was not labeled and reported as an AE. Moreover, serious adverse event (SAE) was defined as AE that led to serious deterioration of health, permanent impairment of body structure or function, re- or prolonged hospitalization, or death. Concomitant or prescribed medications were also listed.

Sample Size

The rate of incisional hernia varies a lot between different reports, probably very much related to different definitions of incisional hernia used at follow-up. For sample size calculation, proportion of patients having incisional hernia of 5.6% till 12 months as reported by a previous study [16] was considered in the PDS® suture arm. The anticipated proportion of the patients having incisional hernia in the PD Synth® suture arm till 12 months was assumed as 6.0%. Considering type I error, power and margin of non-inferiority as, 5%, 80% and 15% respectively, requirement of sample size was calculated as 38 in each arm, providing a total sample size of 76. Further, considering 20% drop out and post-randomization exclusion, the required sample size was increased to 92. This sample size was adjusted to 96 for block randomization, with 48 subjects to be enrolled in each arm.

Sample size calculation formula:

Two-sample Parallel Non-inferiority $\pi_1 - \pi_2 \geq \delta$ $n_i = \frac{(Z_\alpha + Z_\beta)^2 (\pi_1 (1-\pi_2) + \pi_2 (1-\pi_2))}{(\pi_1 - \pi_2 - \delta)^2}$

n_i: Sample size required in each group

Z_α: Conventional multiplier for alpha

Z_β: Conventional multiplier for power

π_1: Incidence rate of incisional hernia in the standard PDS® arm

π_2: Incidence rate of incisional hernia in PD Synth® arm

δ: Margin of non-inferiority difference

π_1-π_2: Size of difference of clinical importance

Randomization and Blinding

Block randomization with variable block length, stratified per trial site was performed using sequentially numbered opaque sealed envelope technique. Eligible subjects were randomized in 1:1 ratio to receive either of the sutures. An interactive, automated randomization number was generated before the initiation of the study by an independent programmer (not a member of the study team).

Post-operative controls were performed at each center by a physician or support staff, not directly involved in the study and they were kept blind to the particular suture used in each patient, along with the patient himself/herself. However, the operating staff cannot be blinded to allocation due to the nature of the intervention; they were instructed not to disclose the allocation status at any time point.

Statistical Analysis

Per-protocol or PP analysis set was used for subjects, who had complete data for primary endpoint at 12 months follow-up, without major protocol deviations that could impact the primary outcome. The t-test and its non-parametric equivalent (Mann-Whitney U test) were used for comparing mean±SD for all continuous variables. Frequencies and percentages of all qualitative variables were calculated by applying Chi-square test. Data of primary endpoint was expressed as proportion/percentage of subjects having incisional hernia and compared using Chi-square test. Depending on quantitative or qualitative nature of the variables, secondary endpoints were expressed as mean±SD or as proportions/percentages. Data were analyzed using SPSS version 28.0 (SPSS, Chicago, Illinois, USA), considering p value <0.05 as significant.

Results

Between December 2020 and June 2022, a total of 96 participants were screened for eligibility. Final analysis included 88 subjects, randomized in PD Synth® (n=45) and PDS® (n=43) groups, who have completed the trial. Reason for exclusion of rest of the subjects is presented in Figure *1*.

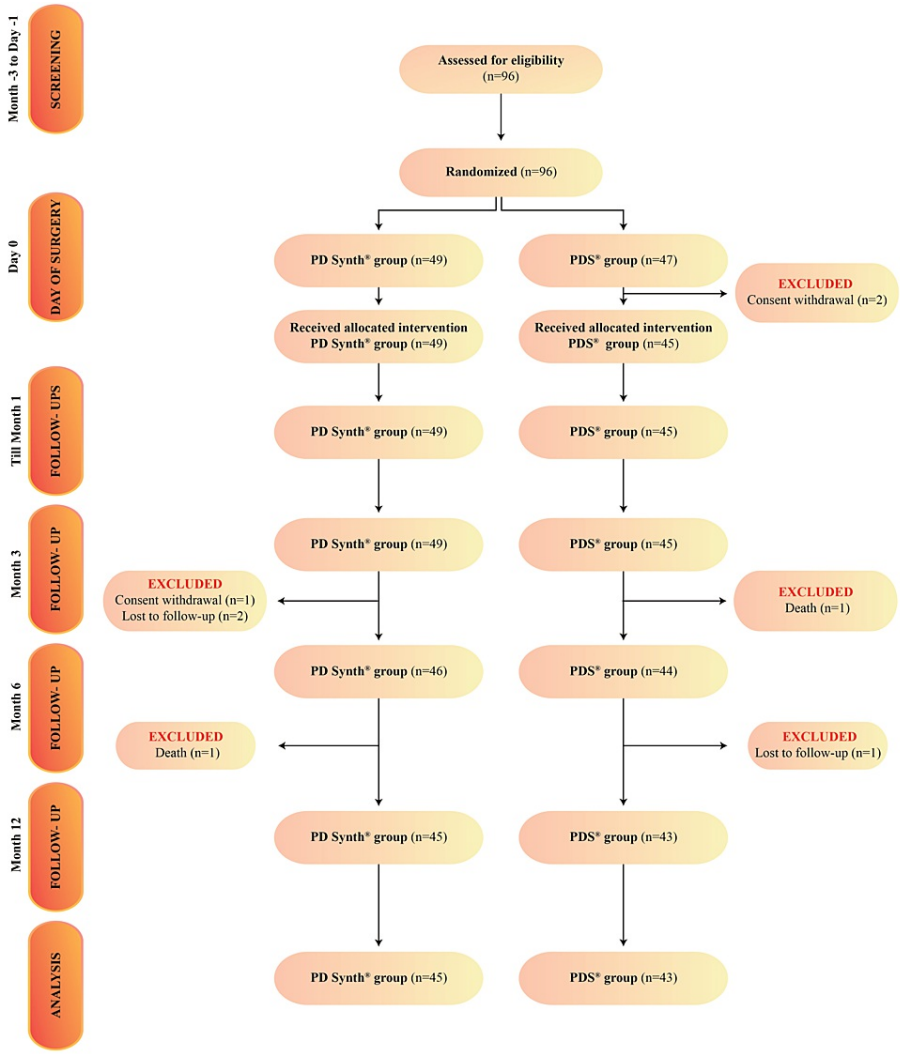


FIGURE 1: CONSORT flow chart of the study

n= number of patients

Demographics and Other Relevant Characteristics

Demographics of subject in terms of age, ethnicity, gender, occupation, alcohol consumption and smoking history were comparable. All subjects of PDS® group were Indians; 44 (97.8%) subjects in PD Synth® group were Indians and one (2.2%) subject was non-Indian Asian (p=0.33). In PD Synth® and PDS® group, 22 (48.9%) and 20 (46.5%) subjects respectively were females, and remaining were males (p=0.82). Both groups were comparable with respect to occupation, vital signs, alcohol and smoking history, and medical/surgical history (Table *1*).

Subject characteristics	PD Synth® (n=45)	PDS® (n=43)	p value
Age (years)	41.3±12.0	43.6±10.8	0.12
Alcohol consumption history	6 (13.3)	7 (16.3)	0.70
Smoking history	5 (11.1)	2 (4.7)	0.26
Medical/surgical history	38 (84.4)	36 (83.7)	0.99
Weight (kg)	60.0±10.4	59.1±9.5	0.69
Height (cm)	161.2±8.9	159.3±7.7	0.48
BMI (kg/m^2)	23.0±3.1	23.22±2.8	0.71
Occupation			
Desk job	3 (6.7)	0	0.62
Hard strenuous job	9 (20.0)	9 (20.9)	
Mild strenuous job	17 (37.8)	16 (37.2)	
Housewife	16 (35.6)	18 (41.9)	
Vital signs			
Pulse rate (beats per minute)	84.3±9.7	85.8±7.7	0.22
Respiratory rate (respiration per minute)	18.4±2.3	18.1±2.3	0.79
Systolic blood pressure (mmHg)	118.0±11.1	121.6±10.1	0.62
Diastolic blood pressure (mmHg)	75.2±8.8	77.9±6.9	0.11

TABLE 1: Baseline characteristics of the study participants

n= number of patients, Data is presented as mean±SD or n (%)

Pre-surgery radiation therapy was required in one subject of both PD Synth® (2.2%) and PDS® (2.3%) groups (p=0.97). Physical examination revealed abnormal gastrointestinal system (100.0% vs. 97.7%, p=0.30), skin (2.2% vs. 4.7%, p=0.53), joint and extremities (0 vs. 2.3%, p=0.30) and lymph nodes (2.2% vs. 4.7%, p=0.53) in PD Synth® and PDS® group.

Primary Endpoint Analysis

Post-operative incidence of incisional hernia was evaluated at Month 1, 6 and 12 follow-ups. There was no incidence of incisional hernia at Month 1 among the subjects of both groups. However, at 6 and 12 month follow-ups, one (2.2%) subject of PD Synth® group was diagnosed with incisional hernia at umbilicus. Ultrasound examination showed that the subject had intact linea alba, but bulging at umbilicus with and without Valsalva maneuver at both visits. At Month 6, the size of the defect was 6 mm that increased to 10 mm at Month 12 follow-up, and omentum fat was present in the defect. At the last follow-up, presence of incisional hernia at umbilicus was marked in one (2.3%) subject of PDS® group, who had focal defect at umbilical region. The subject had bulging with Valsalva maneuver along with a defect measuring 1.7 cm. Also, fatty tissue was present in the defect. The result was comparable between the groups at Month 6 (p=0.96) and Month 12 (p=0.97) follow-ups.

Secondary Endpoint Analysis

Intraoperative Profile

Intraoperative antibiotic prophylaxis was given to all study participants. General anesthesia was used in 42 (93.3%) and 41 (95.3%) subjects of PD Synth® and PDS® group respectively; rest were given spinal anesthesia (p=0.69). Intraoperative suture handling characteristics were comparable for both suture groups; none of the characteristics were graded as “poor” (Figure *2*),

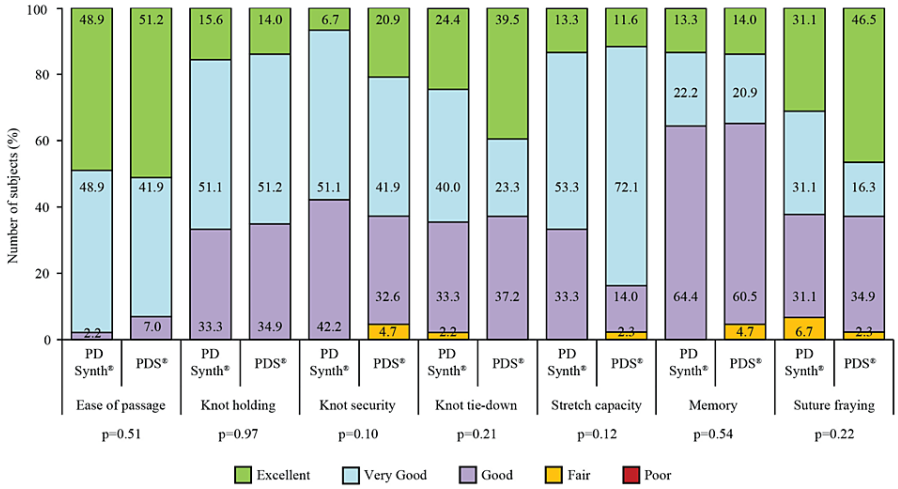


FIGURE 2: Intraoperative suture handling characteristics in subjects assigned to PD Synth® (n=45) and PDS® (n=43) groups

and no intraoperative suture related challenge was reported. Continuous suturing with size no. 1 suture of 150.00 cm was done in all subjects of both groups. Round bodied needle of 50 mm in PD Synth® group and of 48 mm in PDS® group was used. Suture and wound length ratio was 4:1 in both groups. Thrombosis prophylaxis, deep vein thrombosis pump (2.2% vs. 2.3%), clexane, (37.8% vs. 41.9%) and heparin (0 vs. 2.3%) were used in both PD Synth® and PDS® groups (p=0.37). During the surgery, blood loss occurred in 28 (62.2%) and 26 (60.5%) subjects of PD Synth® and PDS® group respectively (p=0.34). Epidural catheter was used in 13 (28.9%) subjects of PD Synth® and 15 (34.9%) subjects of PDS® group (p=0.55). None of the subjects reported perioperative complications (p=1.00). Good outcome of surgery was noted in both groups (p=1.00). Other intraoperative details are summarized in Table *2*.

Subject profile	PD Synth® (n=45)	PDS® (n=43)	p value
Intraoperative profile			
Length of incision (cm)	15.5±3.1	15.7±3.4	0.27
Number of sutures used	1.6±0.7	1.7±0.5	0.70
Total operative time (hours)	3.0±2.6	3.2±2.1	0.41
Blood loss amount (ml)	331.6±229.6#	524.6±548.6##	0.81
Number of sutures used			
1	20 (44.4)	16 (37.2)	0.69
2	23 (51.1)	26 (60.5)	
3	1 (2.2)	1 (2.3)	
4	1 (2.2)	0	
Type of drain administered			0.88
Abdominal	1 (2.2)	0	
Pelvic	3 (6.7)	5 (11.6)	
Subcutaneous	0	1 (2.3)	
Esophagojejunal anastomosis site	1 (2.2)	0	
Duodenal stump	0	1 (2.3)	
Morrisons pouch	1 (2.2)	0	
Left hypochondrium	1 (2.2)	0	
Left splenic bled	1 (2.2)	0	
Left flank	0	1 (2.3)	
Flat drain	1 (2.2)	0	
Ryles tube	1 (2.2)	0	
Post-operative profile			
Length of ICU stay (days)	0.6±0.8	0.6±0.8	0.87
Length of hospital stay (days)	9.1±7.8	8.8±6.2	0.86
Time taken to return to normal day to day activities (days)	19.4±9.0	17.3±9.8	0.21
Time taken to return to work (days)	38.3±16.3	35.6±18.5	0.54

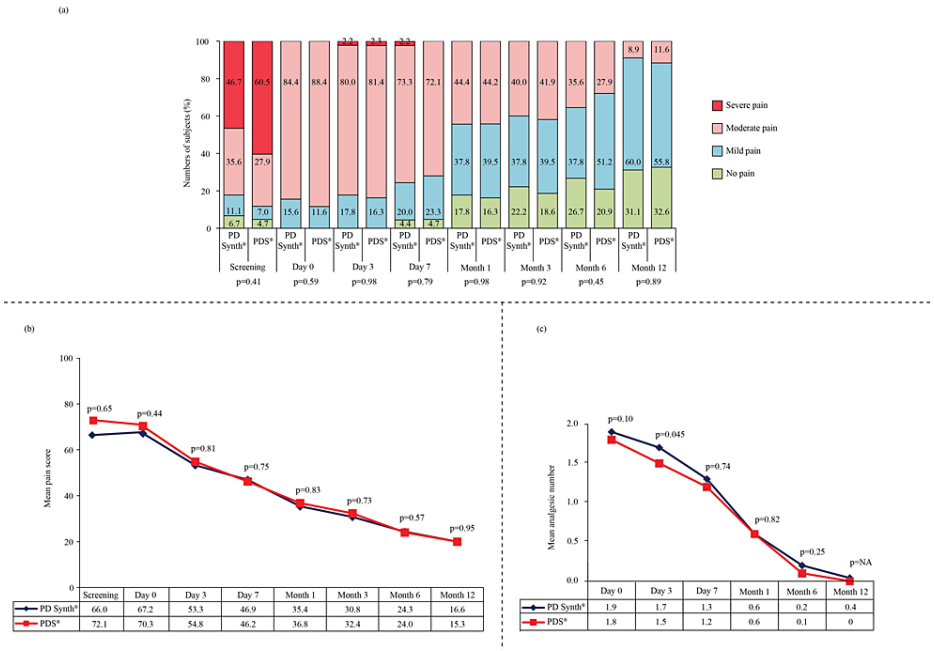
TABLE 2: Intraoperative and post-operative characteristics of the study participants

Data is presented as mean ± SD or n (%); # n=28; ## n=26; ICU: Intensive Care Unit

Post-Operative Profile

All subjects were screened for fascial dehiscence at Day 3 and 7, and for suture sinus at Month 1, 6 and 7, and no occurrence of the same were noted. However, in PDS® group, one (2.3%) subject developed superficial incisional SSI on each Day 2 (p=0.99) and Day 7 (p=0.99). In both PD Synth® and PDS® groups, two (4.4%) and one (2.3%) subjects respectively had superficial incisional SSI at Month 1; the finding is non-significant (p=0.58). Two (4.7%) subjects of PDS® group had seroma on Day 7 (p=0.98). Although no medications were prescribed for the complications, but no further incidence of superficial incisional SSI and seroma were recorded on the subsequent visits. Other post-operative complications, viz., deep incisional, hematoma, scar tenderness, re-suturing, and other suture related complications did not occur in any subjects of both groups. Pain started at 4.3±2.0 and 4.3±2.7 hours of surgery in subjects randomized to PD Synth® and PDS® group,

respectively (p=0.65). On Day 0, 3 and 7, all subjects of PD Synth® and PDS® groups had pain. However, proportion of subjects, experiencing no pain was increased with time, and by Month 12, none of them had severe pain (Figure 3a).



(b)	Screening	Day 0	Day 3	Day 7	Month 1	Month 3	Month 6	Month 12
PD Synth®	66.0	67.2	53.3	46.9	35.4	30.8	24.3	16.6
PDS®	72.1	70.3	54.8	46.2	36.8	32.4	24.0	15.3

(c)	Day 0	Day 3	Day 7	Month 1	Month 6	Month 12
PD Synth®	1.9	1.7	1.3	0.6	0.2	0.4
PDS®	1.8	1.5	1.2	0.6	0.1	0

FIGURE 3: (a) Mean pain score with VAS, (b) grade of pain, and (c) number of analgesics in subjects assigned to PD Synth® (n=45) and PDS® (n=43) groups.

*p<0.05

Improvement in intragroup pain with each follow-up was apparent in both groups, as depicted in Figure 3b. In addition, requirement for analgesics was declined with each passing visit (Figure 3c), and at Month 3, only 3 (6.7%) subjects in PD Synth® group and 3 (7.0%) subjects in PDS® group were taking analgesics (p=0.95). None of the subjects in both groups reported have complications on Month 3 follow-up, viz., peri-incisional swelling, infection, fever, back pain, abdominal colic, vomiting, constipation, distension of abdomen and difficulty in respiration. At the discretion of the Investigator, in PD Synth® and PDS® group ultrasound was performed in one (2.2%) and 4 (9.3%) subjects respectively at Month 6 (p=0.15), and in 8 (17.8%) and 7 (16.3%) subjects respectively at Month 12 (p=0.85) follow-ups. Among them, presence of incisional hernia was only confirmed in one subject of PD Synth® group (at both Month 6 and 12) and in one subject of PDS® group (at only Month 12), details of which is provided earlier. In addition, non-intact linea alba was noted in one subject of PD Synth® group at Month 12 and in one subject of PDS® group at both Month 6 and 12, though incisional hernia was not diagnosed in these subjects. Similar findings of intensive care unit (ICU) stay, hospital stay and time to return to normal day to day activities and work were recorded (Table 2).

The subjects of both groups reported to have some problems in mobility, self-care, usual activities, pain/discomfort and depression/anxiety at screening visit that improved after undergoing midline laparotomy. Analysis of each dimension of EQ-5D showed that overall proportion of no problems was increased with each post-operative follow-up in both PD Synth® and PDS® groups (Figure 4 a-e).

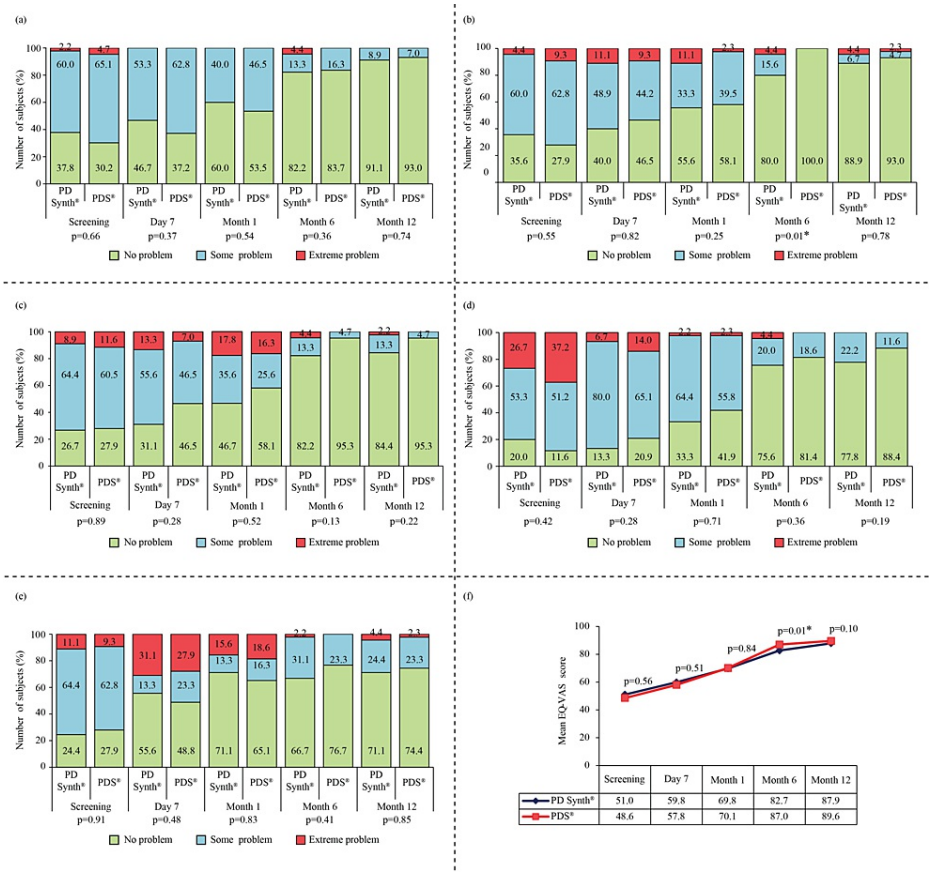


FIGURE 4: EuroQoL five-dimensional three-level questionnaire for overall well-being: (a) mobility, (b) self-care, (c) usual activities, (d) pain/discomfort and (e) depression/anxiety, and (f) EuroQol-visual analogue scale for global assessment of health in subjects assigned to PD Synth® (n=45) and PDS® (n=43) groups.

*p<0.05

Between the groups, a significant (p<0.05) difference in self-care was detected only at Month 6. However, the results for all dimensions were comparable at final follow-up. Additionally, the EQ-VAS score gradually improved with each post-operative visit (Figure *4f*). Although at Month 6, a significant (p<0.05) difference in EQ-VAS score was found between PD Synth® (82.73±18.15) and PDS® (86.95±11.82) group, but the mean result was increased and at Month 12, a comparable (87.89±12.02 vs. 89.58±7.60) improvement was noted between the groups.

Adverse events and SAEs, occurring within the course of the study were documented. Twelve and thirteen non-serious mild AEs were reported in PD Synth® and PDS® group, respectively. The incidents were not related to the study device. Vomiting and giddiness (2.2%), constipation (2.2%), fat necrosis (2.2%), resuture of skin (2.2%), headache (4.4%), vomiting (2.2%), burning micturition (2.2%), diarrhea (2.2%), hypertrophic scar (4.4%) and general body pains (2.2%) were reported in PD Synth® group. Chest pain (2.3%), skin gaping (2.3%), thrombocytosis (2.3%), wound discharge (2.3%), resuture of skin (4.7%), abdominal pain (2.3%), headache (2.3%), headache and nausea (2.3%), anemia (2.3%), cough, constipation and pain localized to upper abdomen (2.3%), cold (2.3%), and constipation (2.3%) were recorded in PDS® group. One (2.3%) subject in PDS® group was readmitted due to vomiting and abdominal distension at Month 1, and discharged after treatment to continue the study. This was reported as SAE and not related to the study device. Although other SAEs took place but not included in the PP analysis set due to unavailability of primary endpoint data. The SAEs were as follows: readmission at Month 1 (due to pleural effusion) and Month 3 (due to left sided chest pain and dyspnea), and death (due to intracapsular neck of femur fracture after falling) of one subject in PD Synth® group; and at Month 6, death (due to hemorrhagic shock) of one subject in PDS® group. Both subjects were excluded from the study, as shown in Figure *1*. Analgesics, antibiotics and medications for gastrointestinal were prescribed to the subjects during the study; details of some of them are given in Table *3*.

Prescribed medications	PD Synth® (n=45)	PDS® (n=43)
Analgesics		
Paracetamol	45 (100.0)	42 (97.7)
Tramadol	28 (62.2)	29 (67.4)
Diclofenac	16 (35.6)	10 (23.3)
Fentanyl	15 (33.3)	12 (27.9)
Antibiotics		
Cefoperazone+Sulbactam	18 (40.0)	15 (34.9)
Metronidazole	16 (35.6)	19 (44.2)
Cefuroxime	17 (37.8)	13 (30.2)
Ceftriaxone	7 (15.6)	9 (20.9)
Gastrointestinal		
Pantoprazole	33 (73.3)	39 (90.7)
Ondansetron	15 (33.3)	20 (46.5)

TABLE 3: Concomitant or prescribed medications

n= number of patients, Data is presented as n (%)

Discussion

Midline laparotomy offers advantage of exposure and ease of access to several organs, but still poses risk of impaired wound healing due to avascular nature of linea alba [17]. Development of incisional hernia is a frequent and common complication of laparotomy, elevating the healthcare burden [18]. Increase in intra-abdominal pressure, abdominal distension and inadequate healing of a previous incision, which is necessary for providing strength and preventing development of hernia, are the contributing factors of hernia development [9, 19]. Moreover, higher incidence of incisional hernia is evident with midline incisions as compared to transverse and paramedian incisions [17, 20]. Continuous closure of abdominal fascia after midline laparotomies using slowly absorbable monofilament suture material, with a suture length:wound length ratio above 4:1 provides stability and mechanical strength [21]. A significant improvement in outcomes of midline laparotomy was reported with the use of polydioxanone suture, along with a reduced incidence of incisional hernia compared to polypropylene suture (30.9% vs. 51.1%) [22]. The present study is first to compare PD Synth® and PDS® slowly absorbed polydioxanone sutures for the incidence of incisional hernia, occurring within 12 months of abdominal fascial closure following midline laparotomy. The study sheds light on the efficacy and safety of both sutures for elective/emergency midline laparotomy.

Both PD Synth® and PDS® sutures had satisfactory handling properties regarding ease of passage through tissue, first-throw knot holding, knot tie-down smoothness, knot security, surgical handling and suture fraying. None of the participants has faced perioperative complications, and as a result good outcome of surgery was noted in both groups. However, at the end of the study, 2.2% and 2.3% subjects of PD Synth® and PDS® group respectively appeared to have incisional hernia at umbilicus. Time-dependent development of incisional hernias are reported by previous studies; 7.7% incidence within 2 years [12], 12.8% within 23.7 months (~2 years) [23], and 5% requirement of incisional hernia repair within 5 years of midline laparotomy [24]. A recent study recorded 54% incidence of incisional hernia, mostly at the infra umbilical region of Indian patients within 3 years of midline incision [18]. Reduction of incisional hernia by 5% is associated with a cost saving of 4 million Euros in French public hospitals [25]. A relatively fewer incidence of incisional hernia in the present study contrary to previous findings regarded to reduce the economic as well as healthcare burden of the patients.

Patients undergoing elective laparotomy usually have adequate nutritional status and less chances to develop dehiscence because of lower risk factors, compared to emergency patients with multiple risk factors [26]. Incidence of post-laparotomy wound dehiscence is reported as 0.2-5% in elective surgeries, and 45% in emergency surgeries; in developing countries the rate is 30% after undergoing laparotomy for various reasons [8]. A prospective cohort study recorded 12.4% incidence of burst abdomen or wound dehiscence after emergency midline laparotomy [27]. A previous randomized controlled trial observed 12.5% cases of

wound dehiscence within one month of emergency midline laparotomy. The authors also noted a significantly higher frequency of abdominal wound dehiscence using interrupted suture technique (20.5%) than continuous suture technique (4.5%) [28]. Similarly, Chalya et al., found lower incidence of wound dehiscence with continuous suturing than interrupted technique (5.4% vs. 22.1%), and with absorbable suture than non-absorbable suture (7.6% vs. 9.3%) [12]. On the other hand, Sharma et al., favored use of interrupted suture over continuous suture technique, as 7.9% rate of wound dehiscence/burst abdomen was found with the former technique in comparison to continuous suturing of rectus sheath, which resulted in 19.5% incidence of wound dehiscence after 7th day of midline incision [29]. In addition, higher occurrence of fascial dehiscence was evident in a retrospective observational study after midline incision (8.1%), compared to transverse incision (3.6%) for elective abdominal surgery [30]. In the present study, patients requiring laparotomy through midline incision in both elective and emergency settings were included, and post-laparotomy abdominal fascia closure was accomplished using PD Synth® and PDS® polydioxanone sutures in continuous manner. Contrary to the above-mentioned studies, subjects of this study did not develop early post-operative fascial dehiscence within 7 days of the surgery.

Other post-operative complications that were noted within 1 month of midline laparotomy were superficial incisional SSI (in both PD Synth® and PDS® groups) and seroma (only in PDS® group). Incidence of wound infection and seroma after midline laparotomy were found across many previous studies. A study from Central India reported wound infection in 7/60 patients and seroma in 4/60 patients, who underwent elective/emergency midline laparotomy [1]. A recent retrospective cohort study recorded 16.3% and 3.0% incidence of wound infection and seroma respectively in adults undergoing midline emergency laparotomy [31]. Clinically 16.7% patients developed seroma following abdominal surgery through midline incision [32]. Overall 27.9% incidence of wound infection after midline laparotomy in one study [29] and 41.9% in another study were reported [12]. Hempel et al. observed a significant difference in occurrence of SSI after elective abdominal surgery between midline and transverse incision (27.6% vs. 16.8%) [30]. However, with the use of polydioxanone suture, a significantly reduced SSI was registered compared to non-absorbable polypropylene suture (23.2% vs. 45.5%) [14].

Post-operative medical and operation-related complications lead to prolonged hospital stay and greater mortality, as found after emergency midline laparotomy [31]. Surgical site infection (20%) was indicated as the major cause for re-hospitalization, followed by sub-acute intestinal obstruction, gastrointestinal causes, burst abdomen, stoma-related, and other causes [33]. Another study also recorded 17.4% unplanned readmission after laparotomy; most common causes were viscus perforation and small bowel obstruction [34]. However, readmission was noted in only one subject in PDS® group of the current study, because of vomiting and abdominal distension, which had no marked impact as the subject completed the next follow-ups successfully. The readmission was not related to the device and reported as SAE. Hospital stay was ~9 days in both PD Synth® and PDS® groups, which is comparable to some previous studies that demonstrated post-laparotomy hospital stay of ~10 days [35] and 11-12 days [26].

Chronic persistent post-surgical pain following laparotomy was demonstrated at post-operative day 90 in 38.1% patients (all had moderate pain) undergoing staging laparotomy that impacted patient's quality of life [36]. In our study, by 3rd Month, 40.0% and 41.9% subjects of PD Synth® and PDS® group respectively had moderate pain, and only three subjects in each group required analgesics. However, improvement in pain and number of analgesic is clearly visible, and at the end of the study 8.9% and 11.6% patients had moderate pain; rest of the patents experienced mild or no pain. Quality of life has also improved, as demonstrated by the results of EQ-5D-5L. No problem in mobility, self-care, usual activities, pain/discomfort and anxiety/depression was witnessed in majority of subjects of both groups after 1 year of surgery. Also, a higher EQ-VAS score of 87.9 and 89.6 in PD Synth® and PDS® group respectively were recorded at the end of the study. A similar EQ-5D score (80.4±16.7) was reported by Fortelny et al., after 1 year of fascial closure with absorbent elastic suture material [37]. Furthermore, subjects of both arms have returned to normal day to day activities as well as work at a similar time, indicating favorable outcome of the surgery.

Although the study subjects were blinded to the suture material that was used, hospital staff and practitioners were not blinded due to nature of the intervention. Hence, there is probability of potential bias in the reporting if practitioners favored one suture or another. Nonetheless, comprehensive, systematic and explicit design of the study and careful consideration of inclusion/ exclusion criteria are strengths of the study. Comparable outcomes regarding both sutures indicated use of PD Synth® slowly absorbed polydioxanone suture for all surgeries, indicated for PDS® slowly absorbed polydioxanone suture.

Conclusions

To conclude, incisional hernia is a common outcome of elective/emergency midline laparotomy, and our study is no exception. However, frequency of the incidence is not too many and is non-significant between the studied groups. In addition, at the end of 12 months, results of secondary outcomes of the study showed non-significant differences between the groups. The findings manifested that PD Synth® and PDS® slowly absorbed polydioxanone sutures are clinically equivalent. Therefore, both PD Synth® and PDS® sutures can be used in subjects requiring abdominal fascial closure following elective or emergency midline laparotomy.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. 1) Institutional Ethics Committee, King George Hospital, Visakhapatnam; 2)Institutional Ethics Committee, Vydehi Institute of Medical Sciences & Research Center; 3)Kasturba Medical College And Kasturba Hospital Institutional Ethics Committee; 4) Scientific Research & Ethical Review Committee, Batra Hospital & Medical Research Center issued approval 1)dated 10/11/2021; 2)VIEC/2020/APP/0377SUPPL, dated 03/02/2023; 3)283/2020, dated 05/07/2020; 4)dated 22/11/2022. This study was approved by Institutional Ethics Committee of King George Hospital, Vydehi Institute of Medical Sciences & Research Center, Kasturba Medical College and Kasturba Hospital, and Scientific Research & Ethical Review Committee of Batra Hospital & Medical Research Center. Informed consent was obtained from all patients prior to participation. . **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** Authors Ashok Kumar Moharana and Deepak TS are employees of Healthium Medtech Limited, India, who are manufacturers of PD Synth® suture. Authors Amritha Prabha Shankar, Stanley Mathew, V.S.S.Nagababu.T, Keerthi B.R, Saleem Naik, Ravinder K. Pandita, Badareesh L, Naveena Kumar AN, Venkata Narasimha Rao V and Bharath Kumar Bhat declare no competing interest.

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