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Medical Device Material Performance Study

Polypropylene Safety Profile

Prepared for
U.S. FDA Center for Devices and Radiological Health

Submitted to

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Table of Contents

Table of Tables

Executive Summary

Key Points

1. Searches identified 1252 citations; 158 articles were selected for inclusion.
2. Local host responses to polypropylene (PP) used in surgical mesh included pain, foreign body sensation, seroma, and hematoma. When PP mesh was used in other surgeries (female stress urinary incontinence [SUI] mesh or mini-sling, transvaginal or transabdominal prolapse mesh), the primary local responses were erosion/exposure followed by dyspareunia and pain. Studies reported these complications from immediately post surgery to 5 years post surgery. Evidence suggested that lightweight PP mesh was less likely than heavier weight PP mesh to cause pain or foreign body sensation.
3. Low quality evidence from cohort studies showed no association with systemic reactions.
4. There were no studies elucidating patient– or material-related factors contributing to systemic responses.
5. ECRI's PSO data pointed to infection in 40% of event reports associated with PP mesh. There were 5 deaths, and when patient harm was reported, 44% required intervention or hospitalization.
6. Evidence gaps:
    a. Studies of local and systemic host response to PP as a material.
    b. Studies examining local or systemic host response to diaphragmatic hernia mesh.
    c. Better quality evidence regarding local responses such as inflammation, mesh migration, and pain and regarding systemic responses to mesh such as allergy, autoantibody development and systemic inflammation.

Project Overview

FDA engaged ECRI to perform a comprehensive literature search and systematic review to identify the current state of knowledge with regard to medical device material biocompatibility. Additionally, data derived from ECRI's patient safety organization (PSO), accident investigations, problem reporting network (PRN), and healthcare technology alerts were analyzed. This report focuses on answering five key questions, provided by FDA and summarized below, regarding a host's local and systemic response to the PP. If data did not exist to sufficiently address these questions, a gap was noted in this report. These gaps could represent areas of further research.

1. What is the typical/expected local host response to polypropylene?

Local responses in most studies included pain, foreign body sensation, seroma, and hematoma. PP mesh leads to an inflammatory response that decreases over time but does not completely resolve. ECRI surveillance data revealed infection to be the most common incident, and five deaths were associated with mesh complications.

a. Can that response vary by location or type of tissue the device is implanted in or near?

i. Most of the general surgical mesh literature evaluated mesh used for inguinal hernia repair.
ii. For surgeries other than general surgical mesh most studies reported erosion/exposure, dyspareunia, and pain
iii. Lightweight PP mesh was less likely to cause pain or foreign body sensation compared to heavyweight PP mesh
iv. The overall quality of evidence related to local host responses to general surgical mesh and transvaginal prolapse mesh were moderate to low.
v. No evidence was found regarding local host responses for diaphragmatic heria meshes and male SUI mesh.

b. Over what time course does this local host response appear?

i. A local host response could occur at any time with incidents reported both immediately post-surgery, 5 years post-surgery, and chronically occurring.
ii. Hematoma and seroma were usually short-term outcomes that were likely related to the surgical procedure

2. **Does the material elicit a persistent or exaggerated response that may lead to systemic signs or symptoms – beyond known direct toxicity problems?**

    a. *What evidence exists to suggest or support this?*

    Few studies reported data regarding systemic manifestations related to PP implants. The quality of evidence based on two cohort studies is low.

    b. *What are the likely systemic manifestations?*

    Included literature reported a lack of association between PP implants and systemic problems.

    c. *What is the observed timeline(s) for the systemic manifestations?*

    The included cohort studies reported no association of systemic manifestations with mesh-based hernia repair up to 6 years follow-up.

    d. *Have particular cellular/molecular mechanisms been identified for such manifestations?*

    We did not find evidence concerning cellular/molecular mechanisms of systemic manifestations.

3. **Are there any patient-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?**

    None of the studies provided useful information regarding material-related factors that may affect a sustained immunological/systemic response.

4. **Are there any material-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?**

    None of the studies provided useful information regarding material-related factors that may affect a sustained immunological/systemic response.

5. **What critical information gaps exist and what research is needed to better understand this issue?**

    All gaps listed here indicate could benefit from future research.

    i. Evidence of local and systemtic host response to PP as a material (i.e., independent of a specific medical device) includes only 3 animal studies that reported low quality of evidence of inflammation, granulation tissue proliferation, and fibrous capsule formation. None of these included studies reported whether there were systemic responses to PP.
    ii. Studies indicate low quality of evidence of local responses to PP mesh such as inflammation, mesh migration, and pain.
    iii. Systemic responses to PP mesh are varied and associated with very low to low quality of evidence.
    iv. No studies met inclusion critera for diaphragmatic hernia mesh and male SUI mesh with regard to either local or systemic host responses.

Project Overview

FDA engaged ECRI to perform a comprehensive literature search and systematic review to identify the current state of knowledge with regard to medical device material biocompatibility. Specific materials were selected by FDA based on current priority. For 2020, the following six materials were chosen:

1. Siloxane (Si)
2. Polypropylene (PP)
3. Polyether ether ketone (PEEK)
4. Poly(lactic-co-glycolic acid) (PLGA)
5. Polyurethane (PUR)
6. Polyethylene terephthalate (PET)

The systematic review was guided by key questions mutually agreed upon by FDA and ECRI. Data were extracted from literature articles and ECRI surveillance databases accordingly.

Key Questions:

1. What is the typical/expected local host response to the material?
    - Over what time course does this local host response appear?
    - Can that response vary by location or type of tissue the device is implanted in or near?
2. Does the material elicit a persistent or exaggerated response that may lead to systemic signs or symptoms – beyond known direct toxicity problems?
    - What evidence exists to suggest or support this?
        - In-vivo/clinical studies/reports?
        - Bench or in-vitro studies?
    - What are the likely systemic manifestations?
    - What is the observed timeline(s) for the systemic manifestations?
    - Have particular cellular/molecular mechanisms been identified for such manifestations?
3. Are there any patient-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?
4. Are there any material-related factors that may predict, increase, or decrease the likelihood and/or severity of an exaggerated, sustained immunological/systemic response?
5. What critical information gaps/research are needed to better understand this issue?

If data did not exist to sufficiently address these questions, a gap was noted in this report. These gaps could represent areas of further research.

Safety Profiles were written for the six materials listed above to include the summary of key findings from the systematic review and surveillance search and are included in this report.

Literature Search and Systematic Review Framework

The ECRI-Penn Evidence-based Practice Center (EPC) conducts research reviews for the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care (EHC) Program. ECRI's scientific staff within our Center for Clinical Excellence has authored hundreds of systematic reviews and health technology assessments on 3,500+ technologies/interventions for ECRI's public- and private-sector clients. In addition to this work, ECRI staff have coauthored several methods papers on evidence synthesis published on the AHRQ Effective Health Care website and peer-reviewed journals.

For this project, the clinical and engineering literature was searched for evidence related to biocompatibility of each material. Searches of PubMed/Medline and Embase were conducted using the Embase.com platform. Scopus was used initially to search non-clinical literature however it was determined that the retrieved citations did not meet inclusion criteria and that database was subsequently dropped from the search protocol. Search limits included publication date 2010 – 2020 and English as the publication language. ECRI and FDA agreed on appropriate host and material response search concepts as follows:

- **Material Response**
  - Strength
  - Embrittlement
  - Degradation
  - Migration
  - Delamination
  - Leaching

- **Host Response**
  - Local
    - Inflammation
    - Sensitization
    - Irritation
    - Scarring/fibrosis
      - *Keloid formation*
      - *Contracture*
    - Ingrowth
    - Erosion
  - Systemic
    - Cancer
    - Inflammation
    - Immune Response
    - Fatigue
    - Memory Loss
    - Rash
    - Joint Pain
    - Brain Fog

Search strategies were developed for each concept and combined using Boolean logic. Several search approaches were used for comprehensiveness. Strategies were developed for devices of interest as indicated by the FDA as well as the material-related strategies. Each of these sets were combined with the material and host response strategies. Detailed search strategies and contextual information are presented in Appendix B. Resulting literature was screened by title review, then abstract review, and finally full article review. Data were extracted from the articles meeting our inclusion criteria to address the key questions for each material.

ECRI Surveillance Search Strategy

There are four key ECRI sources for medical device hazards and patient incidents. These databases were searched by key terms and device models. Relevant data were extracted to address the key questions agreed upon by FDA and ECRI. Patient demographics were extracted when available. All data presented were redacted and contain no protected health information (PHI).

ECRI PSO

ECRI is designated a Patient Safety Organization by the U.S. Department of Health and Human Services and has collected more than 3.5 million serious patient safety events and near-miss reports from over 1,800 healthcare provider organizations around the country. Approximately 4% of these reports pertain to medical devices. Most of these reports are acute (single event) reports and do not include patient follow-up. These data were filtered by complication, and relevant reports were included in the analysis. "Harm Score" refers to the National Coordinating Council Medication Error Reporting and Prevention (NCC MERP) taxonomy of harm, ranging from A to I with increasing severity (see Figure 1). The entire PSO database was included in the search, with reports ranging from year 2004 through May 2020, unless otherwise noted.

Figure 1. NCC MERP "harm score," which is now regularly used by patient safety organizations.

Category A (No Error)
Circumstances or events that have the capacity to cause error.

Category B (Error, no harm)
An error occurred, but the error did not reach the patient (an "error of omission" does reach the patient).

Category C (Error, no harm)
An error occurred that reached the patient but did not cause patient harm.

Category D (Error, no harm)
An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm.

Category E (Error, harm)
An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention.

Category F (Error, harm)
An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization.

Category G (Error, harm)
An error occurred that may have contributed to or resulted in permanent patient harm.

Category H (Error, harm)
An error occurred that required intervention necessary to sustain life.

Category I (Error, death)
An error occurred that may have contributed to or resulted in patient death.

Definitions
Harm: Impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom.
Monitoring: To observe or record relevant physiological or psychological signs.
Intervention: may include change in therapy or active medical/ surgical treatment.
Intervention necessary to sustain life: includes cardiovascular and respiratory support (eg CPR, defibrillation, intubation).

Accident Investigation

ECRI has performed thousands of independent medical-device accident investigations over more than 50 years, including on-site and in-laboratory investigations, technical consultation, device testing and failure analysis, accident simulation, sentinel event and root-cause analyses, policy and procedure development, and expert consultation in the event of litigation. Our investigation files were searched by keywords, and the search was limited to the past 10 years unless we found landmark investigations that are particularly relevant to biocompatibility.

Problem Reporting Network (PRN)

For more than 50 years, ECRI's Problem Reporting Network (PRN) has gathered information on postmarket problems and hazards and has been offered as a free service for the healthcare community to submit reports of medical device problems or concerns. Each investigation includes a search and analysis of the FDA MAUDE database for device-specific reports. Based on our search findings, we may extend our analysis to all devices within that device's FDA-assigned product code. The PRN database was searched by keywords, and the search was limited to the past 10 years.

Healthcare Technology Alerts

We regularly analyze investigation and PRN data to identify trends in use or design problems. When we determine that a device hazard may exist, we inform the manufacturers and encourage them to correct the problem. ECRI publishes the resulting safety information about the problem and our recommendations to remediate the problem in a recall-tracking management service for our members. The Alerts database contains recalls, ECRI exclusive hazard reports, and other safety notices related to Medical Devices, Pharmaceuticals, Blood Products, and Food Products. This database was searched by keywords and specific make and model, and the search was limited to the past 10 years.

Safety Profile - Polypropylene

Full Name: Polypropylene

CAS Registry Number: 9003-07-0

Search Overview

The systematic review included clinical and engineering literature on biocompatibility (i.e., host response and material response) of polypropylene (PP) used in medical devices. In addition to fundamental material biocompatibility, we focused on specific devices known to be made of PP. The devices in Table 1 were recommended by FDA CDRH to guide ECRI in searching this literature and ECRI's surveillance data. In the latter, only those devices listed in Table 1 were included.

Table 1: Medical devices containing polypropylene provided by FDA to guide ECRI searches

Regulatory Description	Pro Code	Class
Diaphragmatic hernia mesh	OWU	II
Prolapse mesh, transvaginal	OTP	III
Male SUI mesh	OTM	II
Female SUI mesh, synthetic	OTN	II
Female SUI mini-sling, synthetic	PAH	II
Prolapse mesh, transabdominal, apical and uterine repair	OTO	II
General surgical mesh	FTL	II

Systematic Review Safety Brief

The Safety Brief summarizes the findings of the literature search on toxicity/biocompatibility of PP. Inclusion/exclusion criteria and quality of evidence criteria appear in Appendix A in the Appendices document. Quality of evidence ratings reflected a combination of the quality of comparative data (study designs), quantity of evidence (number of

relevant studies), consistency of evidence, magnitude of effect, directness of evidence, and evidence for a dose response or response over time. The search strategy appears in Appendix B, and a flow diagram documenting inclusion/exclusion of studies appears in Appendix C. Summary evidence tables with individual study data appear in Appendix D, and a reference list of studies cited in the Safety Brief appears in Appendix E.

A summary of our primary findings is shown in Table 2. We then turn to a detailed discussion of research on polypropylene as a material as well as research on the various device categories.

Table 2: Summary of primary findings from our systematic review

Application	**Local host responses**	**Quality of evidence (local responses)**	**Systemic responses**	**Quality of evidence (systemic responses)**
Polypropylene as a material 3 animal studies	Inflammatory response, granulation tissue proliferation, fibrous capsule formation	Low	Did not report whether any animals exhibited systemic problems	Very low
General surgical mesh 45 human studies, 39 animal studies	Pain, damage to smooth muscle of the vas, dysejaculation, inflammation, mesh erosion, mesh migration, mesh transmigration, mesh contraction, nerve damage, neuroma-type lesion, orchialgia, segmental testicular atrophy, sexual pain, spermatocele, stretched blood capillaries, hematoma, seroma, soft tissue necrosis, numbness in groin, foreign body sensation, oxidative stress markers, anti-sperm antibodies, fistula, ischemic orchitis, adhesions, cellulitis, testicular atrophy, itching, neuralgia, tightness, sperm concentration, sperm motility, sperm morphology	Moderate for pain and foreign body sensation Low for all other local responses	Allergy, arthralgias/arthritis, ASIA, autoantibody presence, cognitive symptoms, dry eyes/mouth, elevated ACE, elevated CK, elevated CRP, elevated IgE, fatigue, IBS, increased IgG/IgG subclasses, livedo reticularis, localized pain, lymphadenopathy, myalgia/muscle weakness, pyrexia, Raynaud's stroke-like symptoms, systemic autoimmune inflammatory disorders	Low

Application	Local host responses	Quality of evidence (local responses)	Systemic responses	Quality of evidence (systemic responses)
Prolapse mesh, transvaginal 45 human studies, 11 animal studies	Mesh exposure, erosion, extrusion, umbilical hernia, vaginal bleeding, vaginal discomfort, vaginal shrinkage, vaginal dryness, de novo dyspareunia, chronic pelvic pain, excessive fibrosis, de novo stress incontinence, de novo urgency incontinence, pelvic inflammatory disease, urinary retention, vaginal adhesions, granulated tissue, cystitis, hematoma, constipation, hypergastralgia, polyp, elevated CRP and/or mild fever	Moderate for pain, dyspareunia and erosion/exposure Low for all other local responses	Allergy, anemia, arthralgias/arthritis, ASIA, autoantibody presence, cognitive symptoms, dry eyes/mouth, elevated ACE, elevated CK, elevated CRP, elevated IgE, fatigue, IBS, increased IgG/IgG subclasses, livedo reticularis, localized pain, lymphadenopathy, myalgia/muscle weakness, pyrexia, Raynaud's stroke-like symptoms, sclerosis, systemic autoimmune inflammatory disorders, anaphylactoid breakout, endometrial cancer	Very low
Prolapse mesh, transabdominal apical and uterine 5 human studies, 2 animal studies	Chronic inflammation, degradation, exposure, erosion, fibrosis, pain, sclerosis, shrinkage	Moderate for erosion/exposure Low for all other local responses	No issues reported in included studies	Very low
Female SUI mesh, synthetic 9 human studies, 1 animal study	Cystitis, de novo urgency, repeated cystitis, erosion, temporary elevated PVRV, transient groin pain, urethrolysis, urinary obstruction, voiding difficulty requiring ISC, dyspareunia, inguinal pain extending to legs, perineal pain, urinary retention, vaginal erosion, worsening urgency, vaginal discharge, vaginal bleeding, foreign body granuloma	Moderate for erosion/exposure Low for all other local responses	Allergy, arthralgias/arthritis, ASIA, autoantibody presence, cognitive symptoms, dry eyes/mouth, elevated ACE, elevated CK, elevated CRP, elevated IgE, fatigue, IBS, increased IgG/IgG subclasses, livedo reticularis, localized pain, lymphadenopathy, myalgia/muscle weakness, pyrexia, Raynaud's, stroke-like symptoms, sclerosis	Very low
Female SUI mini-sling, transvaginal 6 human studies, 1 animal study	Degradation, exposure, fibrosis, inflammation, pain, protrusion, abdominal abscess, bleeding, foreign-body granuloma, purulent or rufus discharge, urgency	Moderate for erosion/exposure Low for all other local responses	Anaphylactoid reaction Cancer (evidence did not support an association)	Low for cancer Very low for anaphylactoid reaction
Diaphragmatic hernia mesh, male SUI mesh	No studies	Very low (no evidence)	No studies	Very low (no evidence)

ACE: angiotensin converting enzyme; ASIA: autoimmune syndrome induced by adjuvants; CK: creatine kinase; CRP: C-reactive protein; IBS: inflammatory bowel syndrome; IgE: immunoglobulin E; IgG: immunoglobulin G; SUI: stress urinary incontinence

Polypropylene as a material: 3 animal studies (2 observational comparative studies,[2,3] 1 case series[1]). One study evaluated a PP discoid implanted subcutaneously in mice, one study evaluated a PP net implanted subcutaneously in rats, and the remaining study evaluated PP threads implanted in muscle tissue in rats. For more information, see Table 1 in Appendix D.

Local host responses: The animal studies all reported inflammatory responses related to PP. One study that provided more detail on the inflammatory response reported granulation tissue proliferation, inflammatory cell-rich granulation, and thin fibrous tissue capsule formation.

Systemic responses: None of the studies reported whether the animals exhibited any systemic responses.

Overall quality of evidence: The evidence for local responses in animal studies was based on a small number of studies, although the findings concerning inflammatory response were relatively consistent across studies. Since the number of studies is small and the evidence was not from human studies, the quality of evidence supporting local host responses is low.

No studies evaluated systemic responses, so the corresponding quality of evidence is very low.

General surgical mesh: 45 human studies (2 systematic reviews,[35,44] 21 randomized controlled trials [RCTs],[4-6,10,12,14,15,17,19,23,24,26,27,32,36,38,39,41-43,45] 22 observational studies[7-9,11,13,16,18,21,22,25,28-31,33,34,37,40,46-48]); 39 animal studies (1 meta-analysis,[77] 26 RCTs,[42,49-51,55,56,58-60,62-65,67-73,75,76,78,82-84] and 18 observational studies[52-54,57,61,66,74,77,79-81,85,86]). For more information, see Tables 2 and 3 in Appendix D.

Local host responses: 42 human studies reported on local host reactions potentially related to PP general surgical mesh. The most common were pain (reported in 25 studies), seroma (21 studies), hematoma (14 studies), and foreign body sensation (15 studies). Other local host responses mentioned in one or more studies included damage to smooth muscle of the vas, dysejaculation, inflammation, mesh erosion, mesh migration, mesh transmigration, mesh contraction, nerve damage, neuroma-type lesion, orchialgia, segmental testicular atrophy, sexual pain, spermatocele, stretched blood capillaries, soft tissue necrosis, numbness in groin, foreign body sensation, oxidative stress markers, anti-sperm antibodies, fistula, ischemic orchitis, adhesions, cellulitis, testicular atrophy, itching, neuralgia, tightness, and changes in sperm concentration, motility, and morphology.

The largest study[35] was a systematic review and meta-analysis of 11 RCTs comparing heavyweight PP mesh (Prolene, Premilene, Atrium, Surgipro) with lightweight mesh (mostly PP mesh: Opilene, Vypro, Vypro II, SURGIMESH, ULTRAPRO, TiMESJ) in a total of 2,231 patients who had Lichtenstein inguinal hernia repair. The individual study duration ranged from 2 months to 5 years. The meta-analysis found that pain was significantly lower with lightweight mesh (OR = 0.64; 95% confidence interval [CI] 0.51-0.82) as was foreign body sensation (OR = 0.56; 95% CI 0.40-0.78). Testicular atrophy, hematoma, and seroma did not differ significantly between mesh types.[35] Another systematic review[44] meta-analyzed 10 RCTs comparing the lightweight Vypro II mesh (50% PP/50% polyglactin) to heavyweight PP mesh (Prolene, Premilene, Atrium, Surgipro) in 2027 patients undergoing Lichtenstein, total extraperitoneal (TEP), or transabdominal preperitoneal (TAPP) inguinal hernia repair. Individual study duration ranged from 2 months to 5 years. The meta-analysis found no significant difference in pain, seroma, or testicular atrophy between Vypro II and heavy PP mesh, but Vypro II mesh was associated with a significantly lower rate of foreign body sensation (OR 0.58, 95% CI 0.42–0.80).[44] The two systematic reviews had some overlap in that 5 RCTs appeared in both reviews. A more recent RCT[14] comparing lightweight ULTRAPRO mesh to heavyweight Prolene mesh reported that significantly more patients had pain in the ULTRAPRO group at 1 year postsurgery, which conflicts with earlier systematic review[35] findings. Another RCT[27] comparing ULTRAPRO to Prolene reported more foreign body sensation in the Prolene group but no significant between-group difference in pain. In an RCT comparing Bilayer (PP and polytetrafluoroethylene [PTFE]) mesh (Ventralex vs. CA.B.S.s'air), pain, foreign body sensation, and late complications were significantly lower for CA.B.S.'air than for Ventralex at 1 month and 3 months. A recent RCT[5] comparing ProLite PP mesh to bovine mesh reported significantly higher short-term pain (1 day to 3 months) for ProLite but no difference in pain at 6 months.

Thirty-nine animal studies reported local host responses possibly related to PP general surgical mesh. Several RCTs and comparative studies reported higher inflammatory response with PP mesh compared to non-PP mesh.[42,49,51,53,55,56,62,76,77] A meta-analysis of several studies found that natural devices had a lower adhesion rate than PP mesh. The same review reported that non-PP mesh had more shrinkage than PP mesh.[77] An RCT reported that PTFE mesh had a lower adhesion rate and more shrinkage than PP mesh.[78] Lightweight PP mesh generated fewer adhesions compared to heavyweight PP.[68]

Systemic responses: 3 human studies (2 cohort, 1 case-control) reported systemic responses potentially related to PP general surgical mesh. One cohort study[47] included 40 patients diagnosed with autoimmune syndrome induced by adjuvants (ASIA) who had been treated with PP mesh for hernia, stress urinary incontinence (SUI) or pelvic organ prolapse (POP). Of these patients, 45% developed an autoimmune disease (e.g., rheumatoid arthritis) and 25% had immunodeficiencies (e.g., IgG subclass deficiency) detected at more than 3 years follow-up. Abnormal laboratory findings were detected in most patients (see Table 2 in Appendix D for more details). However, this study lacked a control group, so it does not address whether the risk of ASIA was higher among patients who received PP mesh. Another very large cohort study[48] by the same author analyzed 26,575 patients who underwent hernia repair with PP mesh and 71,271 undergoing colonoscopy (control group). The study found no association between PP mesh and the risk of developing systemic/autoimmune disorders up to 6 years follow-up. A very large cohort study (Chughtai et al.[46]) analyzed 27,425 patients who underwent PP mesh-based hernia repair compared to 13,339 patients who underwent cholecystectomy (control group). This study found that mesh-based hernia repair was not associated with an increased risk of cancer up to 6 years follow-up. No animal studies reported systemic response data.

Patient-related or material-related factors associated with systemic response: No studies reported adequate data on factors related to systemic responses.

Overall quality of evidence: Several studies reported that general surgical PP mesh was associated with pain and foreign body sensation during postsurgical follow-up. In addition, a 2013 meta-analysis of 11 RCTs found that lightweight mesh (mostly PP mesh) were associated with less pain and foreign body sensation than heavyweight PP mesh. It is unclear whether these findings are representative of the newest models of lightweight and heavyweight PP mesh, and whether material properties beyond weight and size contribute to pain and foreign body sensation. The overall quality of evidence linking PP mesh with pain and foreign body sensation is moderate. Several studies reported hematoma and seroma, but these are likely to occur because of the surgical procedure; hematoma and seroma rates were generally similar between mesh types. Therefore, the quality of evidence linking PP mesh to hematoma and seroma is low. For other reported local responses the quality of evidence is also low.

Although 3 studies provide evidence concerning systemic adverse events, the 2 large studies looked at the risk of specific events (systemic/autoimmune disorders, cancer) and found no association between PP mesh and an increased risk of developing these disease/disorders. These studies may have had unmeasured confounding factors that could have influenced the findings. The remaining small study reported on cases of ASIA among patients who had received PP mesh, but the lack of a control group precluded any analysis of the risk of ASIA among patients receiving a PP mesh. The quality of evidence for systemic responses based on the large comparative studies is low.

Prolapse mesh, transvaginal: 45 human studies (1 systematic review,[99] 3 RCTs, [90,91,106,129] 41 observational studies[47,87-89,92-98,100-105,107-128,130-132]), and 11 animal studies (1 systematic review,[99,] 4 RCTs,[63,134,136,140] 6 observational studies[66,133,135,137-139]). For more information, see Tables 4 and 5 in Appendix D.

Local host responses: 42 human studies reported local host responses. The most common event was mesh exposure/erosion (38 studies) followed by dyspareunia (18 studies) and pain (15 studies). Other local responses include umbilical hernia, vaginal bleeding, vaginal discomfort, vaginal shrinkage, vaginal dryness, excessive fibrosis, de novo stress incontinence, de novo urgency incontinence, pelvic inflammatory disease, urinary retention, vaginal adhesions, granulated tissue, cystitis, hematoma, constipation, hypergastralgia, polyp, elevated c-reactive protecin (CRP) levels, and/or mild fever. The systematic review included 6 human studies and reported that PP mesh elicits an inflammatory response that decreases over time without complete resolution. All the animal studies reported that PP mesh elicits an inflammatory response.

Systemic responses: 4 human observational studies reported systemic response data. One cohort study[47] included 40 patients diagnosed with ASIA who had been treated with PP mesh for hernia, SUI, or POP. Of these patients, 45% developed an autoimmune disease (e.g., rheumatoid arthritis) and 25% had immunodeficiencies (e.g., IgG subclass

deficiency) detected at more than 3 years of follow-up. Abnormal laboratory findings were detected in most patients (see Table 9 in Appendix D for more details). However, this study lacked a control group, so it does not address whether the risk of ASIA was higher among patients who received a PP mesh. A large cohort study[132] (2,102 patients) reported that PP mesh-based surgery was not associated with an increased risk of developing systemic autoimmune inflammatory disorders after 2 to 6 years of follow-up. Another cohort study[118] with 524 patients reported one case of endometrial cancer at 3 years after ProLift implantation. The remaining study (128 patients) reported one case of anaphylactoid breakout that occurred from 2 to 9 months postsurgery and disappeared upon mesh removal.

Patient-related or material-related factors associated with systemic response: No studies reported adequate data on factors related to systemic responses.

Overall quality of evidence: The evidence for erosion/exposure, dyspareunia, and pain was consistent across several studies, but most studies were observational and the quality of evidence was therefore moderate. For other local symptoms the quality of evidence was low.

The evidence for systemic manifestations was sparse and appeared only in observational studies, each of which reported a different manifestation. The quality of evidence linking systemic manifestations to transabdominal PP mesh is very low.

Prolapse mesh, transabdominal apical and uterine: 5 human studies (1 RCT,[144] 1 cohort study,[143] 3 case series[126, 141,142]) and 2 animal studies (both RCTs). For more information, see Tables 6 and 7 in Appendix D.

Local host responses: All 5 human studies reported local responses, the most common of which was exposure (reported in all studies), followed by pain (2 studies). The human cohort study also reported chronic inflammation, fibrosis, sclerosis, degradation, and shrinkage. Both animal studies reported exposure, and one also reported inflammatory response.

Systemic responses: We did not identify any studies reporting systemic responses to transabdominal apical and uterine prolapse mesh.

Overall quality of evidence: The evidence supporting mesh exposure was consistent (reported in all studies), but most human studies were observational and the quality of evidence was therefore moderate. The quality of evidence for other local responses was low and for systemic responses it was very low (due to no evidence).

Female SUI mesh, synthetic: 9 human studies (1 RCT,[150] 8 observational studies[47,131,143, 147-149,151,152]) and 1 animal study (comparative observational study[153]). For more information, see Tables 8 and 9 in Appendix D.

Local host responses: 8 human studies reported local responses, the most common being erosion (7 studies), followed by pain (5 studies), obstructive urinary symptoms (4 studies), and vaginal discharge (3 studies). Other reported local responses include cystitis, de novo urgency, urethrolysis, voiding difficulty requiring intermittent self-catheterization, dyspareunia, urinary retention, worsening urgency, vaginal bleeding, and foreign body granuloma. The RCT reported that chronic urinary retention was significantly higher with the PP T-sling compared to the anterior vaginal wall sling. The animal study reported adhesions, inflammation, exposure, and fibrosis.

Systemic responses: One cohort study[47] included 40 patients diagnosed with ASIA who had been treated with PP mesh for hernia, SUI, or POP. Of these patients, 45% developed an autoimmune disease (e.g., rheumatoid arthritis) and 25% had immunodeficiencies (e.g., IgG subclass deficiency) detected at more than 3 years follow-up. Abnormal laboratory findings were detected in most patients (see Table 9 in Appendix D for more details). However, this study lacked a control group, so it does not address whether the risk of ASIA was higher among patients who received PP mesh.

Patient-related or material-related factors associated with systemic response: No study reported adequate data on factors related to systemic responses.

Overall quality of evidence: The evidence for erosion/exposure was consistent across all studies, but most studies were observational and the quality of evidence was therefore moderate. For other local symptoms the quality of evidence was low. The only study that reported systemic responses was small and lacked a control group, so the quality of evidence was very low.

Female SUI mini-sling, transvaginal: 6 human studies (2 systematic reviews,[154,155] 4 observational studies[101,131,156,157]),. and 1 animal study (RCT[158]). For more information, see Tables 10 and 11 in Appendix D.

Local host responses: 5 human studies reported local responses. The most frequently reported response was erosion/exposure (5 studies) followed by pain (2 studies). Other local responses included degradation, exposure, fibrosis, inflammation, protrusion, abdominal abscess, bleeding, foreign-body granuloma, purulent or rufus discharge, and urgency. The animal RCT reported inflammation, foreign body giant cell reaction, and fibrosis.

Systemic responses: 1 systematic review and 1 uncontrolled case series reported data related to systemic manifestations. The SR reviewed 10 studies with a total of 4,835 patients (primarily from 2 large cohort studies with mean follow-up of 42 to 60 months) that found no evidence that PP mini-slings were associated with cancer risk. However, there is a possibility of bias from unmeasured confounders and that longer follow-up may be needed to detect an association. The case series reported a case of anaphylactoid reaction that occurred from 2 to 9 months postsurgery and disappeared upon mesh removal.

Patient-related or material-related factors associated with systemic response: No studies reported adequate data on factors related to systemic responses.

Overall quality of evidence: The evidence for erosion/exposure was consistent across all studies, but most studies were observational and the quality of evidence was therefore moderate. For other local symptoms the quality of evidence was low. For systemic responses, the quality of evidence from a systematic review of observational studies suggesting that cancer was not a major risk factor associated with PP slings was low. The evidence for anaphylactoid reaction was based on 1 case in 1 uncontrolled study, so the quality of evidence is very low.

Diaphragmatic hernia mesh and male SUI mesh: Our literature searches did not identify any studies of these devices that met inclusion criteria.

ECRI Surveillance Data

ECRI surveillance data comprise ECRI Patient Safety Organization (PSO) event reports, accident investigations, problem reporting network (PRN) reports, and alerts. The PSO, investigations, and PRN reports included in this report include mostly acute patient events. We rarely find chronic conditions or patient follow-up reports, which are more prevalent in the clinical literature. Complications are reported directly by clinical staff, thus reports vary greatly in the level of detail provided.

The most common complication reported within surveillance data for PP mesh was infection, accounting for nearly 40% of all PSO reports regarding PP mesh. Additional reported complications are consistent with clinical literature, including material erosion, pain, and exposure. Most complications that resulted in harm had a harm score of E (27%) requiring temporary intervention and F (17%) requiring temporary hospitalization. Five deaths associated with mesh complications were reported. The majority of ECRI alerts were unrelated to host responses to PP and involved manufacturing, packaging, and device labeling errors.

Patient Safety Organization

Search Results: ECRI PSO identified 1,714 reports of incidents that included PP materials that occurred between 10/2005 and 5/2020. 378 of these involved complications (see Table 3). The top 5 complications were 1) Infection - 141 (37.3%), 2) Erosion - 46 (12.2%), 3) Pain - 43 (11.4%), 4) Hemorrhage/hematoma – 30 (7.9%), 5) Iatrogenic injury - 20 (5.3%). Harm occurred in 47% of the events, and the majority of events were associated with harm scores ranging from C through F (Table 4). Harm scores C and D refer to errors that did not cause harm to the patient. E and F resulted in patient harm, incidents with a score of F required initial or prolonged hospitalization. Abdominal and vaginal mesh complications were the most commonly reported, with abdominal complications having a higher percentatge of reports of prolonged harm (harm score F, 25%) than the vaginal complications (1%). Inguinal mesh complications were reported far less often, but a significant percentage of these incidents were associated with prolonged harm (24%).

All individual PSO event reports are redacted and included in Appendix F.

Table 3: Complications in polypropylene-related PSO event reports.

Complications	Abdominal	Vaginal	Inguinal	Unknown	Umbilical	Suburethral	Diaphragmatic	Midurethral	Total
Infection	101	6	6	20	6	1	1		141
Erosion	1	42		1		2			46
Pain	9	25	4	3	1			1	43
Hemorrhage/Hematoma	11	2	15	1	1				30
Iatrogenic injury	9	8	1	1	1				20
Incarceration	10	1	2	1	2				16
Adhesions	11		1	1	2				15
Exposure	1	10							11
Small bowel obstruction	4		3	1					8
Leakage	4	1		1					6
Seroma	4		2						6

Complications	Abdominal	Vaginal	Inguinal	Unknown	Umbilical	Suburethral	Diaphragmatic	Midurethral	Total
Incontinence		5							5
Clinical Manifestations	3			1					4
Torsion/strangulation			2				1		3
Mesh broke	1	1						1	3
Urinary Incontinence	1			2					3
Dehiscence	2	1							3
Hernia repair		3							3
Small bowel resection	1	1							2
Migration	1			1					2
Urinary retention				2					2
Necrotizing fasciitis	1		1						2
Ischemic bowel	1								1
Fenestration	1								1
Debridement		1							1
Compartment syndrome	1								1
Total	**178**	**107**	**37**	**36**	**13**	**3**	**2**	**2**	**378**

Table 4: Harm score associated with polypropylene-related event reports

Harm Scores (NCC-MERP)

Category	Severity	Abdominal	Vaginal	Inguinal	Unknown	Umbilical	Suburethral	Diaphragmatic	Midurethral	Total
A	No Error	4	1		3					8
B1	Error, No Harm									
B2	Error, No Harm	1	12							13
C	Error, No Harm	6	46		4	1	3		2	62
D	Error, No Harm	20	7	4	4	1				36
E	Error, Harm	52	26	11	9	3		2		103
F	Error, Harm	45	1	9	8	4				67

Category	Severity	Abdominal	Vaginal	Inguinal	Unknown	Umbilical	Suburethral	Diaphragmatic	Midurethral	Total
G	Error, Harm	2								2
H	Error, Harm	1								1
I	Error, Death	2		1		2				5
NULL *		45	14	12	8	2				81
Total		**178**	**107**	**37**	**36**	**13**	**3**	**2**	**2**	**378**

**Harm score was not reported*

Accident Investigations

Search Criteria: Mesh. Investigation files from 2010 were searched to recover cases pertaining to the PP mesh categories provided by FDA.

Search Results: 2 investigations were recovered as summarized in Table 5. Reported patient incidents were associated, in part, with device misuse, including excessive force during sling anchor placement and inserting mesh fixation screws into bone instead of collagenous structures – both of which increase the likelihood of a host response.

All individual investigations are redacted and included in Appendix F.

Table 5: Accident investigations of patient incidents involving polypropylene devices.

Device Type	# Investigations	Reported Problem and Findings (number of investigations)
Diaphragmatic hernia mesh (OWU)	1	*Rupture / tear* – iatrogenic at implantation
Female SUI mini-sling, synthetic (PAH)	1	*Fracture* – distal tip separated after excessive force

ECRI Problem Reports

Search Criteria: Mesh

Search Results: The search returned 4 reports submitted by ECRI members (Table 6). The reports include pain and obstructed bowel, general pain, and counterfeit materials concern.

All problems reports are redacted and included in Appendix F.

Table 6: ECRI Problem Report Summary

Device Type	# Problem Reports	Reported Problem (number of problem reports)
Abdominal mesh (OWU)	2	*Pain and obstructed bowel*
Unspecified mesh	1	*Pain*
Transvaginal mesh (OTP)	1	*Counterfeit materials concern*

Alerts

Search Criteria: Specific devices and search terms are included in Appendix G.

Search Results: The search returned 91 alerts related to PP mesh devices, summarized in Table 7.

Table 7: Summary of regulatory and manufacturer alerts

Device Type	# Alerts	Problems
Prolapse mesh, transvaginal (OTO)	18 4 issued by regulatory agencies 14 manufacturer-issued	• Health Canada finds that nonabsorbable synthetic transvaginal mesh should no longer be used for a certain type of POP repair. • FDA orders manufacturers to discontinue marketing of transvaginal surgical mesh for repair of pelvic organ prolapse • Sales discontinued • Manufacturing errors • Labeling errors • Packaging errors
Male SUI mesh (OTM)	4 All manufacturer-issued	• Labeling error • Sterility compromised • Updated IFU
Female SUI mesh synthetic (OTN)	3 all manufacturer-issued	• Sales discontinued • Manufacturing errors • Labeling error
Female SUI mini-sling, transvaginal (PAH)	1 manufacturer-issued	• Manufacturer ceases production
Prolapse mesh, transabdominal, apical and uterine Repair (OTO)	12 4 issued by regulatory agencies 8 manufacturer-issued	• FDA orders manufacturers to discontinue marketing of transvaginal surgical mesh for repair of pelvic organ prolapse • Update to the directions for use of warnings, precautions, and adverse events • Health Canada finds that nonabsorbable synthetic transvaginal mesh should no longer be used for a certain type of POP repair • Sales discontinued • Labeling errors • Packaging

Device Type	# Alerts	Problems
General Surgical Mesh (FTL)	53 all manufacturer issued	• Sales discontinued • Manufacturing errors • Regulatory approvals missing or false • Labeling errors • Packaging errors • Sterility concerns • IFU updated
Diaphragmatic Hernia mesh (OWU)	No results for product code OWU in 510k, MAUDE, or PMA (or Google)	Intentionally blank

Potential Gaps

ECRI surveillance searches reflect mostly acute patient incidents that involved medical devices made of PP. Areas of particular concern involve incidents that result in direct tissue exposure to the material if there is moderate to high-quality evidence of acute or systemic reaction to this exposure, as determined by the systematic review. Topics with very low or low quality of evidence represent areas of potential gaps in the literature. If the literature revealed areas of new concern (e.g., systemic response to long-duration contact) and there is little supporting evidence, these are considered gaps.

Polpropylene as a material: Only three animal studies reported local response of PP material resulting in low-quality of evidence of inflammation, granulation tissue proliferation, and fibrous capsule formation, None of the three studies reported whether the animals exhibited any systemic responses. Based on the results of ECRI's search, there is a gap in the literature regarding the local and systemic host response to PP as a material, indicating areas of potential future research.

Mesh: For general surgical mesh, studies indicated moderate quality of evidence for local pain and foreign body sensation; however there was low quality of evidence associated with inflammation, mesh migration, and pain. Further research is indicated to address these local responses associated with low quality of evidence.

There were no studies that met inclusion criteria for diaphragmatic hernia mesh or male SUI mesh regarding either local or systemic host responses. In addition, we found very little data in our surveillance searches indicating issues with these meshes. This is likely less of a concern unless potential additional research on PP as a material signals a biocompatibility risk.

There was very low to low quality of evidence associated with systemic responses including allergy, autoantibody presence, localized pain, and systemic autoimmune inflammatory disorders. Further research is indicated to address these local responses.

A gap in the literature exists for PP-involved patient-related or material-related factors that influence the likelihood and/or severity of sustained, exaggerated systemic responses, indicating areas of potential further research.

Appendix A. Inclusion/Exclusion Criteria and Quality of Evidence Criteria

Inclusion Criteria

1. English-language publication
2. Published between January 2010 and July 2020
3. Human and animal studies
4. Systematic reviews, randomized controlled trials, cohort studies, case-control studies, cross-sectional studies, case series
5. Studies that evaluate toxicity/biocompatibility of polypropylene or priority devices that include this material

Exclusion Criteria

1. Foreign-language publication
2. Published before January 2010
3. Not a study design of interest (e.g., in vitro lab study, case report, narrative review, letter, editorial)
4. Off-topic study
5. On-topic study that does not address a key question
6. No device or material of interest
7. No relevant outcomes (adverse events or biocompatibility not reported)
8. Study is superseded by more recent or more comprehensive systematic review

Quality of Evidence Criteria

1. **Quality of comparison** – is there evidence from systematic reviews including randomized and/or matched study data and/or randomized or matched individual studies?
2. **Quantity of data** – number of systematic reviews and individual studies (human and animal) providing relevant data.
3. **Consistency of data** – are the findings consistent across studies that report relevant data?
4. **Magnitude of effect** – in human and animal studies, what is the likelihood of adverse effects compared to controls (with no device, lower dosage, shorter exposure time), and possibly number of patients likely to have harms.
5. **Directness of evidence** – do human studies isolate the effect of the device (i.e., can the adverse effects be attributed to the device)? Animal studies are indirect but may provide the best evidence for the material itself.
6. Is there evidence of a **dose response or time response** (e.g., adverse effects increase with longer exposure time)?

Appendix B. Search Summary

Strategies crafted by ECRI's medical librarians combine controlled vocabulary terms and free-text words in conceptual search statements that are joined with Boolean logic (AND, OR, NOT).

Most medical bibliographic databases such as Medline and Embase include detailed controlled vocabularies for medical concepts accessible through an online thesaurus. Controlled vocabularies are a means of categorizing and standardizing information. Many are rich ontologies and greatly facilitate information transmission and retrieval. Frequently seen examples of controlled vocabularies include ICD-10, SNOMED-CT, RxNorm, LOINC, and CPT/HCPCS.

Citations in PubMed are indexed with MeSH terms and those in Embase are indexed with terms from EMTREE. These terms are assigned either by a medical indexer or an automated algorithm. Several terms are selected to represent the major concept of the article – these are called "major" headings. This "major" concept can be included in search strategies to limit search retrieval. The syntax in Embase for this is /mj. We have used this convention in our strategies sparingly since indexing is subjective and we are using a sensitive search approach which errs in the direction of comprehensiveness.

Database providers build functionality into their search engines to maximize the usefulness of indexing. One of the most frequently used shortcuts is term explosion. "Exploding" in the context of hierarchical controlled vocabularies means typing in the broadest (root or parent) term and having all the related more specific terms included in the search strategy with a Boolean OR relationship. We use term explosions whenever feasible for efficiency. Feasibility depends on whether you wish to include all of the related specific terms in your strategy. For example, in one of our approaches we explode the Emtree concept mechanics. This explosion automatically added the all the following terms (n = 174) and their associated entry terms (lexical variants and synonyms) to the strategy using an "OR" without the searcher having to type them in. That's one of the major advantages to searching using controlled vocabularies. We don't rely exclusively on controlled vocabulary terms since there are possible limitations such as inconsistent indexing and the presence of unindexed content. That's why we also include free text words in our strategies.

Set Number	Concept	Search statement
1	**Polypropylene**	polypropylene* OR polypropene* OR propene OR polipropene* OR polypropilene* OR (poly NEAR/1 propene*) OR (propene NEAR/1 polymer*) OR 'polypropylene'/exp OR 'polypropylene suture'/exp

Material Response

Set Number	Concept	Search statement
2		'biocompatibility'/de OR biocompat* OR tribolog* OR 'bio compat*' OR 'biological* compat*' OR 'biological* evaluation'
3		'degradation'/exp OR degradation OR degrad* OR split OR splitting OR split* OR wear OR deteriorat* OR atroph* OR migrat* OR movement OR shift* OR transfer* OR 'delamination'/exp OR delamina* OR leach* OR filtrate OR filter* OR seep*
4		Leachable* OR extractable*
5		(swell* OR shrink* OR contract* OR stretch* OR retract* OR extension OR extend* OR deform* OR creep OR plasticity OR degrad* OR disintegrat*) NEAR/3 (implant* OR mesh* OR sling* OR tape* OR suture*)
6		'mechanics'/exp [see Emtree explosions section at the end of the strategy]

Set Number	Concept	Search statement
7		'device material'/exp/mj
8		'Biomedical and dental materials'/exp/mj
9	**Combine sets**	**#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19**

Devices

Set Number	Concept	Search statement
10	Atrium	'prolite' OR 'vitamesh' OR 'proloop' OR (('C-QUR' OR 'CQUR') NEAR/2 (mesh OR plug* OR sling* OR patch*))
11	B.Braun	'optilene' OR 'premilene' OR 'Obtryx'
12	BARD	'marlex'/exp OR 'marlex' OR 'polysoft' OR 'composix' OR 'bard mk' OR 'perfix' OR 'speramesh' OR 'ventralex' OR 'ventrio' OR 'Avaulta' OR 'pelvitex' OR (('influx' OR 'bard' OR '3d max' OR '3dmax' OR 'kugel') NEAR/2 (mesh OR plug* OR sling* OR patch*))
13	Boston Scientific	'obtryx' OR 'prefyx' OR 'solyx' OR 'upsylon' OR (('advantage' OR 'lynx' OR 'pinnacle' OR 'uphold' OR 'arise') NEAR/2 (mesh OR plug* OR sling* OR patch*))
14	Ethicon/J&J	vypro* OR 'prolene' OR 'prolift' OR 'gynemesh' OR (('proceed' OR 'ultrapro') NEAR/2 (mesh OR plug* OR sling* OR patch*))
15	Medtronic Covidien	'Perietene' OR 'Parietex ProGrip' OR 'SurgiPro' OR 'Pelvetex' OR 'Uretex' OR ((Tunneler OR IVS) NEAR/2 (mesh OR plug* OR sling* OR patch*))
16	Other brands	'Trelex' OR 'Serapren' OR 'Seramesh' OR 'Dynamesh' OR 'Prolus' OR 'SURGIMESH' OR 'Evexar' OR 'TiMesh' OR 'TiLene' OR 'Promesh' OR 'Dolphin Mesh' OR 'IntePro' OR 'Desara' OR 'Vertessa' OR 'Ugytex'
17	**Combine sets**	**#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8**
18	**Combine sets**	**#1 OR #9**
19	Limit by language and publication date	#10 AND [english]/lim AND [2010–2020]/py
20	Limit by publication type	#11 NOT ('book'/it OR 'chapter'/it OR 'conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'editorial'/it OR 'erratum'/it OR 'letter'/it OR 'note'/it OR 'short survey'/it OR 'tombstone'/it)

Host Response

Set Number	Concept	Search statement
21		Host NEAR/2 (reaction* OR response*)

Set Number	Concept	Search statement
22		'toxicity'/exp OR toxic*:ti OR cytotox* OR teratogenic* OR genotox* 'carcinogenicity'/exp OR carcinogen*:ti
23		('fibrosis'/exp OR fibrosis OR fibrotic) AND ('postoperative complication'/exp OR implant* OR mesh* OR sling* OR tape*)
24		'immune response'/exp OR 'immunity'/exp/mj OR 'hypersensitivity'/exp OR 'immunopathology'/exp/mj
25		Immun*:ti OR autoimmun*:ti OR hypersens*:ti
26		'inflammation'/exp OR inflamm*:ti
27		'foreign body reaction' OR granuloma*
28		('adhesion'/exp OR 'tissue adhesion'/exp OR 'biomechanics'/exp OR biocompat*)
29		('tissue adhesion'/exp OR adhes*) AND ('postoperative complication'/exp OR implant* OR mesh* OR sling* OR tape*)
30		('erosion'/exp OR 'mesh erosion'/exp OR eros* OR erod*)
31		Expos* AND (implant* OR mesh* OR sling* OR tape* OR suture*)
32		(protrude* OR protrus*) NEAR/3 (implant* OR mesh* OR sling* OR tape* OR suture*)
33		Migrate OR migration
34	**Combine sets**	**#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33**

Alternate Approaches

Set Number	Concept	Search statement
35	By periodical title	(material* OR biomaterial*):jt

Set Number	Concept	Search statement
36		('physical parameters'/exp/mj OR 'mechanics'/exp/mj) AND ([humans]/lim OR [animals]/lim)
37	**Combine sets**	**#35 AND #36**
38	**(Polypropylene OR Devices) AND Material Response**	**#12 AND #20**
39	**(Polypropylene OR Devices) AND Host Response**	**#12 AND #34**
40	**(Polypropylene OR Devices) AND alternate**	**#12 AND #37**
41	**Combine all**	**#38 OR #39 OR #40**

Emtree term explosions

"Exploding" in the context of hierarchical controlled vocabularies means typing in the broadest (root or parent) term and having all the related more specific terms included in the search strategy. In one of our approaches, we explode the Emtree concept mechanics. This explosion automatically added the following 5 pages of terms plus the entry terms (lexical variants and synonyms) associated with those terms to the strategy. That's one of the major advantages to searching using controlled vocabularies. Possible limitations are inconsistent indexing and the presence of unindexed content. That's why we also include free text words in our strategies.

Mechanics/exp

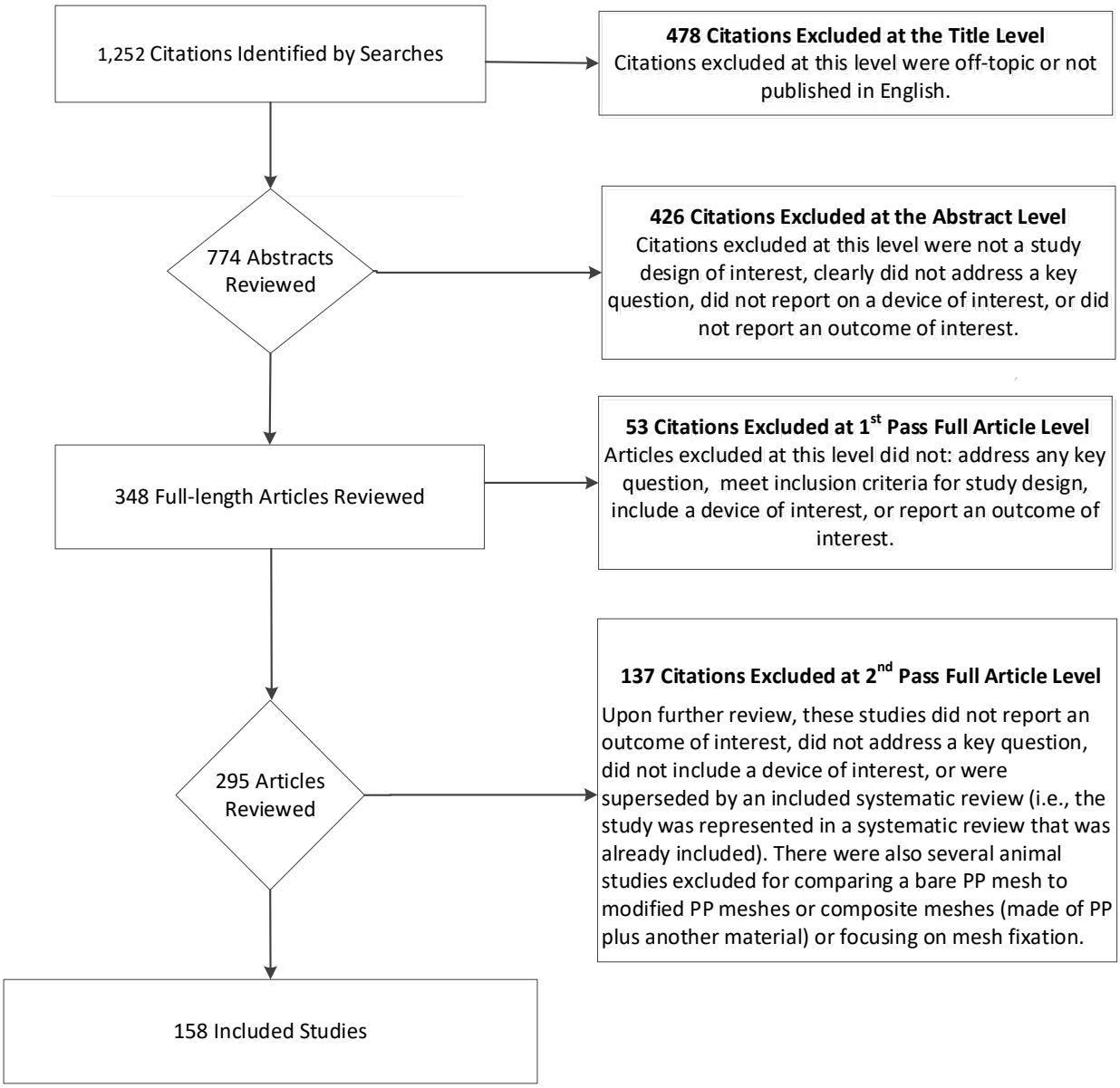
- Biomechanics
- Compliance (physical)
    - Bladder compliance
    - Blood vessel compliance
        - Artery compliance
        - Vein compliance
    - Heart muscle compliance
        - Heart left ventricle compliance
        - Heart ventricle compliance
    - Lung compliance
- Compressive strength
- Dynamics
    - Compression
    - Computational fluid dynamics
    - Decompression
        - Explosive decompression
        - Rapid decompression

        - Slow decompression
    - Gravity
        - Gravitational stress
        - Microgravity
        - Weight
            - Body weight
                - Birth weight
                    - High birth weight
                    - Low birth weight
                        - Small for date infant
                        - Very low birth weight
                            - Extremely low birth weight
            - Body weight change
                - Body weight fluctuation
                - Body weight gain
                    - Gestational weight gain
                - Body weight loss
                    - Emaciation
                - Body weight control
                - Fetus weight
                - Ideal body weight
                - Lean body weight
                - Live weight gain
            - Dry weight
            - Fresh weight
            - Molecular weight
            - Organ weight
                - Brain weight
                - Ear weight
                - Heart weight
                - Liver weight
                - Lung weight
                - Placenta weight
                - Spleen weight
                - Testis weight
                - Thyroid weight
                - Uterus weight
            - Seed weight
            - Tablet weight
            - Thrombus weight
        - Weightlessness
    - Hydrodynamics
        - Hypertonic solution
        - Hypotonic solution
        - Isotonic solution
        - Osmolality
            - Hyperosmolality
            - Hypoosmolality
            - Plasma osmolality
            - Serum osmolality
            - Urine osmolality
        - Osmolarity
            - Blood osmolarity
            - Hyperosmolarity
            - Hypoosmolarity

                - Plasma osmolarity
                - Serum osmolarity
                - Tear osmolarity
                - Urine osmolarity
            - Osmosis
                - Electroosmotic
                - Osmotic stress
                    - Hyperosmotic stress
                    - Hypoosmotic stress
    - Photodynamics
        - Photoactivation
            - Photoreactivation
        - Photodegradation
        - Photoreactivity
            - Photocytotoxicity
            - Photosensitivity
            - Photosensitization
            - Phototaxis
            - Phototoxicity
        - Photostimulation
    - Proton motive force
    - Shock wave
        - High-energy shock wave
    - Stress strain relationship
    - Thermodynamics
        - Adiabaticity
        - Enthalpy
        - Entropy
- Elasticity
    - Viscoelasticity
    - Young modulus
- Force
- Friction
    - Orthodontic friction
- Hardness
- Kinetics
    - Adsorption kinetics
    - Flow kinetics
        - Electroosmotic flow
        - Flow rate
        - Gas flow
        - Laminar airflow
        - Laminar flow
        - Powder flow
            - Angle of repose
            - Hausner ration
        - Pulsatile flow
        - Shear flow
        - Thixotropy
        - Tube flow
        - Turbulent flow
        - Vortex motion
        - Water flow
    - Motion
        - Coriolis phenomenon

        - Rotation
        - Vibration
            - Hand arm vibration
            - High frequency oscillation
            - Oscillation
            - Oscillatory potential
            - Whole body vibration
    - Velocity
        - Acceleration
        - Deceleration
        - Processing speed
        - Wind speed
- Mass
    - Biomass
        - Fungal biomass
        - Immobilized biomass
        - Microbial biomass
    - Body mass
    - Bone mass
    - Dry mass
    - Fat free mass
    - Fat mass
    - Heart left ventricle mass
    - Kidney mass
- Materials testing
- Mechanical stress
    - Contact stress
    - Contraction stress
    - Shear stress
    - Surface stress
    - Wall stress
- Mechanical torsion
- Molecular mechanics
- Plasticity
- Pliability
- Quantum mechanics
    - Quantum theory
- Rigidity
- Torque
- Viscosity
    - Blood viscosity
        - Plasma viscosity
    - Gelatinization
    - Shear rate
    - Shear strength
    - Shear mass
    - Sputum viscosity
    - Viscoelasticity

Appendix C: Study Flow Diagram



Appendix D. Evidence Tables

Table 8: Polypropylene as a Material – Health Effect (In Vivo) Animal Studies

Local Response/Toxicity

Source Citation: Tomida et al. (2011)[1]

Study Design: Case series

Device or Material: PP discoid 0.54 mm thick

Route: Subcutaneously in the dorsal area.

Dose: NA

Frequency/Duration: Unclear

Response - Granulation tissue proliferation, inflammatory cell-rich granulation, thin fibrous tissue capsule formation.

Species (strain): mice, ddY

Gender: all male

Number per group: 6 in PP group

Observations on adverse effects (brief): See Response

Timing of adverse effects: Inflammatory granulation 1 week, thin fibrous tissue capsule formation 12 weeks.

Source Citation: Drobnik et al. (2017)[2]

Study Design: Comparative study

Device or Material: PP net 3 cm x 2 cm

Route: Subcutaneously in the left lumbar region.

Dose: NA

Frequency/Duration: Unclear

Response: Low intensity inflammation.

Species (strain): rats, Wistar

Gender: all male

Number per group: 28 per group (3 groups)

Observations on adverse effects (brief): Inflammation, but low intensity. Weight of granulated tissue increased from 24 mg to 42 mg from weeks 2-24. Water content of tissue decreased from 90% to 72% weeks 2-24. Glycosaminoglycan content increased during weeks 4-8. Total collagen gradually increased weeks 2-24. Soluble collage decreased from 26 ug/mg at 2 weeks to almost 0 at 24 weeks. Breaking strength of granulated tissue decreased during weeks 4-8 but increased at week 24.

Timing of adverse effects: Timing of adverse effects

Source Citation: Zywicka et al. (2016)[3]

Study Design: Comparative study

Device or Material: PP threads diameter 3/0 USP

Route: Muscle tissue

Dose: NA

Frequency/Duration: Unclear

Response: Inflammatory response

Species (strain): Rats, Wistar

Gender: NR

Number per group: 10

Observations on adverse effects (brief): Adhesion, inflammatory response, narrow formed band of connective tissue, increasing in thickness over days 14-90.

Timing of adverse effects: 0-14 days

Table 9: General Surgical Mesh – Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Gutlic et al. 2019[4]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact Duration: 3-year follow-up

Dose: TEP technique with unfixed heavyweight mesh (3DMax) versus Lichtenstein technique with lightweight mesh (Parietene) fixed with PP suture.

Frequency/Duration: Single administration

Response: Pain (at 1 and 3 years)

Patient characteristics (gender, mean age): 100% male, 54 years

Number per group: 3DMax: 188 at 1 year, 180 at 3 years. Parietene: 208 at 1 year, 194 at 3 years.

Observations on adverse effects: No significant difference between groups on pain at 1 or 3 years.

Timing of adverse effects: Assessments at 1 and 3 years.

Factors that predict response: NR.

Source Citation: Sun et al. 2019[5]

Study Design: RCT (Non-inferiority of bovine mesh)

Device or Material: Polypropylene mesh

Contact duration: 6-month follow-up

Dose: ProLite versus bovine mesh (Balance)

Frequency/Duration: Single administration

Response: Pain, Foreign body sensation

Patient characteristics (gender, mean age): ProLite: 93.9% male, 61.4 years. Bovine: 84.8% male, 58.2

years.

Number per group: 66

Observations on adverse effects: Pain significantly higher for ProLite than for bovine mesh at 1 day, 1 week, 1 month and 3 months; both groups reported no pain at 6 months. No cases of foreign body sensation in bovine mesh group, 4 cases in PP group (no significant difference).

Timing of adverse effects: Assessments at 1 day, 1 week, and 1, 3, and 6 months.

Factors that predict response: NR

Source Citation: Yang et al. 2019[6]

Study Design: Case series

Device or Material: Polypropylene mesh

Contact duration: Median months implanted: 59 (range 8 to 176)

Dose: NR

Frequency/Duration: Single administration

Response: Pain, Foreign body sensation, Seroma

Patient characteristics (gender, mean age): 100% male. 45.0 (SPMM-66), 47.5 (PFM) years.

Number per group: 52 SPMM-66, 50 PFM.

Observations on adverse effects: No chronic pain reported in any patients at 1-year follow-up. No significant difference in foreign body sensation (17 SPMM-66 vs 15 PFM) or seroma (3 PFM, 6 SPMM-66).

Timing of adverse effects: n/a

Factors that predict response: NR

Source Citation: Iakovlev et al. 2018[7]

Study Design: Case series

Device or Material: Polypropylene mesh

Contact duration: Median months implanted: 59 (range 8 to 176)

Dose: NR

Frequency/Duration: Single administration

Response: Damage to smooth muscle of the vas, Dysejaculation, Inflammation, Mesh erosion, Mesh migration, Mesh transmigration, Nerve damage, Neuroma-type lesion, Orchialgia, Segmental testicular atrophy, Sexual pain, Spermatocele, Stretched blood capillaries

Patient characteristics (gender, mean age): 100% male. 52 years (range 23 to 72).

Number per group: 13 with severe chronic post-herniorrhaphy pain and involvement of spermatic cord/vas deferens.

Observations on adverse effects: Mesh migration through the spermatic cord and vas deferens caused sexual pain, dysejaculation, and orchialgia post-herniorrhaphy. Complications: 3 transmigration through the vas with complete fibrous replacement, 3 mesh migration and erosion, 6 sexual pain, 3 dysejaculation, inflammation, stretched blood capillaries, 1 neuroma type lesion, 1 spermatocele, 1 segmental testicular atrophy, autonomic and somatic nerve damage, damage to smooth muscle of the vas.

Timing of adverse effects: 8 to 176 months post-implant.

Factors that predict response: NR

Source Citation: Koscielny et al. 2018[8]

Study Design: Matched-pair analysis

Device or Material: Polypropylene mesh vs. SIS mesh

Contact duration: 24-month follow-up

Dose: 12 ULTRAPRO, 12 Vypro

Frequency/Duration: Single administration

Response: Hematoma, Seroma, Soft tissue necrosis

Patient characteristics (gender, mean age): 58% male. 58±9.3 years SIS, 60±9.9 PP.

Number per group: 24 each group.

Observations on adverse effects: Significantly more surgical site occurrences (seroma, hematoma, soft tissue necrosis) with SIS (19 SIS, 12 PP). Complications: 12 seroma (20.8% PP, 29.2% SIS), 10 hematoma (16.7% PP, 25% SIS), 9 soft tissue necrosis (12.5% PP, 25% SIS).

Timing of adverse effects: NR

Factors that predict response: Female gender was associated with more complications.

Source Citation: Pathrose Kamalabai et al. 2018[9]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: Mean duration in days: 219.69 (range, 88 to 419)

Dose: Double-layer G-patch (45 g/m2)

Frequency/Duration: Single administration

Response: None

Patient characteristics (gender, mean age): 80% male. 37.1 years (range 18 to 62).

Number per group: 35 undergoing decompressive craniectomy (DC).

Observations on adverse effects: Use of double-layer G-patch prevented the occurrence of adhesions.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Wong et al. 2018[10]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 1-year follow-up

Dose: Lightweight PP/ poliglecaprone mesh (Ultrapro) versus heavyweight polyester mesh (Parietex)

Frequency/Duration: Single administration

Response: Pain, Seroma, Urinary retention

Patient characteristics (gender, mean age): ULTRAPRO: 92% male, median age 62. Parietex: 100% male, median age 58.

Number per group: 39 ULTRAPRO, 38 Parietex.

Observations on adverse effects: No significant differences in pain between groups. Seroma was lower with UL-TRAPRO (2) vs Parietex (9)(p=0.02). Urinary retention occurred in 3 cases for ULTRAPRO and 0 for Parietex (not statistically significant).

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Henrikson et al. 2017[11]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: 12-month follow-up

Dose: TYRX

Frequency/Duration: Single administration

Response: Pocket hematoma

Patient characteristics (gender, mean age): 24% female, 70.8±11.5 years.

Number per group: 1,129 undergoing CIED replacement with an ICD (n=459) or CRT (670) treated with TYRX.

Observations on adverse effects: Pocket hematoma occurred in 18 (1.6%) patients treated with TYRX.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Nikkolo et al. 2017[12]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 3-year follow-up

Dose: Sutured lightweight PP mesh (Optilene LP) versus self-gripping polyester mesh (Parietex ProGrip)

Frequency/Duration: Single administration

Response: Chronic pain, Foreign body sensation

Patient characteristics (gender, mean age): NR

Number per group: 66 Optilene, 65 Parietex.

Observations on adverse effects: No significant differences in pain or foreign body sensation between groups.

Timing of adverse effects: 3 years.

Factors that predict response: Severe preoperative and early postoperative pain.

Source Citation: Ahmad et al. 2016[13]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: 11 months to 2 years

Dose: NR

Frequency/Duration: Single administration

Response: Epidydimorchitis, Numbness in groin, Occasional pain/pain after exertion, Pain, Seroma

Patient characteristics (gender, mean age): 100% male. Mostly 61 to 70 years.

Number per group: 158 undergoing hernioplasty.

Observations on adverse effects: Seroma and epidydimorchitis occurred in <2% of patients. Complications: 2 (1.26%) seroma, 48 (30.4%) pain, 1 (0.63%) epidydimorchitis, 8 (5.06%) numbness in groin, 6 (3.8%) occasional pain/pain after exertion.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Burgmans et al. 2016[14]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 1- and 2-year follow-up

Dose: Lightweight (ULTRAPRO: 55 g/m2), heavyweight (Prolene: 80 g/ m2)

Frequency/Duration: Single administration

Response: Foreign body sensation, Pain

Patient characteristics (gender, mean age): 100% male. 55 years.

Number per group: 950 with TEP inguinal hernia repair (478 ULTRAPRO, 471 Prolene).

Observations on adverse effects: Complications: Number of patients with relevant pain (NRS >3) but without recurrent hernia was significantly higher with ULTRAPRO at 1 year. Foreign body sensation was higher with ULTRAPRO (13.8% vs 12.2%) at 1 and 2 years.

Timing of adverse effects: NR

Factors that predict response: Multivariate analysis indicated that light-weight ULTRAPRO was significantly associated with pain at 1 year. Weakness of lightweight mesh may have contributed to increased pain.

Source Citation: Donati et al. 2016[15]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 12-day follow-up

Dose: Lightweight versus heavyweight PP mesh (same manufacturer [Hertra]), both sutured

Frequency/Duration: Single administration

Response: Inflammation markers (IL-6, TNF-α), Oxidative stress markers (GSH, LOOH)

Patient characteristics (gender, mean age): NR. 60.17 (light), 59.06 (heavy) years.

Number per group: 29 light, 32 heavy.

Observations on adverse effects: No significant differences between groups in IL-2 levels. Significantly higher TNF-α for heavy than for light (14.3 pg/mL vs. 3.67, $p = 0.016$) at 3 days. Significantly lower GSH for heavy than for light (64.93 nmol/mL vs. 81.93, $p = 0.01$) at 6 hours. Significantly higher LOOH for heavy than for light (19.45 nmol/mL vs. 6.61, $p = 0.019$) at 3 days.

Timing of adverse effects: Assessments at 6 hours, 3 days, and 12 days.

Factors that predict response: Number of plugs.

Source Citation: Karaca et al. 2016[16]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: mean months follow-up: 40 to 44 (based on graft use)

Dose: mean months follow-up: NR

Frequency/Duration: Single administration

Response: Hematoma

Patient characteristics (gender, mean age): 83% male. 48 years.

Number per group: 246 with incarcerated inguinal hernia.

Observations on adverse effects: Hematoma occurred in 29 patients.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Kassem & El-Haddad 2016[17]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: Mean month follow-up: 28.7

Dose: Standard PP mesh (Prolene) versus composite mesh (PROCEED, PHYSIOMESH)

Frequency/Duration: Single administration

Response: Pain

Patient characteristics (gender, mean age): Prolene: 33.3% male, 46.9 years. Composite: 40% male, 46.1 years.

Number per group: 30

Observations on adverse effects: No significant difference in pain between groups.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Krnic et al. 2016[18]

Study Design: Case control

Device or Material: Polypropylene mesh

Contact duration: % months

Dose: Bard mesh

Frequency/Duration: Single administration

Response: Decrease in PI, Decrease in RI, Increase ASA, Increase EDV, Increase PSV

Patient characteristics (gender, mean age): 100% male. 57 years (range 40 to 81) elective open mesh hernia repair, 64 years (range 28 to 80) incarcerated hernia repair.

Number per group: 50 (25 each arm).

Observations on adverse effects: Early postoperative changes in all patients included an increase in ASA, EDV, and PSV. Response in all patients: increase in postoperative ASA; increase in EDV and PSV. Response in urgent repair only: significant decrease in resistive index (RI) and pulsative index (PI).

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Nikkolo et al. 2016[19]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 3 year follow-up

Dose: Large-pore lightweight composite mesh (ULTRAPRO) versus small-pore lightweight PP mesh (Optilene LP), both sutured

Frequency/Duration: Single administration

Response: Chronic pain, Foreign body sensation

Patient characteristics (gender, mean age): NR

Number per group: 65 ULTRAPRO, 63 Optilene.

Observations on adverse effects: Significantly higher rate of chronic pain for ULTRAPRO than for Optilene (33.9% vs. 15.9%, p = 0.025). Foreign body sensation also higher for ULTRAPRO (23.1% vs 15.9%, difference not significant).

Timing of adverse effects: NR

Factors that predict response: Age, severe preoperative pain.

Source Citation: Evans 2015[20]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: Median months: 23 (2-78)

Dose: NR

Frequency/Duration: Single administration

Response: Mesh erosion

Patient characteristics (gender, mean age): 93% female. 59±16 years (entire cohort).

Number per group: 2051 undergoing laparoscopic ventral rectopexy (LVR); 1325 with PP.

Observations on adverse effects: 23 mesh erosions with PP occurred from 12 months to 84 months. Complications: 23 mesh erosion (significantly higher incidence of mesh erosion with polyester (6.4%) vs. PP (1.7%).

Timing of adverse effects: Erosions occurred at 12 months (4), 24 months (6), 36 months (6), 60 months (5), 72 months (1), and 84 months (1).

Factors that predict response: NR

Source Citation: Ho et al. 2015[21]

Study Design: Cohort

Device or Material: PP vs. SIS

Contact duration: Median follow-up 18 months

Dose: 10 x 15 cm

Frequency/Duration: Single administration

Response: Chronic pain, Epididymitis, Ileus, Seroma

Patient characteristics (gender, mean age): 94.3% male PP, 83.3% male SIS. 53 years both arms.

Number per group: 70 PP (108 hernias), 12 SIS (17 hernias).

Observations on adverse effects: Overall complications were higher with SIS (but not significantly different): chronic pain (25% SIS, 7.1% PP), seroma (25% SIS, 7.1% PP), epididymitis (1.4% PP), ileus (8.3% SIS).

Timing of adverse effects: NR

Factors that predict response: Degradation of SIS was associated with recurrence.

Source Citation: Akkary and Olgers 2014[22]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: Mean months follow-up: 12±6

Dose: NR

Frequency/Duration: Single administration

Response: Bone

Patient characteristics (gender, mean age): 77.5% females. 49±11.56 years.

Number per group: 102 with LAGB surgery.

Observations on adverse effects: No mesh erosions were observed.

Timing of adverse effects: n/a

Factors that predict response: n/a

Source Citation: Basile et al. 2014[23]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 3-year follow up

Dose: PP vs. composite PP (Combi Mesh Plus (PP-PU))

Frequency/Duration: Single administration

Response: Abdominal wall hypo-mobility, abscess, Atypical sensation, Discomfort, Hematoma, Pain, Seroma

Patient characteristics (gender, mean age): 79.2% male. 62.6±15.9 years (PP).

Number per group: 24

Observations on adverse effects: 4 (16.7%) patients reported abdominal pain with PP. Complications: 4 (16.7%) abdominal pain, 3 (12.5%) superficial wound infection/seroma/hematoma/abscess, 1 (4.2%) abdominal wall hypomobility, discomfort, atypical sensation.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Bensaadi et al. 2014[24]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: Mean month follow-up: 42

Dose: Bilayer (PP and polytetra-fluoroethylene) mesh: Ventralex versus CA.B.S.'Air

Frequency/Duration: Single administration

Response: Pain, Foreign body sensation, Late complications

Patient characteristics (gender, mean age): 47% male, 42.6 years.

Number per group: 41 Ventralex, 42 Cabs'Air.

Observations on adverse effects: : Pain, foreign body sensation and late complications significantly lower for Cabs'Air than for Ventralex at 1 month and 3 months.

Timing of adverse effects: Assessments at 1 week, 1 month, and 3 months.

Factors that predict response: NR

Source Citation: Bontinck et al. 2014[25]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: ≥12 months

Dose: PROCEED Ventral Patch (PVP), lightweight mesh

Frequency/Duration: Single administration

Response: Foreign body sensation, Hematoma, Mesh contraction, Seroma

Patient characteristics (gender, mean age): 67% male. 54±13.3 years.

Number per group: 101 with primary umbilical hernia or another abdominal wall hernia.

Observations on adverse effects: : Mesh contraction was observed in 10 patients undergoing abdominal wall hernia repair with PVP. Complications (mean 16 months): 10% mesh contraction, 3% seroma, 2% hematoma, 11% foreign body sensation.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Demetrashvili et al. 2014[27]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 3-year follow-up

Dose: LWM (ULTRAPRO) vs. HWM (Prolene)

Frequency/Duration: Single administration

Response: Foreign body sensation, Hematoma, Pain, Seroma

Patient characteristics (gender, mean age): 92% male. 54.7± 14.3 years LWM, 51.3± 17.5 HWM.

Number per group: 226 with inguinal hernia; 113 each group.

Observations on adverse effects: Benefits to LWM included significantly fewer patients with foreign body sensation from 1 to 3 years. Early complications: 1 hematoma in each group, 10 seroma (4 LWM, 6 HWM). Late complications: Significantly more patients with foreign body sensation with HWM at 1 year (17 vs. 6), 2 years (11 vs. 2), and 3 years (9 vs. 1). No difference in pain.

Timing of adverse effects: Pain from 7 days to 3 years.

Factors that predict response: NR

Source Citation: Kulikovsky et al. 2014[28]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: 7 days

Dose: NR

Frequency/Duration: Single administration

Response: High concentration of cytokines, Seroma

Patient characteristics (gender, mean age): NR

Number per group: 52 with incisional hernia.

Observations on adverse effects: Seromas formed in 18 (34.6%) individuals. Complications: 18 seroma, high concentrations of cytokines (TNFa, IL 1B, IL 2, IL 6, IL 8, IL 10, IL 1 RA) up to Day 7 postoperatively in drainage from subcutaneous fat.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Peres et al. 2014[29]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: 5-year follow-up

Dose: NR

Frequency/Duration: Single administration

Response: Chronic Pain, Hematoma, Seroma

Patient characteristics (gender, mean age): 63% female. 49 years (range 33 to 82).

Number per group: 24 undergoing subcostal incisional hernia repair.

Observations on adverse effects: Seroma occurred in 3 (12.5%) patients. Complications: 3 (12.5%) seroma, 1 (4.1%) hematoma, 1 chronic pain.

Timing of adverse effects: Pain persisted for 6 months in 1 patient.

Factors that predict response: NR

Source Citation: Sorour 2014[30]

Study Design: Case series

Device or Material: Polypropylene mesh

Contact duration: mean months follow-up: 46.8±20.3

Dose: Prolene

Frequency/Duration: Single administration

Response: Seroma

Patient characteristics (gender, mean age): 87.6% female. 59.3±11.7 years.

Number per group: 105 with large ventral hernia.

Observations on adverse effects: Seroma occurred in 12 (11.4%) patients. Complications: 12 seroma formation.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Klosterhalfen and Klinge 2013[31]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: Mean months explanted: 35±21 (large pore), 23±15 (small pore)

Dose: 18 large pore (Vypro, ULTRAPRO), 152 small pore (Marlex, Atrium, Prolene)

Frequency/Duration: Single administration

Response: Collagen I/III ratio fistula, Inflammation (high infiltrate [IF]), Pain

Patient characteristics (gender, mean age): 76.2% males (overall explants). NR.

Number per group: 170 PP mesh samples from abdominal wall hernias explanted for pain (other mesh explanted for recurrence or infection); 75% with mesh placed in groin area, 27% in anterior abdominal wall.

Observations on adverse effects: Tissue explanted for mesh-related pain had a high presence of IF, and mostly normal collagen I/III ratio. Complications: IF was higher with presence of pain vs. absence (32±12 vs. 28±14). Normal

collagen I/III ratio was reported in 70% of patients, lowered collagen I/III ratio in 30% of patients. Intense inflammation was linked to predominance of collagen type I.

Timing of adverse effects: : Latest explanation for chronic pain was undertaken at 96 months.

Factors that predict response: Intense inflammation with high IF was correlated with female gender but not with age.

Source Citation: Pielacinski et al. 2013[32]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 6-month follow-up

Dose: HWM PP (100 g/m2) vs composite (PP/polyglactin) LWM

Frequency/Duration: Single administration

Response: Discomfort (pinching, tightness, pulling), Foreign Body sensation, Hematoma, Ischemic orchiti, Seroma

Patient characteristics (gender, mean age): 100% male. 59 years (range 20 to 89).

Number per group: 76 HWM, 73 composite LWM (n/a).

Observations on adverse effects: After 6 months postoperatively, 23 (43%) patients complained of foreign body sensation or other discomfort in the operated groin. Early complications (number not specified for HWM): 22 hematoma, 3 seroma. Late complications (3 to 6 months; n=54): 9 (17%) chronic pain in the groin, 32 (59%) foreign body sensation, prickly/pinching sensation, tightness and pulling or other unspecified discomfort in operated groin.

Timing of adverse effects: Complaints of discomfort after 3rd month (59%) and after 6th month (43%) postoperative.

Factors that predict response: ASA III was significantly associated with a higher risk for early complications (OR 5.23, 95% CI: 1.36 to 20.03). Being obese and overweight (IRR 4.05, 95% CI: 0.8 to 12.4) and having a hernia type II (IRR 5.7, 95% CI: 1.8 to 17.6) were significantly associated with more intense chronic pain.

Source Citation: Souza and Dumanian 2013[33]

Study Design: Case series

Device or Material: Polypropylene mesh

Contact duration: Median months follow-up: 23 (range, 6 to 64)

Dose: Soft Prolene

Frequency/Duration: Single administration

Response: Adhesions, Cellulitis, Hematoma, Seroma, Pain

Patient characteristics (gender, mean age): 55% male. 56.8±12.3 years.

Number per group: 87 with hernia repair.

Observations on adverse effects: 2 patients were admitted to the hospital at 6 months and 2 years postoperatively with pain possibly due to adhesions. 1 patient with hematoma occurring immediately postoperatively had been “continuously anticoagulated for a cardiac indication.” Complications: 4 hematoma, 2 cellulitis, 1 seroma, 2 with pain possibly due to mesh-induced adhesions.

Timing of adverse effects: Adhesions occurred at 6 months and 2 years postoperatively. 1 hematoma occurred immediately postoperatively.

Factors that predict response: 1 hematoma requiring reoperation occurred in a patient who was “continuously anticoagulated for a cardiac indication.”

Source Citation: Yang F. 2013[34]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: Mean months follow-up: 12.5±6.5

Dose: Marlex (90 g/m2)

Frequency/Duration: Single administration

Response: Seroma, Foreign body sensation

Patient characteristics (gender, mean age): 61% male. 52.5±10.2 years.

Number per group: 23 with contaminated large ventral hernias.

Observations on adverse effects: Repair of contaminated large ventral hernias with Marlex mesh caused seroma and chronic foreign body sensation in 3 patients each.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Zhong et al. 2013[35]

Study Design: Systematic review (11 RCTs)

Device or Material: Polypropylene mesh

Contact duration: 2-month to 5-year follow-up

Dose: Lightweight (Opilene, Vypro, Vypro II, SURGIMESH, ULTRAPRO, TiMESH) versus heavyweight (Prolene, Premilene, Atrium, Surgipro)

Frequency/Duration: N/R

Response: Pain, Foreign body sensation, Testicular atrophy, Hematoma, Seroma

Patient characteristics (gender, mean age): NR

Number per group: Lightweight: 1,120 (of whom all reported on pain and 633 reported on testicular atrophy); heavy-weight: 1,061 (all reported on pain, 616 on atrophy).

Observations on adverse effects: 9/9 studies reported on pain; pain lower with lightweight mesh (OR = 0.64; 95% CI = 0.51-0.82). 4/9 reported on foreign body sensation (lower with lightweight mesh, OR = 0.56; 95% CI = 0.40-0.78; P < .05). 4/9 studies reported on atrophy; no significant difference between groups. No significant difference in hematoma or seroma.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Magnusson et al. 2012[36]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 12-month follow-up

Dose: Prolene (PHS®), Lichenstein technique with PP mesh, ULTRAPRO composite (UHS®)

Frequency/Duration: Single administration

Response: Foreign body sensation, Hematoma, Itching, Neuralgia, Pain, Sensory disturbance, Seroma, Tightness

Patient characteristics (gender, mean age): 100% male. Range 46 to 66 years.

Number per group: 309 with inguinal hernia (109 Lichenstein (LS), 99 PHS, 102 UHS).

Observations on adverse effects: Pain at rest and inguinal discomfort peaked at 6 months and was slightly higher with LS up to 12 months. Early complications (<30 days): 8 hematoma (5 LS, 3 PHS), 1 seroma with PHS. Late complications (30 days to 12 months): 2 sensory disturbance (LS), 1 hematoma with PHS, 6 foreign body sensation (3 LS, 3 PHS), 2 neuralgia (LS). Pain at rest peaked at 6 months (28% LS, 25% PHS) then declined similarly at 12 months (22% LS, 18.4% PHS). Inguinal discomfort (tightness, foreign body sensation, sensory loss, itching): 3 months: 46% LS, 43% PHS; 6 months: 49% LS, 47% PHS; 12 months: 42% LS, 35% PHS.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Ali et al. 2011[37]

Study Design: Case series

Device or Material: Polypropylene mesh

Contact duration: Weeks follow-up: 1 to 12

Dose: NR

Frequency/Duration: Single administration

Response: Scrotal hematoma, Seroma

Patient characteristics (gender, mean age): 100% males. 46 years (range 18 to 72).

Number per group: 420 with inguinoscrotal hernia.

Observations on adverse effects: 420 with inguinoscrotal hernia.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Bittner et al. 2011[38]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 1-year follow-up

Dose: Extralight titanized PP mesh (TiMESH) with no fixation versus standard heavyweight (Prolene) with absorbable sutures.

Frequency/Duration: Single administration

Response: Pain, Seroma, Hematoma

Patient characteristics (gender, mean age): Prolene: 86.7% male, 52.4 years. TiMESH: 90% male, 53.5 years.

Number per group: 150

Observations on adverse effects: No significant differences between groups in pain or hematoma. Seroma was significantly lower in the TiMESH group ($p = 0.04$).

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Pielacinski et al. 2011[39]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 6-month follow-up

Dose: Heavyweight PP (100 g/m2) vs. lightweight composite Vypro II (V, 80 g/m2)

Frequency/Duration: Single administration

Response: Foreign body sensation, Pain

Patient characteristics (gender, mean age): 93% male. 59±15.1 years.

Number per group: 59 with inguinal hernia (34 PP, 25 V); 24 PP and 17 V at 6 months.

Observations on adverse effects: Mesh type did not significantly influence chronic pain (>3 months) occurrence. Early complications (>3 months): 5 pain in groin (8.8% PP, 8% V). Late complications (>6 months): 3 pain in groin (5.9% PP, 4% V), foreign body sensation (no significant difference).

Timing of adverse effects: NR

Factors that predict response: Hernia type 2 was significantly associated with pain up to 6 months.

Source Citation: Agarwal et al. 2010[40]

Study Design: Case series

Device or Material: Polypropylene mesh

Contact duration: Months follow-up: 12 to 31

Dose: PPM (100 g/m2), LWM (45 gm/ m2)

Frequency/Duration: Single administration

Response: Pain, Seroma

Patient characteristics (gender, mean age): 100% male. 49 years.

Number per group: 57 patients (114 TEP herniorrhaphy); 84 PPM (n=42), 30 LWM (n=15).Observations on adverse effects: : Benefits with LWM included significantly lower pain scores and fewer seromas. Complications: Significantly higher pain scores (10 point VAS) with PPM up to 3 months. Higher incidence of seroma with PPM (15 vs. 2).

Timing of adverse effects: Seromas were detected at week 3 (14) and month 3 (3).

Factors that predict response: NR

Source Citation: Ammar S. 2010[41]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 6- to 28-month follow-up

Dose: Proline® vs. conventional fascial repair

Frequency/Duration: Single administration

Response: Hematoma, Seroma

Patient characteristics (gender, mean age): 76% male. 51.4±5.67 years (PP).

Number per group: 37 undergoing PP mesh hernioplasty for complicated umbilical hernia.

Observations on adverse effects: Complications were limited to 4 (10.8%) hematoma/seroma.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Arslani et al. 2010[42]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 2-year follow-up

Dose: Prolene mesh with Prolene sutures versus dual component fibrin mesh (DCFM) with no fixation

Frequency/Duration: Single administration

Response: Acute postoperative pain (in first 5 days), Chronic pain, Testicular atrophy

Patient characteristics (gender, mean age): 98% male, 52.3 years.

Number per group: 45 Prolene, 52 DCFM.

Observations on adverse effects (brief): Acute postoperative pain significantly higher for Prolene than for DCFM; no significant differences on chronic pain or testicular atrophy.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Chui et al. 2010[26]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 1-year follow-up

Dose: Lightweight (DynaMesh) versus heavyweight (Surgipro)

Frequency/Duration: Single administration

Response: Pain, Foreign body sensation

Patient characteristics (gender, mean age): 97.8% male, 61.6 years.

Number per group: 50 (within-subject design).

Observations on adverse effects: : Higher pain score for heavyweight mesh but $p > 0.10$. Significantly more patients had foreign body sensation with heavyweight mesh at every time point.

Timing of adverse effects: Up to 1 year.

Factors that predict response: NR

Source Citation: Di Vita et al. 2010[43]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 48-hour follow-up

Dose: Heavyweight PP (2/0 Prolene) versus hybrid (Vypro II)

Frequency/Duration: Single administration

Response: Inflammatory response(leukocytes, cytokines, C-reactive protein, α1-antitrypsin)

Patient characteristics (gender, mean age): 100% male, age 21-65 years

Number per group: 15

Observations on adverse effects: In both groups, leukocytes, acute phase proteins, and cytokines increased significantly, and growth factors decreased significantly, but all returned to near baseline levels by 48 hours except for C-reactive protein, α1-antitrypsin. Prolene > Vypro on lymphocytes at 24 hours; otherwise, the two groups did not differ significantly.

Timing of adverse effects: Measurements at 6, 24, and 48 hours.

Factors that predict response: NR

Source Citation: Gao et al. 2010[44]

Study Design: Systematic review

Device or Material: Polypropylene mesh

Contact duration: 8 week to 5 year follow-up

Dose: Vypro II (50% polyglactin and 50% PP) versus PP mesh (Prolene, Premilen, Atrium, Surgipro)

Frequency/Duration: NR

Response: Pain, Foreign body sensation, Testicular atrophy, Seroma

Patient characteristics (gender, mean age): NR

Number per group: Vypro II: 1014 (of whom 758 reported on pain and 295 on testicular atrophy); other:1013 (769 pain, 282 atrophy).

Observations on adverse effects: 4/10 studies reported pain within 1 year; no significant difference between Vypro II and PP mesh. 3/10 studies reported testicular atrophy; no significant difference between Vypro II and PP. Vypro II had significantly lower foreign body sensation than PP mesh (OR 0.58, 95% CI 0.42–0.80). No significant difference for seroma.

Timing of adverse effects: NR

Factors that predict response: NR. Note: Substantial overlap with Zhong et al.35

Source Citation: Peeters et al. 2010[45]

Study Design: RCT

Device or Material: Polypropylene mesh

Contact duration: 1-year follow-up

Dose: Lightweight (Vypro II, TiMESH) versus standard (Marlex)

Frequency/Duration: Single administration

Response: α-glucosidase, Sperm morphology, Sperm concentration, Sperm motility

Patient characteristics (gender, mean age): 100% male. Median age 43.5 (Marlex), 34.5 (Vypro II), 37 (TiMe).

Number per group: 20 Marlex, 20 Vypro II, 19 TiMesh.

Observations on adverse effects: At 1 year, patients receiving Vypro II or TiMesh had significantly greater decreases from baseline in sperm motility than patients receiving Marlex. Sperm concentration, sperm morphology, and α-glucosidase level did not differ significantly across groups.

Timing of adverse effects: NR

Factors that predict response: At 1 year, patients receiving Vypro II or TiMesh had significantly greater decreases from baseline in sperm motility than patients receiving Marlex. Sperm concentration, sperm morphology, and α-glucosidase level did not differ significantly across groups.

Source Citation: Chughtai et al. 2018[46]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: Mean 6 year follow-up (range 5 to 7 years)

Dose: NR

Frequency/Duration: NR

Response: Examined risk of cancer (no increased risk)

Patient characteristics (gender, mean age): 100% male. 56.9 years mesh-based hernia repair, 55.1 cholecystectomy, 65.4 TKA

Number per group: 27,425 mesh-based hernia repair; 13,339 cholecystectomy; 11,435 TKA.

Observations on adverse effects: Mesh-based hernia repair was not associated with an increased risk of cancer up to 6 years follow-up.

Timing of adverse effects: n/a

Factors that predict response: n/a

Source Citation: Cohen Tervaert JW 2018[47]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: >3-year follow-up

Dose: NR

Frequency/Duration: NR

Response: Allergy, Arthralgias/arthritis, ASIA, Autoantibody presence, Cognitive symptoms, Dry eyes/mouth, Elevated ACE, Elevated CK, Elevated CRP, Elevated IgE, Fatigue, IBS, Increased IgG/IgG subclasses, Livedo reticularis, Localized pain, Lymphadenopathy, Myalgia/muscle weakness, Pyrexia, Raynauds, Stroke-like symptoms

Patient characteristics (gender, mean age): 80% female, 49.5 years (range 28 to 75).

Number per group: 40 with mesh repair of hernia (18) SUI (4) and POP (18).

Observations on adverse effects: : Of the 40 patients diagnosed with ASIA, 45% developed an autoimmune disease (e.g., RA) and 25% had immunodeficiencies (e.g. IgG subclass deficiency) detected >3 years follow-up. Abnormal laboratory findings were detected in most patients. Complications: ASIA symptoms: 98% fatigue, 95% myalgias/muscle weakness, 90% arthralgias/arthritis, 78% cognitive symptoms, 80% pyrexia, 85% dry eyes/dry mouth, 17% stroke-like symptoms. Additional symptoms: 78% localized pain, 30% Raynaud's, 80% IBS, 75% allergy, 48% livedo reticularis, 75% lymphadenopathy. Laboratory findings: 33% elevated CRP, 24% elevated ACE, 26% elevated CK, 20% elevated IgE, 24% increased IgG or IgG subclasses, 38% autoantibodies (ANCA, ANA or ACL).

Timing of adverse effects: : 61% of patients experienced symptoms <1 year, 25% within 1-3 years, and 14% >3 years post implantation.

Factors that predict response: 7% of patients had a preexisting allergic disease. Note: 2 patients committed suicide due to unbearable severe weight loss from abdominal pain.

Source Citation: Chughtai et al. 2017[48]

Study Design: Cohort

Device or Material: Polypropylene mesh

Contact duration: 6 years

Dose: NR

Frequency/Duration: NR

Response: Examined risk of systemic/autoimmune disorders (SAID)

Patient characteristics (gender, mean age): 100% male, 58 years

Number per group: 26,575 undergoing hernia repair, 71,271 undergoing colonoscopy.

Observations on adverse effects: PP mesh was not associated with an increased risk of developing SAID up to 6 years follow-up.

Timing of adverse effects: NR

Factors that predict response: NR

ACE: angiotensin converting enzyme; ACL: anti-cardiolipin antibodies; ANA: antinuclear antibodies; ANCA: anti-neutrophil cytoplasmic antibodies; ASA: antisperm antibodies; ASIA: autoinflammatory/autoimmunity syndrome induced by adjuvants; CIED: cardiovascular implantable electronic device; CI: confidence interval; CK: creatinine kinase; CRP: C-reactive protein; CRT: cardiac resynchronization therapy device; EDV: end-diastolic velocity; GSH: glutathione; HWM: heavy weight mesh; IBS: irritable bowel syndrome; ICD: implantable cardioverter-defibrillator; IF: inflammatory infiltrate; IgE: immunoglobulin E; IgG: immunoglobulin G; IRR: incidence rate ratio; LABG: laparoscopic adjustable gastric band; LOOH: lipid hydroperoxide; LWM: light weight mesh; n/a: not applicable; nmol/mL: nanomole/milliliter; NR: not reported; NRS: numeric rating scale; OR: odds ratio; pg/mL: picogram/milliliter; PI: pulsative index; PP: polypropylene; PPM: heavy PP mesh; PSV: peak systolic velocity; RA: rheumatoid arthritis; RCT: randomized controlled trial; RI: resistive index; SIS: small intestinal submucosa; TEP: totally extra-peritoneal; TKA: total knee arthroplasty; TNF-α: tumor necrosis factor alpha; VAS: visual analog scale.

Table 10: General Surgical Mesh – Health Effect (In Vivo) Animal Studies

Local Response/Toxicity

Source Citation: Amigo et al. 2020[49]

Study Design: RCT

Device or Material: PP (Prolene), PGA, UBM (Gentrix Surgical Matrix Plus), control

Route: Hiatal hernia

Dose: NR

Frequency/Duration: Single administration/ 3 months

Response: cellular infiltration of implant, FBGC, fibrosis, fibrous encapsulation, lymphocytes, macrophages, necrosis

neovascularization, plasma cells, scaffold incorporation and degradation

Species (strain): Pig (Landrace)

Gender: Female

Number per Group: 5

Observations on adverse effects: PP group had a higher overall composite score (less favorable outcomes) and higher scores for all subcategories of inflammation (cells, lymphocytes, plasma cells, macrophages, FBGCs, necrosis, fibrosis and fibrous encapsulation, neovascularization, cellular infiltration of implant analysis, and scaffold incorporation and degradation vs. all other groups.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Damous et al. 2020[50]

Study Design: RCT

Device or Material: PP mesh

Route: Inguinotomy

Dose: 1 x 1 cm

Frequency/Duration: Single administration/ 30 and 90 days

Response: cell proliferation, collagen I/III ratio, gene expression, spermatogensis

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 20

Observations on adverse effects: Use of PP mesh preserved spermatogenesis and did not impair the vas deferens or testicles.

Timing of adverse effects: NR

Factors that predicts response:

Source Citation: Pineda Molina et al. 2019[51]

Study Design: RCT

Device or Material: Non-resorbable PP mesh (Bard) vs other non-PP mesh types

Route: Abdominal hernia

Dose: 1 x 1 cm

Frequency/Duration: Single administration/ 3, 7, 14, 21, and 35 days

Response: chronic inflammation

Species (strain): Rat (Sprague-Dawley)

Gender: NR

Number per Group: 10

Observations on adverse effects: Multinucleate giant cells were detected around mesh at 7 days and persisted until 35 days. Infiltrated macrophages were localized at material interface. Macrophages with an M1-like phenotype were lowest with Strattice mesh at 7 days. Persistent pro-inflammatory TNF-α expression at 35 days around PP Bard® Mesh, TIGR®, and GORE® BIO-A® in comparison to the expression of this marker around Phasix™ and Strattice™.

Timing of adverse effects: 7 to 35 days.

Factors that predicts response: macrophage phenotype.

Source Citation: Bronzatto and Ricetto 2018[52]

Study Design: Comparative

Device or Material: SW-PP, LW-PP

Route: Abdomen

Dose: g/m2: 72 and 16

Frequency/Duration: Single administration/4 or 30 days

Response: Il-1 expression, inflammatory response, MMP-2 expression, MMP-3 expression

Species (strain): Rat (NR)

Gender: Female

Number per Group: 20 side-by-side mesh implant

Observations on adverse effects: IL-1, MMP-2, and MMP-3 expression increased over time with no significant differences between LW and SW mesh.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Dreger et al. 2018[53]

Study Design: Comparative

Device or Material: PP, PEUs

Route: Hernia

Dose: NR

Frequency/Duration: Single administration/ 2 and 3 months

Response: capsule thickness, inflammation, lymphocytes, multinucleated giant cells, necrosis, neutrophils, number of inflammatory cells, plasma cells, single macrophages, mechanical properties

Species (strain): Rat (Sprague-Dawley)

Gender: Female

Number per Group: 7

Observations on adverse effects: Significantly smaller fibrous capsule thickness with all five PEUs (vs. PP). Higher degree of inflammation (exhibited by neutrophils, lymphoctyes, plasma cells, single macrophages, multinucleated giant cells, and necrosis) with PP at 3 months. The Young's moduli of the 5 PEUs tested was comparable to those of PP (105 ± 30 to 269 ± 12 MPa); 2% branched poly(1-VAL-8) maintained the greatest mechanical properties at 3 months.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Dreger et al. 2018[54]

Study Design: Comparative

Device or Material: PP, SIS-ECM, 30% PHE6 P(1-VAL-8)

Route: Hernia

Dose: 1 cm diameter discs

Frequency/Duration: Single administration / 7 and 14 days

Response: lymphocytes, macrophages, mechanical properties, multinucleated giant cells, necrosis, neutrophils,

plasma cells, stiffness

Species (strain): Rat (NR)

Gender: NR

Number per Group: NR

Observations on adverse effects: 30% PHE6 P(1-VAL-8) induced the lowest overall inflammatory response at 7 days, while SIS-ECM induced the lowest inflammatory response at 14 days. Young's moduli value for 30% PHE6 P(1-VAL-8) was significantly higher vs. PP.

Timing of adverse effects: Nr

Factors that predicts response: NR

Source Citation: Zaworonkow et al. 2018[55]

Study Design: RCT

Device or Material: PP (Optomesh), no mesh, TiNI-based alloy mesh (TNM)

Route: Abdominal wall

Dose: 2.5 x 3.5 cm

Frequency/Duration: Single administration/ 14, 28, 56 and 90 days

Response: adhesions, hernia recurrence, implant dislocation, inflammatory response, stiffening of abdominal wall,

white blood cell count

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 20

Observations on adverse effects: White blood cell count (WBC) was significantly higher with PP compared to NM (no mesh) and TNM at days 7 and 14; infiltration of neutrophilic leukocytes concentrated around the mesh at day 14; distinguishable granulation tissue capsule around mesh. Rigidity of the abdominal wall, skin suture dehiscence (25%), implant dislocation due to growth and weight gain (30%), hernia recurrence (25%); omentum-to-implant adhesions (70%); intestinal adhesions (40%), significantly higher surgical complication rate compared to TNM at 3 months.

Timing of adverse effects: 7 to 90 days.

Factors that predicts response: growth and weight gain.

Source Citation: Ibrahim et al. 2017[56]

Study Design: RCT

Device or Material: Non-resorbable polypropylene mesh (Prolene)

Route: Subcutaneous implant

Dose: 2 cm-long cylinders

Frequency/Duration: Single administration/ 14, 30, 60, 90, and 180 days

Response: fibrous capsule formation, FBGC, inflammatory foreign body reaction

Species (strain): Mouse (C57BL/6)

Gender: Female

Number per Group: 15

Observations on adverse effects: Compared to polyvinyl alcohol, silicone, and expanded polytetrafluoroethylene, PP mesh had the thickest capsule on day 30, the highest number of macrophages at 30, 60, 90, and 180 days indicating a robust foreign body response, and the highest number of multinucleated giant cells at 180 days.

Timing of adverse effects: 30 to 80 days

Factors that predicts response: NR

Source Citation: Utrabo et al. 2017[57]

Study Design: Comparative

Device or Material: Prolene, Bard Soft®

Route: Ventral wall

Dose: g/m2: 100 Prolene, 44 Bard; 1 x 2 cm defect

Frequency/Duration: Single administration/ 30, 60 and 120 days

Response: resistance

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 10

Observations on adverse effects: No complications were reported. Greater resistance was shown with macroporous mesh versus microporous mesh.

Timing of adverse effects: n/a

Factors that predicts response: Pore size and weight.

Data Quality: n/a

Source Citation: Chan et al. 2016[58]

Study Design: RCT

Device or Material: HW-PP (Prolene)

Route: Abdominal wall

Dose: 4 x 4 cm

Frequency/Duration: Single administration/ 56 months

Response: FBGC, mesh fixation and contraction, stiffening of abdominal wall

Species (strain): Rabbit (New Zealand White)

Gender: NR

Number per Group: 5 animals in 3 groups

Observations on adverse effects: Skin and subcutaneous host tissue tethered to implant and grown into interstices of the mesh causing a rigid, inflexible implant area. Mesh contraction (24%) caused stiffening of the abdominal wall and distorted implant area. Layer of inflammatory cells surrounding mesh fibers, FBGCs adjacent to implant, and dis-organized collagen within spaces of the mesh filaments.

Timing of adverse effects: 56 months

Factors that predicts response: NR

Source Citation: De Maria et al. 2016[59]

Study Design: RCT

Device or Material: HW-PP, LW-PP

Route: Abdomen

Dose: g/m2: 48 LW-PP, 220; 2 x 2 cm

Frequency/Duration: Single administration/ 7 and 30 days

Response: inflammation, macrophages, mechanical behavior, multinucleated giant cells

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 6

Observations on adverse effects: Lower signs of inflammation and foreign body reaction (macrophages, multinucleated giant cells) with LW-PP at 30 days. The mechanical behavior of LW-PP is similar to human abdominal wall tissue.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Lambertz A. 2016[60]

Study Design: RCT

Device or Material: PP, polycarbonate-based thermoplastic urethane (TPU)

Route: Abdomen

Dose: 3 x 3 cm2

Frequency/Duration: Single administration/ 7 and 21 days

Response: adhesions, apoptotic cells, CD68, collagen type I/III ratio, foreign body granulomas,

Ki67

Species (strain): Rabbit (New Zealand White)

Gender: Female

Number per Group: 8

Observations on adverse effects: Significantly more adhesions (at both follow-ups), and smaller outer granuloma sizes (at 21 days) with PP. No significant differences were reported in immunohistochemical observations (inflammatory cells (CD68), proliferating cells (Ki67), and apoptotic cells)), or collagen type I/III ratio. Elastic properties of TPU mesh remained at 7 and 21 days.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Garcia-Moreno et al. 2015[61]

Study Design: Comparative

Device or Material: 2 PP composites (Ventralex, Proceed), non-PP composite (Parietex)

Route: Ventral hernia

Dose: 1.5 cm diameter

Frequency/Duration: Single administration/ 2 weeks, 6 weeks, 6 months

Response: collagen I, foam cells, macrophages, multinucleated FBGC, seroma

Species (strain): Rabbit (New Zealand White)

Gender: Male

Number per Group: 6

Observations on adverse effects: Results with Proceed included significantly higher adhesion formation up to 6 weeks, and most intense macrophage response at 2 weeks and 6 months.

Earlier complications: Seroma was detected in 17% Ventralex, 67% Proceed, and 28% Parietex implants. Late complications (6 months): macrophages, multinucleated foreign-body giant cells, and foam cells were detected in Ventralex implants, macrophages were detected in Parietex implants, collagen I expression increased gradually for all implant groups, macrophages labeled with RAM-11 monoclonal antibody were detected in Ventralex and Parietex implants; significantly lower than Proceed, Parietex showed the best anti-adhesive properties at all time points.

Timing of adverse effects: NR

Factors that predicts response: Implant deployment mechanism with Parietex.

Source Citation: Mazroa et al. 2015[62]

Study Design: RCT

Device or Material: PP (Euromesh)

Route: Anterior abdominal wall

Dose: 0.5 x 0.5 cm

Frequency/Duration: Single administration/ 4 weeks

Response: FBGC, irregularly arranged collagen fibers, lymphocyte infiltration, macrophage count

Species (strain): Rat (albino)

Gender: Male

Number per Group: 10

Observations on adverse effects: The inflammatory reaction (e.g., increased mean number of lymphocytes and macrophages) with PP mesh was significantly higher vs. controls.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Fan et al. 2014[63]

Study Design: RCT

Device or Material: Polypropylene mesh

Route: Implanted in vagina and abdomen

Dose: Gynemesh

Frequency/Duration: Single administration, 12 weeks indwelling

Response: erosion, inflammation degree, necrosis

Species (strain): New Zealand white

Gender: Female

Number per Group: 20

Observations on adverse effects: Placement of vaginal PP resulted in a moderate-to-severe inflammatory response (including necrosis) and higher inflammation scores vs. other subgroups (vaginal cUBM, abdomen cUBM, abdomen PP). Erosion occurred in 8/12 (67%) rats with vaginal Gynemesh.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: García-Moreno et al. 2014[64]

Study Design: RCT

Device or Material: 2 PP composites (Ventralex, Proceed), non-PP composite (Parietex)

Route: Umbilical hernia

Dose: 1.5 x 1.5 cm

Frequency/Duration: Single administration/ 2 and 6 weeks

Response: visceral adhesion formation

Species (strain): Rabbit (New Zealand White)

Gender: Male

Number per Group: 18 (9 per time period)

Observations on adverse effects: Omental adhesions between mesh and parietal peritoneum present at 2 weeks (n=3) and 6 weeks (n=3); subcutaneous seroma (n=1); loose and disorganized connective tissue surrounding filaments at 6 weeks.

Timing of adverse effects: 2 to 6 weeks

Factors that predicts response: NR

Source Citation: Jerabek et al. 2014[65]

Study Design: RCT

Device or Material: Two LW-PP and one HW-PP (pore sizes: 3 [PP3], 1 [PP1], and .5 mm [PP.5])

Route: Abdominal hernia

Dose: g/m2: 47 PP3, 40 PP1, 81 PP.5; 10 x 10 cm

Frequency/Duration: Single administration/ 90 days

Response: chronic inflammatory reaction, foreign body granuloma, shrinkage

Species (strain): Rabbit (New Zealand White)

Gender: NR

Number per Group: 7

Observations on adverse effects: Temporary seromas were present in two pigs in the PP.5 group and two in the PP1 group, one which became infected. Mesh shrinkage was observed in all groups, with the PP3 group having significantly less shrinkage compared to the PP1 and PP.5 groups, which had similar shrinkage. Lower shrinkage may contribute to reduced rates of hernia recurrence. PP3 was significantly more elastic than PP.5, however, the higher elasticity is lost once the mesh structure is fixed in the connective tissue. Lymphocytes and macrophages were significantly higher in PP3 than PP.5. Both inner and outer width of foreign body granulomas were decreased as pore size increased. At the mesh-tissue interface, PP3 showed better biocompatibility compared to both PP1 and PP.5, and PP1 showed better biocompatibility compared to PP.5.

Timing of adverse effects: 90 days

Factors that predicts response: pore size

Source Citation: Karabulut et al. 2014[66]

Study Design: Case control

Device or Material: Polypropylene mesh

Route: Implanted in vagina and abdomen

Dose: Atrium®

Frequency/Duration: Single administration, 9 weeks indwelling

Response: fibrosis, foreign body type reaction, granulocyte, inflammation degree, lymphocyte, macrophages, mast cells, necrosis

Species (strain): Wistar albino rats

Gender: Female

Number per Group: 37 (10 each control, menopause, steroid + menopause; 7 DM plus menopause).

Observations on adverse effects: Mesh at the abdominal region had more intense granulocyte infiltration while mesh at the vaginal region showed more prominent inflammation and necrosis.

Timing of adverse effects: NR

Factors that predicts response: Menopause increased tissue response, while steroid use reduced the response.

Source Citation: Müller-Stich B. 2014[67]

Study Design: RCT

Device or Material: PP (Prolene), PET (Parietex STD), PTFE (GORE INFINIT)

Route: Esophageal hiatus

Dose: g/m2: 85 PP, 116 PET, 70 PTFE; 55 x 55-mm with a 16.5 mm eccentric hole

Frequency/Duration: Single administration/ 8 weeks

Response: collagen I, collagen I/III ratio, collagen III, foreign body reaction , Ki-67 staining , mononuclear cell count

shrinkage

Species (strain): Pig (landrace)

Gender: NR

Number per Group: 8

Observations on adverse effects: All 3 mesh types produced a chronic inflammatory reaction with no significant differences for mononuclear cell count, Ki-67 positive cells, collagen I, collagen III and collagen I/III ratio. PTFE was associated with highest mesh shrinkage (34.9% PTFE, 19.8 PP vs. 12.1 PET) and correlating enlargement of the aperture for the esophagus (100.8% PTFE, 47.0 PP, 35.9 PET).

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Senft et al. 2014[68]

Study Design: RCT

Device or Material: HW-PP (small and large-porous), and LW-PP (large-porous)

Route: Esophageal hiatal hernia

Dose: g/m2: 85 Surgipro, 75 and 38 Parietene; Circular

Frequency/Duration: Single administration/ 8 weeks

Response: adhesion formation, chronic inflammatory reaction, mesh shrinkage

Species (strain): Pig (Landrace)

Gender: NR

Number per Group: 8

Observations on adverse effects: There were signs of chronic inflammatory reaction within all groups, with less inflammatory activity observed with the light-weight large porous (LW-LP) mesh, providing evidence that reducing mesh weight may be associated with higher biocompatibility. Mesh shrinkage was present within all groups and was the highest for LW-LP mesh (25.5%). Large pore size was associated with the best form stability. Small pore size had superior tissue integration, which may prevent mesh migration. Solid adhesions covering large parts of the mesh area were present with heavy-weight small porous (HW-SP) and heavy-weight large porous (HW-LP) mesh, while there were significantly fewer adhesions with LW-LP mesh. Solid fixation of the esophagogastric junction by adhesions may contribute to a reduction of hernia recurrence.

Timing of adverse effects: 8 weeks

Factors that predicts response: mesh weight, pore size.

Source Citation: Xu et al. 2014[69]

Study Design: RCT

Device or Material: HW and LW monofilament non-resorbable PP, ePFTE

Route: Hernia repair surrounding the vas deferens and spermatic vessels

Dose: NR

Frequency/Duration: Single administration/90 days

Response: abnormal spermatogenesis process, decreased sperm motility, dense adhesion formation, increased anti-sperm antibodies

Species (strain): Rat (Sprague-Dawley)

Gender: Male

Number per Group: 8

Observations on adverse effects: HW- and LW-PP produced dense adhesions to the spermatic cord on greater than 50% of the mesh area at 3 months compared to the thin adhesions produced e-PTFE on less than 25% of the mesh area. An abnormal spermatogenesis process was found in rats implanted with PP mesh (including congestion of necrotic tissue in the seminiferous tubules, damaged germinal epithelium, and reduced spermatogenic cell layers). There was a significant increase in levels of anti-sperm antibodies (AsAbs) and hypoxia-inducible factor-1α (HIF-1α), as well as significantly decreased sperm motility.

Timing of adverse effects: 3 months

Factors that predicts response: NR

Source Citation: Bryan et al. 2013[70]

Study Design: RCT

Device or Material: Commercial monofilament and multifilament, and experimental monofilament light PP.

Route: Subcutaneous implant

Dose: g/m2: 35-140 PP, 70-140 PGA, 35-70 PET; 1 x 1 cm

Frequency/Duration: Single administration/ 2, 5, 7, 14 and 28 days

Response: FBGC, inflammatory response

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 16

Observations on adverse effects: Macrophages present at 48 hours and persistent at 28 days. FBGCs present at 5 days in multifilament mesh and largely absent in monofilament mesh. Mesh surrounded by fibrous tissue at 28 days. Material weight (heavy vs. light) was not found to be a determining factor in host foreign body response.

Timing of adverse effects: 2 to 28 days

Factors that predicts response: filament type, time in vivo

Source Citation: Ditzel M. 2013[71]

Study Design: RCT

Device or Material: PP (Prolene), composite (Parietex), porcine dermis (Strattice, Permacol), small intestinal submucosa (Surgisis)

Route: Incisional hernia

Dose: 2.5 x 3.5 cm

Frequency/Duration: Single administration/30 and 90 days

Response: adhesion coverage, giant cells, lymphocytes, poor mesh incorporation, shrinkage

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 30 days (10 per group), 90 days (7 per group).

Observations on adverse effects: Adhesion formation was significantly reduced at 90 days (vs. 30 days) with Prolene, Strattice, and Permacol. No significant differences were reported for mesh incorporation or shrinkage between mesh.

Timing of adverse effects: Adhesions and shrinkage were noted at 30 and 90 days.

Factors that predicts response: NR

Source Citation: Fan et al. 2013[72]

Study Design: RCT

Device or Material: PP (Gynemesh), porcine UBM (UBM), cross-linked UBM

Route: Abdominal wall

Dose: 1 x 1 cm

Frequency/Duration: Single administration/ 1, 2, 4, 8 and 12 weeks

Response: lymphocytes, macrophages, mRNA expression, plasma cells

Species (strain): Rabbit (New Zealand White)

Gender: Female

Number per Group: 15

Observations on adverse effects: The inflammatory response ranged from a very mild to mild response across groups. mRNA expression levels (IFN-y, IL-2, IL-4, and IL-10) of cross-linked UBM were similar to sham indicating the lowest immunogenic response. Cross-linked UBM showed slow degradation.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Lamber et al. 2013[73]

Study Design: RCT

Device or Material: PP (Marlex), no implant, Parietex Composite

Route: Incisional hernia

Dose: 2 x 2 cm

Frequency/Duration: Single administration/ 21 days

Response: adhesion coverage, number of adhesions

Species (strain): Rat (Wistar)

Gender: Female

Number per Group: 10 (PP, Parietex Composite). 5 (sham).

Observations on adverse effects: Adhesions developing from PP mesh were detected in the center of the mesh and adhered to 30% to 100% of surfaces of the omentum, liver, small intestine, and round ligament of the liver.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Pascual et al. 2013[74]

Study Design: Comparative

Device or Material: LW-PP (Optilene), LW-PTFE (Infinit)

Route: Abdominal wall

Dose: g/m2: 48 Optilene, 70 Infinit; 4 x 4 cm

Frequency/Duration: Single administration/14 days

Response: collagen I/III mRNA expression, macrophage cells, multinucleated FBGC, shrinkage

Species (strain): Rabbit (New Zealand White)

Gender: Male

Number per Group: 8

Observations on adverse effects: Use of PTFE resulted in seroma in 2 implants, a significantly higher macrophage count, significantly greater shrinkage, but no significant difference in collagen I and III mRNA expression patterns (vs. PP).

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Dolce et al. 2012[75]

Study Design: RCT

Device or Material: Novel polypropylene/polylactide composite mesh, PROCEED, ePTFE (DualMesh), Parietex Composite

Route: Abdominal wall

Dose: 4 x 2 cm

Frequency/Duration: Single administration/1, 4, and 16 weeks

Response: stiffness, visceral adhesion formation

Species (strain): Rabbit (New Zealand White)

Gender: NR

Number per Group: 18

Observations on adverse effects: Polypropylene/polylactide mesh led to more adhesions compared to Parietex Composite mesh. No differences in stiffness of mesh or tissue, amount of inflammatory cells or percent of mesothelialization compared to Paritex Composite, Proceed, and DualMesh.

Timing of adverse effects: 4 weeks

Factors that predicts response: NR

Source Citation: Hjort et al. 2012[76]

Study Design: RCT

Device or Material: Non-resorbable PP mesh vs long-term resorbable test mesh (TIGR)

Route: Abdominal wall repair and soft tissue reinforcement

Dose: 8 x 8 cm

Frequency/Duration: Single administration/ 4, 9, 15, 24 and 36 months

Response: chronic inflammatory response, degradation, foreign body granuloma

Species (strain): Sheep (NR)

Gender: Female

Number per Group: 14 (10 received polypropylene mesh).

Observations on adverse effects: Abdominal swelling post-surgery (n=8); chronic inflammatory reaction at the site of the PP mesh at all time periods, including phagocytotic cells infiltrating the mesh, fibroplasia, mature collagen between the fibers and encapsulating the mesh, and foreign-body granulomas surrounding the fibers. At 24 and 36 months, the PP mesh remained stiff and not well integrated. No local adverse effects were observed macroscopically. No sign of material alteration or degradation at 36 months.

Timing of adverse effects: NR

Factors that predicts response: Not reported

Source Citation: Huber et al. 2012[77]

Study Design: Meta analysis

Device or Material: PP, non-PP polymers (non-PP), and natural mesh

Route: Soft tissue repair of abdominal wall

Dose: NR

Frequency/Duration: NR, median endpoint: 28 days post-implant

Response: adhesion grade response, cell proliferation , inflammation grade response, monocyte/macrophage infiltration, shrinkage

Species (strain): mostly rats, pigs, and rabbits.

Gender: NR

Number of studies for inflammation grade response of tissue to device: mostly rats, pigs, and rabbits.

Observations on adverse effects: No significant difference in inflammation grade response with PP vs. natural or non-PP.

Number of studies for adhesion grade response of Tissue to Device: 13 PP vs. natural, 7 PP vs. non-PP.

Observations on adverse effects: Significantly reduced grade of adhesion with natural devices vs PP.

Number of studies for proliferation response of tissue to device: 14 PP vs. non-PP.

Observations on adverse effects: No significant difference in amount of cell proliferation.

Number of studies for monocyte/macrophage infiltration to device: 25 PP vs. non-PP, 20 PP vs. natural

Observations on adverse effects: Non-PP had significantly less monocyte/macrophage infiltration vs. PP. No significant difference between PP and natural mesh.

Number of studies for area shrinkage response of tissue to device: 9 PP vs. non-PP

Observations on adverse effects: Significantly more shrinkage with non-PP vs. PP.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Novotny et al. 2012[78]

Study Design: RCT

Device or Material: LW-PP (Mesh Extra Large Pore), PTFE Mesh

Route: Intraabdominal implant

Dose: g/m2: 47 PP, 44 PTFE; 5 x 5 cm

Frequency/Duration: Single administration/ 90 days

Response: adhesion coverage, adhesion score, fibrous tissue, granulocyte count, lymphocyte count, macrophage count

shrinkage

Species (strain): Rabbits (New Zealand White)

Gender:

Number per Group: 14

Observations on adverse effects: Average area covered with adhesions and overall adhesion score were significantly lower with PTFE. Histologic results indicated significantly less fibrous tissue induced by the mesh (outer layer) with PTFE, slightly more macrophages and lymphoctyes with PTFE, and low granulocyte count in both groups. More shrinkage with PTFE (36.9±12.0% vs. 12.6±8.72%).

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Orenstein et al. 2012[79]

Study Design: Comparative

Device or Material: Polyester (Parietex), HW-PP (Trelex), MWPP (ProLite), LW-PP composite (ULTRAPRO), ePTFE (DualMesh)

Route: Hernia repair

Dose: g/m2: 95 Trelex, 85 ProLite, 28 UltraPro, 78 Parietex, solid laminar sheet DualMesh; 5-mm piece

Frequency/Duration: Single administration/ 4 and 12 weeks

Response: Fibrosis, foreign body reaction, inflammation

Species (strain): Mice (C57BL/6J)

Gender: NR

Number per Group: 6

Observations on adverse effects: Overall, Parietex had the greatest inflammatory response. Fibrosis and foreign body reaction from highest to lowest at both follow-ups: Parietex, DualMesh, Trelex, ProLite, ULTRAPRO

Timing of adverse effects: NR

Factors that predicts response: material composition

Source Citation: Pascual et al. 2012[80]

Study Design: Comparative

Device or Material: HW-PP (Surgipro), LW-PP (Optilene), and PTFE (Infinit)

Route: Abdominal wall

Dose: g/m2: 85 Surgipro, 48 Optilene, 70 Infinit; 4 x 4 cm

Frequency/Duration: Single administration / 90 and 180 days

Response: macrophage cells, mechanical properties, mRNA translation, multinucleated foreign-body giant cells, seroma

Species (strain): Rabbit (New Zealand White)

Gender: Male

Number per Group: 12

Observations on adverse effects: Use of PTFE resulted in the highest macrophage count up to 180 days with seroma in 2 implants. LW-PP had the most efficient collagen I and III mRNA translation. Similar tensile strength and elastic modulus values were reported up to 180 days.

Timing of adverse effects: Seroma at 14 days

Factors that predicts response: NR

Source Citation: Pascual et al. 2012[81]

Study Design: Comparative

Device or Material: HW-PP: Surgipro , LW-PP: Parietene, ULTRAPRO, Optilene Elastic

Route: Abdominal wall repair

Dose: g/m2: Surgipro (85), Parietene (38), ULTRAPRO (28), Optilene Elastic (48); 7 x 5 cm

Frequency/Duration: Single administration/14 days

Response: FBGC, inflammation, macrophages

Species (strain): Rabbit (New Zealand White)

Gender: Male

Number per Group: 6

Observations on adverse effects: A more intense inflammatory reaction was noted with a partially absorbable LWM (ULTRAPRO).

Timing of adverse effects: NR

Factors that predicts response: presence of absorbable material

Source Citation: Anurov et al. 2011[82]

Study Design: RCT

Device or Material: Light and standard wrap-knitted monofilament PP mesh (Parietene Standard and Light; Premilene and Optilene LP)

Route: Abdominal hernia

Dose: 10 x 10 cm

Frequency/Duration: Single administration/ 6 months

Response: deformation of implant, FBGC, fistula, foreign body inflammatory reaction, hemorrhage

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 5

Observations on adverse effects: Light mesh: The light mesh showed pronounced deformation of the implant leading to displacement of the lower edge of the mesh. Hernia was present in 3 rats in the Parietene L group and 2 rats in the Optilene LP group. Light mesh implants led to numerous, sometimes extensive hemorrhages, and a more pronounced foreign body inflammatory reaction compared to the standard mesh. FBGCs found around Parietene L mesh. Standard mesh: Standard mesh showed more pronounced inflammation 3 to 4 weeks post-operatively. Extensive destruction of the transverse fascia and peritoneum covered with hypertrophied omentum was found in 1 rat in the Parietene S group. Ligature fistula at the lower edge of the mesh was found in 1 rat in the Premilene group.

Timing of adverse effects: 6 months

Factors that predicts response: weave structure

Source Citation: Klink et al. 2011[83]

Study Design: RCT

Device or Material: PP, PVDF

Route: Abdominal wall hernia

Dose: m2/m2: 1.1 PP, 2.0 PVDF; 1 x 1 mesh

Frequency/Duration: Single administration/ 7 days, 6 months

Response: CD8 expression, COX2 expression, granuloma size

Species (strain): Rat (Wistar)

Gender: Male

Number per Group: 14

Observations on adverse effects: Significantly smaller granumola sizes with PVDF at both follow-ups. Immunohistochemical observations at 7 days included significantly higher CD68 expression with PVDF, and significantly higher COX-2 expression with PP.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Melman et al. 2011[84]

Study Design: RCT

Device or Material: HW-PP (Bard®), LW-PP composite (ULTRAPRO) vs. mkPTFE (GORE® INFINIT)

Route: Hernia

Dose: 8 x 10 cm

Frequency/Duration: Single administration/ 1, 3, 5 months

Response: fibrosis, focal hemorrhage, inflammatory response, lymphocytes, macrophages, multinucleated giant cells

shrinkage

Species (strain): Mini pig (Yucatan)

Gender: Female

Number per Group: 9 each time point

Observations on adverse effects: Edges of HW-PP mesh appeared distorted (rolled edges). No significant differences were reported in inflammation, fibrosis, tissue ingrowth, shrinkage, or overall response scores between mesh.

Timing of adverse effects: 1 month in HW-PP: macrophages, lymphocytes, multinucleated giant cells, some focal hemorrhage: 3 months with HW-PP: macrophages, lymphocytes, minimal focal hemorrhage, plus fibrosis near mesh fibers.

Factors that predicts response: NR

Source Citation: Arslani et al. 2010[42]

Study Design: RCT

Device or Material: PP mesh

Route: Implant

Dose: 1 sheet (2 x 1.5 cm) of polypropylene mesh (PPM) or dual component fibrin mesh (DCFM)

Frequency/Duration: Single administration, 30 day indwelling

Response: Inflammation degree, Fibrous tissue diameter

Species (strain): Fischer rats

Gender: 51% male

Number per Group: 40 PPM, 38 DCFM

Observations on adverse effects: PPM significantly more likely than DCFM to have high degree of inflammation and thin fibrous tissue diameter.

Timing of adverse effects: NR

Factors that predicts response: NR

Source Citation: Torres-Villalobos et al. 2010[85]

Study Design: Case series

Device or Material: PP mesh with self-expanding Nitinol frame (Rebound)

Route: Abdominal hernia repair

Dose: g/m2: 52

Frequency/Duration: Single administration/90 days

Response: FBGC, inflammatory foreign body reaction

Species (strain): Pig (NR)

Gender: Female

Number per Group: 3

Observations on adverse effects: 3 band-adhesions (2 to the urinary bladder and 1 to the spiral colon). Mesh embedded in thick mature fibrous tissue (up to 4 mm thick). Fibrogranulomatous reaction with a layer of histiocytes and multinucleated giant cells adjacent to the mesh.

Timing of adverse effects: 90 days

Factors that predicts response: size of mesh pores.

Source Citation: Voskerician et al. 2010[86]

Study Design: Comparative

Device or Material: PP (Prolene), compressed PTFE (MotifMESH), expanded PTFE (DualMesh), PET + C (Parietex Composite), and SIS (Surgisis)

Route: Abdominal hernia repair

Dose: 1.5 x 2.5 cm

Frequency/Duration: Single administration/30 days

Response: adhesions, inflammatory response, pus, seroma

Species (strain): Rat (Sprague-Dawley)

Gender: Female

Number per Group: 5

Observations on adverse effects: cPTFE produced a significantly reduced inflammatory and wound healing response vs. all other materials. A significant seroma was detected with PET + C mesh, while “frank pus” was reported in 66% of SIS mesh.

Timing of adverse effects: NR

Factors that predicts response: NR

cPTFE: compressed PTFE; cUBM: cross-linked urinary bladder matrix; DM: diabetes mellitus; ePTFE: expanded PTFE; FBGC: foreign body giant cell; HWM: heavy weight mesh; HW-PP: heavy weight polypropylene; LWM: light weight mesh; LW-PP: low-weight polypropylene; mkPTFE: monofilament knit polytetrafluoroethylene; MWPP: mid-weight polypropylene; n/a: not applicable; NR: not reported; PET: polyethyleneterephthalate; PET + C: polyethyleneterephthalate + collagen; PEU: poly(ester

urea); PGA: polyglycolic acid; PP: polypropylene; PTFE: polytetrafluoroethylene; PVDF: polyvinylidenefluoride; RCT: randomized controlled trial; SIS: small intestine submucosa; SIS-ECM: small intestine submucosa extracellular matrix; SW-PP: standard weight polypropylene; UBM: urinary bladder matrix.

Table 11: Prolapse Mesh, Transvaginal – Health Effect (In Vivo) Human Studies

Local Response/Toxicity

Source Citation: Campagna et al. 2020[87]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: NR

Dose: 35 g/m2 Timsesh®

Frequency/Duration: Single administration

Response: de novo dyspareunia, mesh exposure, umbilical hernia, vaginal bleeding, vaginal discomfort

Patient characteristics (gender, mean age): 100% female. 65.4 years.

Number per group: 217 with stage II-IV POP

Observations on adverse effects: Mesh exposure only occurred in women undergoing incidental colpotomy. Complications (12 months follow-up): 3 (1.4%) mesh exposure, 2 (0.9%) umbilical hernia, 19 (8.7%) nonspontaneous, vaginal discomfort (persisted for 12 months), 2 de novo dyspareunia

Timing of adverse effects: : In 3 women with mesh exposure: vaginal bleeding occurred at 1, 2, and 4 months; spontaneous vaginal pain occurred at 1 and 4 months (n=2), dyspareunia occurred at 2 months (n=1).

Factors that predict response: Mesh exposure was associated with incidental colpotomy.

Source Citation: Campagna et al. 2020[88]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: median months follow-up:14 (12 to 36)

Dose: Restorelle XL

Frequency/Duration: Single administration of Restorelle, previous administration of Calistar and Prolift

Response: mesh erosion, excessive fibrosis

Patient characteristics (gender, mean age): 100% female. 61 years (40 to 75)

Number per group: 20 with POP. recurrence.

Observations on adverse effects: Use of Restorelle XL did not cause any mesh-related complications. Complications: 2 (10%) patients with previous applications of a Calistar and Prolift anterior mesh were affected by anterior vaginal mesh erosion. Excessive fibrosis was reported from previous mesh.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Gillor et al. 2020[89]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: median years follow-up: 3.87

Dose: Uphold™

Frequency/Duration: Single administration

Response: chronic pelvic pain, dyspareunia, mesh exposure

Patient characteristics (gender, mean age): 100% female. 64±10 years.

Number per group: 82 with anterior vaginal wall prolapse ≥ stage 2 POP-Q.

Observations on adverse effects: Chronic pelvic pain and mesh exposure occurred in 5% of patients undergoing prolapse repair with Uphold. Complications: 9 (11%) dyspareunia, 4 (5%) chronic pelvic pain, 4 (5%) mesh exposure.

Timing of adverse effects: NR

Factors that predict response: Nr

Source Citation: Tamanini et al. (2013)[90] , Tamanini et al. (2020)[91]

Study Design: RCT

Device or Material: PP mesh vs no mesh

Contact Duration: 5 years

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure, Slight inguinal pain

Patient characteristics (gender, mean age): all female, mean age 67

Number per group: 43 at 1 yr, 33 at 5 yrs

Observations on adverse effects: Exposure 4 within 1 yr, 2 at 5 yrs. Slight inguinal pain 5

Timing of adverse effects: exposure 0-5 years, slight inguinal pain 2 months.

Factors that predict response: NR

Source Citation: Tsai et al. 2020[92]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 12 months follow-up

Dose: ALYTE (20 g/m2)

Frequency/Duration: Single administration

Response: de novo stress incontinence, de novo urgency incontinence, PID

Patient characteristics (gender, mean age): 100% female. 52.7 (range 33-67) years.

Number per group: 34 with advanced POP-Q stage ≥2.

Observations on adverse effects: De novo symptoms were reported in 4 (12%) patients. Complications: 1 (5.9%) PID, 2/11 (18.2%) de novo stress incontinence, 2 (11.2%) de novo urgency incontinence

Timing of adverse effects: NR

Factors that predict response: Multivariate analysis did not identify factors associated with response.

Source Citation: Dwyer et al. 2019[93]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: median months follow-up: 34 (range 1 to 94)

Dose: Restorelle (19 g/m2)

Frequency/Duration: Single administration

Response: de novo dyspareunia, mesh extrusion, worsening dyspareunia

Patient characteristics (gender, mean age): 100% female. 61±10.3 years.

Number per group: 156 with prolapse.

Observations on adverse effects: 1 mesh extrusion occurred at 40 months with an ultra-lightweight mesh.
Complications: 1 mesh extrusion, 1 worsening dyspareunia, 2 (6.5%) de novo dyspareunia

Timing of adverse effects: : extrusion at 40 months

Factors that predict response: NR

Source Citation: Tennyson et al. 2019[94]

Study Design: Case control

Device or Material: PP mesh

Contact Duration: 1-144 months exposed

Dose: NR*

Frequency/Duration: Single administration

Response: fibroma, increased T cells, T cells located away from mesh-tissue interface., increased TGF-B and CTGF,

thick collagen fibers

Patient characteristics (gender, mean age): 100% female. 52.92±12.38 mesh exposure, 49±11.88 pain

Number per group: 42 with mesh complications due to pain (n=18) or exposure (n=24), 21 controls undergoing additional vaginal biopsy away from site of mesh.

Observations on adverse effects: From 1 to 144 months, T cells were significantly higher in women with mesh complications (exposure and pain) vs. Controls. Fibromas encapsulating mesh fibers were present in both pain and exposure groups. T cells were distinctly located at the "cap" away from the mesh-tissue interface. T-cell populations (CD4+ T helper, and foxp3+ T regulatory) were significantly increased in 42 patients with mesh complications (exposure and pain) vs. Controls. CD8+ cytotoxic T cells were significantly higher in exposure group vs. controls and pain group. Collagen type 1 was significantly increased (+35%) in individuals with mesh complications vs control. TGF-B and CTGF were significantly higher with mesh complications vs. Controls. CTGF was moderately-to-highly correlated with CD4, CD8, and foxp3. A positive correlation between thicker collagen fibers and length of mesh implantation was noted.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Wang et al. 2019[95]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: at least 1.5 year follow-up

Dose: Dynamesh, Gynecare Gynemesh

Frequency/Duration: Single administration

Response: mesh exposure, pain

Patient characteristics (gender, mean age): 100% female. 58±1.6 SIS (n=26), 59±0.9 TVM (n=50).

Number per group: 76 with advanced POP.

Observations on adverse effects: Mesh exposure was significantly higher with SIS graft. Complications: 13 mesh exposures (significantly higher with SIS: 8 vs 5), 4 (15.4) pain with SIS graft, 11 blunt pelvic pain with TVM.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Balsamo et al. 2018[96]

Study Design: Case control

Device or Material: PP mesh vs PVDF mesh

Contact Duration: mean months follow-up: 94±17.3

Dose: 39±3 g/m2

Frequency/Duration: Single administration, Response: mesh exposure, storage symptoms, sexual dysfunction

Patient characteristics (gender, mean age): 100% female. 68.97±10.11 years (PP).

Number per group: 136 with POP (73 PP, 63 PVDF)

Observations on adverse effects: Complications: 3 mesh exposure (1 PP, 2 PVDF), 6 (8.2%) storage symptoms in PP vs 0 in PVDF (p=0.02), sexual dysfunction (12 in PP group, 0 in PVDF group, p = 0.0001).

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Durst and Heit 2018[97]

Study Design: Case control

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 38.6±33.4

Dose: Restorelle (19 g/m2), ULTRAPRO (28 g/m2),Prolene Soft (45 g/m2)Atrium (90 g/m2), Prolene (109 g/m2)

Frequency/Duration: Single administration

Response: mesh exposure

Patient characteristics (gender, mean age): 100% female. 58.7±10.7

Number per group: 133 with mesh exposure.

Observations on adverse effects: Prior surgery for incontinence was associated with mesh exposure.

Timing of adverse effects: NR

Factors that predict response: Prior surgery for incontinence was significantly associated with mesh exposure.

Source Citation: Cheng et al. 2017[98]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 5 (range 1 to 84)

Dose: Apogee, Elevate, GYNEMESH, Perigee, ProLift, PROSIMA

Frequency/Duration: Single administration

Response: Mesh erosion, Recurrent erosion

Patient characteristics (gender, mean age): 100% female, 63 years.

Number per group: 750 with vaginal mesh repair for symptomatic ≥ stage II POP-Q (741 from an original cohort, 9 referrals with erosion).

Observations on adverse effects: Data on mesh type for 47 erosions indicated the following: 40% with Elevate, 32% with ProLift, and 32% with other mesh types (e.g., GYNEMESH, PROSIMA, Apogee, Perigee). Recurrent erosions occurred in 6 patients. Complications: 56 mesh erosions, 6 recurrent erosions

Timing of adverse effects: NR

Factors that predict response: Multivariate analysis indicated that concomitant hysterectomy (OR 27.02, 95% CI: 12.35 to 58.82) and hypertension (OR 5.95, 95% CI: 2.43 to 14.49) were significantly associated with mesh erosion.

Source Citation: Thomas et al. (2017)[99]

Study Design: SR (17 animal, 6 human)

Device or Material: PP mesh

Contact Duration: 4 days to 7.8 years

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Inflammatory response in numerous studies.

Patient characteristics (gender, mean age): all female, age NR

Number per group: 24 to 209

Observations on adverse effects: Authors stated that "PP mesh elicits an inflammatory response that decreases over time; however, no studies documented a complete resolution."

Timing of adverse effects: various

Factors that predict response: NR

Source Citation: Meyer et al. 2016[100]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Mean years follow-up: 7.0±0.7

Dose: ProLift

Frequency/Duration: Single administration

Response: Mesh exposure, Fever, Vaginal tenderness, Vaginal stricture

Patient characteristics (gender, mean age): 100% female, 60.3±9.3 years.

Number per group: 70 with stage I or II POP

Observations on adverse effects: 21 patients complained of vaginal tenderness from ProLift transvaginal mesh. Complications: 3 (6%) mesh exposure, 2 (3%) fever, 4 (8.5%) tenderness in distal vagina, 5 (10.6%) tenderness in middle vagina, 12 (25.5%) tenderness in proximal vagina, 1 (2.1%) vaginal stricture in the proximal vagina

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Nolfi et al. 2016[101]

Study Design: Case control

Device or Material: PP mesh

Contact Duration: Mean months implanted: 36.9±30.3 mesh exposure (n=15), 30.9±18 pain (n=12

Dose: Manufacturers: AMS, Bard, Boston Scientific, Caldera, Coloplast, and Ethicon

Frequency/Duration: NR

Response: Degradation, Exposure, Fibrosis, Inflammation, Pain

Patient characteristics (gender, mean age): 100% female, 52 to 56 years.

Number per group: 27 mesh (15 incontinence mild urethral slings, 12 prolapse); 30 mesh naïve with stage II or III prolapse.

Observations on adverse effects: Mesh explants contained significantly higher cytokines/chemokines (including M1, M2, TNF-a, Interleukin-4), and MMP-9 (pro- and active) and MMP-2 (active) proteolytic enzymes vs. mesh-naïve explants.

Timing of adverse effects: 4.5 to 93 months.

Factors that predict response: NR

Source Citation: Song et al. 2016[102]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 40.4 (range 12 to 63)

Dose: ProLift

Frequency/Duration: Single administration

Response: De novo incontinence, Dyspareunia, Mesh erosion, Pelvic pain, Urinary retention

Patient characteristics (gender, mean age): 100% female, 61.6±9.8.

Number per group: 163 with POP

Observations on adverse effects: De novo incontinence and mesh erosion occurred in 13.5% and 3.1% of patients, respectively. Complications: 2 (1.2%) urinary retention, 4 (2.5%) pelvic pain, 22 (13.5%) de novo incontinence, 5 (3.1%) mesh erosion, 7 (4.3%) dyspareunia.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Arora et al. 2015[103]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 53.4 (range 12 to 104 months)

Dose: Custom bell-shaped Prolene mesh

Frequency/Duration: Single administration

Response: Dyspareunia, Urinary retention

Patient characteristics (gender, mean age): 100% female, 58.5±6.2 years

Number per group: 36 with ≥stage 2 POP-Q

Observations on adverse effects: Dyspareunia occurred at 2 years and 5 years in 7 patients. Early complications: 2 urinary retention <1 week Late complications: 7 dyspareunia

Timing of adverse effects: Dyspareunia occurred at 2 years and 5 years

Factors that predict response: NR

Source Citation: Balchandra et al. 2015[104]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median months follow-up: 28 (range 1 to 48)

Dose: NR

Frequency/Duration: Single administration

Response: De novo SUI, Infective vaginal discharge, Mesh exposure

Patient characteristics (gender, mean age): 100% female. 62 years

Number per group: 159 with POP

Observations on adverse effects: Mesh exposure and de novo SUI occurred in 4% and 7% of patients, respectively. Complications: 6 (4%) mesh exposure, 10 (7%) de novo SUI, 2 infective vaginal discharge

Timing of adverse effects: NR

Factors that predict response: Smoking was associated with exposure in 1 patient.

Source Citation: de Tayrac et al. 2015[105]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: 36 months follow-up

Dose: SURGIMESH (28 g/m2)

Frequency/Duration: Single administration

Response: De novo dyspareunia, Mesh exposure, Pain

Patient characteristics (gender, mean age): 100% female. 67±9 years

Number per group: 111 with stage III/IV POP.

Observations on adverse effects: Mesh exposure in 1 patient was detected at 3-year exam. Complications prior to 36 months: 3 (3.2%) pain, 7/92 (7.6%) spontaneous pain, 2/90 (2.2%) induced pain at exam. Complications at 36 months): 1 (1.3%) mesh exposure, 1 (2.8%) de novo dyspareunia.

Timing of adverse effects: pain 3 days postoperatively

Factors that predict response: NR

Source Citation: Rudnicki et al. (2015)[106]

Study Design: RCT

Device or Material: PP mesh vs no mesh

Contact Duration: 3 years

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure

Patient characteristics (gender, mean age): 100% female, 52 years.

Number per group: 70

Observations on adverse effects (brief): exposure 10 patients

Timing of adverse effects: Exposure 1-3 years

Factors that predict response: No association with POP-Q, age, hormone supplements, or BMI.

Source Citation: Samour et al. 2015[107]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Median months follow-up:18.2 (range 12 to 36)

Dose: GYNECARE GYNEMESH

Frequency/Duration: Single administration

Response: De novo SUI, Dysuria, Fever, Groin pain, Mesh erosion, Persistent Dyspareunia, Vaginal discharge,

Vaginal pain

Patient characteristics (gender, mean age): 100% female, 52 years

Number per group: 152 undergoing repair for cystocele ≥grade 2.

Observations on adverse effects: Mesh erosion occurred from day 3 to 24 months postoperatively. De novo SUI first occurred at 6 months postoperatively. Early complications (<2 weeks): 2 (1.3%) mesh erosion with severe vaginal pain and excessive vaginal discharge, 2 fever, 16 (10.5%) severe vaginal/groin pain. Late complications (n=122): 4 (3.3%) mesh erosion, 4 persistent dyspareunia (90% with varying degrees of dyspareunia), 11 (9%) de novo SUI.

Timing of adverse effects: severe postoperative vaginal/groin pain ≤3 days; early mesh erosion occurred at day 3 and day 4; late mesh erosion occurred at 12, 15, 18, and 24 months; varying degrees of dyspareunia occurred within 3 to 4 months postoperatively; de novo SUI occurred between 6 and 8 months postoperatively.

Factors that predict response: NR

Source Citation: Sharifiaghdas et al. 2015[108]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean months follow-up:24 (range 10 to 36 months)

Dose: Four-arm NAZCA-TC

Frequency/Duration: Single administration

Response: De novo SUI, Lump sensation, Mesh extrusion, Pain (groin/pelvic), Worsening dyspareunia

Patient characteristics (gender, mean age): 100% female, 65.5±8.57 years.

Number per group: 71 with high-stage symptomatic cystocele.

Observations on adverse effects: Extrusion and de novo SUI occurred in 5% and 3% of patients, respectively. Complications (n=64): 3 (4.6%) mesh extrusion, 2 (3.1%) worsening dyspareunia, 2 de novo SUI, 2 lump sensation, 2 pain (groin/pelvic)

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: El-Khawand et al. 2014[109]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 14.3±12.4

Dose: Uphold, Avaulta

Frequency/Duration: Single administration

Response: Mesh exposure

Patient characteristics (gender, mean age): 100% female, 62.2±10.9 years

Number per group: 201 with POP.

Observations on adverse effects: Mesh exposures were detected at median 4.5 months. Complications: 17 (8.5%) mesh exposures.

Timing of adverse effects: Median time to detection of an exposure was 4.5 months (1.1 to 27.3).

Factors that predict response: Lower BMI and concomitant total hysterectomy were significantly associated with mesh exposure.

Source Citation: Jirschele et al. 2014[110]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 12-month follow-up

Dose: Uphold®

Frequency/Duration: Single administration

Response: Mesh exposure

Patient characteristics (gender, mean age): 100% female, 67±11.32 years.

Number per group: 99 with uterovaginal prolapse. Observations on adverse effects: At 1 year follow-up, the mesh exposure rate was 6.52%

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Khan et al. 2014[111]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median months follow-up: 52 (24 to 80)

Dose: Gynecare Prolift™

Frequency/Duration: Single administration

Response: De novo POP , De novo SUI, Granulated tissue, Groin/vaginal pain, Mesh exposure, Vaginal adhesions,

Vaginal tenderness on exam

Patient characteristics (gender, mean age): 100% female, 61±9.6 years

Number per group: 106 with POP ≥grade 2.

Observations on adverse effects: A high rate of de novo POP (19.5%) may be associated with both patient- (high BMI, history of multiple POP repairs) and material-related factors (flexibility and mesh recoil characteristics). Early complications (30- and 90-day): 6 (5.6%) mesh exposure, 2 (1.9%) vaginal adhesions, 6 (5.6%) groin/vaginal pain, 2 (1.9%) granulation tissue, 13 (15.8%) tender on vaginal exam Late complications (median 4 years): 2 (1.8%) de novo SUI, 16 (19.5%) de novo POP in other compartment

Timing of adverse effects: NR

Factors that predict response: De novo POP in the non-operated compartment may be associated with high BMI, history of multiple POP repairs, and flexibility and mesh recoil characteristics.

Source Citation: Larouche et al. 2014[112]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median days follow-up: 340 (IQR) 152 to 644

Dose: Gynemesh PS™, Polyform™

Frequency/Duration: Single administration

Response: Anemia, Cuff cystitis , Cystitis, De novo prolapse in untreated compartment, De novo SUI, Granulation tissue, Hematoma, Mesh exposure, Pelvic pain, Vaginal adhesions, Vaginal bleeding

Patient characteristics (gender, mean age): 100% female, 69±8 years

Number per group: 103 with POP (47 Gynemesh PS, 56 Polyform).

Observations on adverse effects: : Odds of developing mesh exposure were significantly lower with Polyform (OR 0.16, 95% CI: 0.03 to 0.97). Early complications: 3 vaginal bleeding, 2 hematoma, 2 cystitis, 2 cuff cystitis, 4 anemia. Late complications: 13 mesh exposure (11 Gynemesh), 11 granulation tissue (8 Gynemesh), 6 de novo prolapse in untreated compartment (3 each mesh), 6 vaginal adhesions (4 Gynemesh), 13 pelvic pain at 6 month exam (11 Gynemesh), de novo SUI: 8.5% Gynemesh, 7.4% Polyform.

Timing of adverse effects: Pelvic pain was reported at 6 months and ≥1 year.

Factors that predict response: NR

Source Citation: Lo et al. 2014[113]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 19.4±10.9

Dose: Avaulta Plus

Frequency/Duration: Single administration

Response: Mesh exposure, Mesh-related ureteric injury

Patient characteristics (gender, mean age): 100% female, 69.4±11.7 years

Number per group: 70 with stage III/IV POP.

Observations on adverse effects: At 1-year follow-up, mesh exposure occurred in 4 (6.2%) patients. A mesh-related ureteric injury occurred in 1 patient at 28 days. Complications: 4 (6.2%) mesh exposure, 1 mesh-related ureteric injury (right-sided hydroureteronephrosis, right-sided uretero vaginal fistula).

Timing of adverse effects: ureteric injury at 28 days

Factors that predict response: NR

Source Citation: Salamon et al. 2013[114]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 12-month follow-up

Dose: Restorelle Y Smartmesh™

Frequency/Duration: Single administration

Response: None reported

Patient characteristics (gender, mean age): 100% female, 56.6±7.8 years

Number per group: 120 with stage ≥2 apical prolapse (n=118 at 12 months).

Observations on adverse effects: No mesh-related complications, exposures or erosions were reported.

Timing of adverse effects: n/a

Factors that predict response: n/a

Source Citation: Sirls et al. 2013[115]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median days exposed: 96 (15 to 1129)

Dose: Elevate, ProLift

Frequency/Duration: Single administration

Response: Mesh exposure

Patient characteristics (gender, mean age): 100% female. 64±10 with mesh exposure.

Number per group: 335 with POP.

Observations on adverse effects: Lower BMI and a greater decrease in hemoglobin were associated with mesh exposure. Complications: 27 (8.1%) mesh exposure (21 ProLift [8%], 6 Elevate [8.5%]).

Timing of adverse effects: Exposure was detected at a median of 96 days

Factors that predict response: Lower BMI and a greater decrease in hemoglobin were significantly associated with mesh exposure.

Source Citation: Zhang et al. 2013[116]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 1-year follow-up

Dose: NR

Frequency/Duration: Single administration

Response: Constipation, Dysuresia, Fall and expand from cavitas pelvis, Hematomam Hypogastralgia, Incomplete urination, Mesh exposure, Muscular syndrome in cavitas pelvis, Perineal body pain, Ureteral obstruction, Urge incontinence, Urgent incontinence, Vaginal excretion, Vaginal pain, Vaginal shrinkage

Patient characteristics (gender, mean age): 100% female, 64±8 years

Number per group: 114 with Stage III-IV POP.

Observations on adverse effects: Mesh exposures were identified at all follow-ups (2 months, 6 months, 12 months). A 6 cm hematoma was diagnosed in 1 patient at 2 months. Complications at 2 months (n=96): 19 (19.8%) mesh exposures, 34 (35.4%) abnormal excretion in vagina, 20 (20.8%) muscular syndrome in cavitas pelvis, 7 (7.3%) hypogastralgia, 5 (5.2%) fall and expand from cavitas pelvis, 6 (6.3%) perineal body pain, 1 vaginal pain, 1 vaginal shrinkage, 1 urgent incontinence, 4 urge incontinence, 1 dysuresia, 1 incomplete urination, 2 (2.1%) constipation, 1 6- cm hematoma, 1 right ureteral obstruction. Complications at 6 months (n=85): 13 (15.3%) mesh exposure, 29 abnormal excretion in vagina, 6 muscular syndrome in cavitas pelvix, 2 hypogastralgia, 2 fall and expand from cavitas pelvis, 1 perineal body pain, 1 vaginal pain, 1 urge incontinence, 1 incomplete urination. Complications at 12 months (n=77): 6 (7.8%)

mesh exposure, 19 abnormal excretion in vagina, 2 muscular syndrome in cavitas pelvix, 1 hypogastralgia, 1 vaginal pain, 2 urge incontinence, 1 dysuresia, 1 incomplete urination, 1 urgent defecation, 2 constipation.

Timing of adverse effects: Complications occurred at 2, 6, and 12 months

Factors that predict response: Authors noted that age, longer menopause, poor level of estrogen in vaginal mucosa, and high percentage of hysterectomy performed may have been risk factors for mesh exposure. In addition, touched mesh fibres were included in the statistics on mesh exposure.

Source Citation: Chaturvedi et al. 2012[117]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Months follow-up: 6 to 42

Dose: Prolus mesh

Frequency/Duration: Single administration

Response: De novo urgency, Mesh erosion, Perineal pain, Vaginal discharge, Vaginal dryness, Vaginal wall hematoma

Patient characteristics (gender, mean age): 100% female, 54.9 (40 to 71) years.

Number per group: 32 with high-grade POP.

Observations on adverse effects: Late complications included mesh erosion and vaginal dryness in 2 (6.2%) patients each. Early complications: 4 de novo urgency, 3 vaginal discharge, 2 vaginal wall hematoma, 30 perineal pain. Late complications: 2 mesh erosion, 2 vaginal dryness.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: De Landsheere et al. 2012[118]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median months

Dose: ProLift

Frequency/Duration: Single administration

Response: Mesh exposure, Mesh retraction, Rectal compression

Patient characteristics (gender, mean age): 100% female, 64±10.1 years.

Number per group: 524 with POP

Observations on adverse effects: Complications included mesh exposure, mesh retraction and rectal compression. Complications (median follow-up 38 months (15 to 63): 14 (2.7%) mesh exposure, 2 (0.4%) severe symptomatic mesh retraction (combined with exposure in 1 patient), 2 rectal compression causing significant constipation and dyschesia.

Timing of adverse effects: : Median time in months follows: exposure 13 (1 to 49 months); severe symptomatic mesh retraction 14 (11 to 16); rectal compression 18 (12 to 24); symptomatic synechia 25 (11 to 38).

Factors that predict response: Early cystocele stage (stage II) was significantly associated with mesh-related complications

Source Citation: Deffieux et al. 2012[119]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: median months follow-up: 121 (IQR 119 – 132)

Dose: GYNEMESH™

Frequency/Duration: Single administration

Response: Dyspareunia, Persistent mesh exposure, Vaginal pain

Patient characteristics (gender, mean age): 100% female, 81 years (IQR 78-82)

Number per group: 9 with persistent mesh exposure following cystocele repair (n=8 at follow-up).

Observations on adverse effects: No major complications were reported in 8 patients with persistent mesh exposure at long-term follow-up. Complications: 2 (22%) vaginal pain during pelvic exam, 1 (11%) dyspareunia.

Timing of adverse effects: NR

Factors that predict response: NR

Source Citation: Grgic et al. 2012[120]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 12-month follow-up

Dose: Perigee system

Frequency/Duration: Single administration

Response: Bladder erosion, De novo mixed incontinence, De novo stress incontinence, De novo urinary retention, Vaginal erosion

Patient characteristics (gender, mean age): 100% female, 62 (range 42 to 86).

Number per group: 198 with anterior POP ≥grade II.

Observations on adverse effects: Vaginal and bladder erosions occurred in 3 patients by 98 day follow-up. 12 women complained of dyspareunia. Complications through 98 days: 2 (1.0%) vaginal erosion, 1 (0.5%) bladder erosion. Complications through 12 months: 3 (1.5%) de novo stress incontinence, 1 de novo mixed incontinence, 2 (1%) de novo urinary retention, 12 (6.1%) dyspareunia.

Timing of adverse effects: Median days 62 (range 14 to 98)

Factors that predict response: NR

Source Citation: Moore and Lukban 2012[121]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 24

Dose: IntePro (50 g/m2) and IntePro Lite (25.2 g/m2)

Frequency/Duration: Single administration

Response: Mesh erosion, Mesh extrusion

Patient characteristics (gender, mean age): 100% female, 59.5±12.7 years IntePro (IP), 63.5±11.3 years IntePro Lite (IPL).

Number per group: 263 (371 IP implants), 86 (116 IPL implants).

Observations on adverse effects: Use of a lighter weight mesh provided a clinically significant reduction (46%) in extrusion.

Timing of adverse effects: Erosion of IP into the rectum (n=1) occurred at 401 days postoperatively.

Factors that predict response: Higher overall baseline prolapse stage (stage III or IV vs. II) was associated with mesh extrusion.

Source Citation: Cervigni et al. 2011[122]

Study Design: Case series

Device or Material: Collagen –coated PP mesh

Contact Duration: 12-month follow-up

Dose: Avaulta®

Frequency/Duration: Single administration, Response: Cystocele , De novo SUI, De novo dyspareunia, Mesh exposure, Mesh extrusion

Patient characteristics (gender, mean age): 100% female, 62.7±8.8

Number per group: 97 with POP-Q stage ≥2 cystocele

Observations on adverse effects: : Material-related factors may have caused the high exposure rate (21.6%). Complications: 21 (21.6%) mesh exposure, 1 (14.3%) vaginal extrusion, 11 do novo dyspareunia (9 had mesh exposure), 19 (19.5%) de novo SUI.

Timing of adverse effects: : Mesh exposure and de novo SUI were identified by 6 months.

Factors that predict response: 1) stiffness of mesh, 2) collagen coating (which reabsorbed in 15 days) may have provided insufficient protection between tissue and mesh.

Source Citation: Sergent et al. 2011[123]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Mean months follow-up: 58±17

Dose: Parietex® Ugytex

Frequency/Duration: Single administration

Response: Blood transfusion, De novo overactive bladder, De novo SUI, Dyspareunia, Mesh erosion, Mesh exposure, Pelvic hematoma, Persistent vaginal bleeding, Urinary retention, Vaginal pain

Patient characteristics (gender, mean age): 100% female, median 66 years.

Number per group: 114 with recurrent, advanced, or posthysterectomy genital prolapse.

Observations on adverse effects: De novo SUI and overactive bladder occurred in 3% of patients at high-risk of recurring prolapse. Mesh erosion and exposure occurred in 6 and 7 patients, respectively. Early postoperative complications (<6 weeks): 1 (0.8%) urinary retention, 1 (0.8%) pelvic hematoma, 3 (2.6%) blood transfusion, 3 (3%) de novo SUI, 3 (3%) de novo overactive bladder, 3 (2.6%) persistent vaginal bleeding.Late complications: 6 (5.9%) mesh erosion, 10 (9.9%) vaginal pain caused by palpation of the mesh, 7 (6.9%) mesh exposure, 5 (5%) persistent dyspareunia, 4 (4%) de novo dyspareunia. Timing: NR

Timing of adverse effects: Hematoma treated on day 7, mesh erosion occurred between 6 weeks and 6 months.

Factors that predict response: NR

Source Citation: Simon and Debodinance 2011[124]

Study Design: Case series

Device or Material: PPe mesh

Contact Duration: 12 months follow-up

Dose: Gynecare, Prolene Soft, Gynemesh PS

Frequency/Duration: Single administration

Response: Adhesion, Granuloma, Hematoma, Mesh exposure, New-onset IUU, New-onset dyspareunia, New-onset SUI, New-onset urgency, Pain, Polyp, Urine retention

Patient characteristics (gender, mean age): 100% female, 66.7±10.4 years.

Number per group: 100 (88 at 12 months follow-up).

Observations on adverse effects: Grade 1B (e.g., granuloma) and Grade 1A (exposure) healing defects were identified at 2 months to 12 months. Early complications (<1 day): 3 hematoma, 2 acute urine retention. Complications at 2 months: 2 (2%) exposure, 2 Grade 1B defects (polyp, granuloma, adhesion), 6 pain, 8/47 (17%) new-onset SUI, 3/87 (3.5%) new-onset IUU, 4/64 (6.2%) new-onset urgency. Complications at 6 months: 1 (1.1%) exposure, 2 Grade 1B defects (polyp, granuloma, adhesion), 5 pain, 7/43 (16.3%) new-onset SUI, 1/58 (1.7%) new-onset urgency/ Complications at 12 months: 1 exposure, 3/39 (7.7%) new-onset SUI, 2/75 (2.7%) new-onset IUU, 2/75 (5.7%) new- onset urgency, 11.1% new onset dyspareunia/

Timing of adverse effects: Most complications (including exposures) occurred at 2, 6 and 12 months follow-up.

Factors that predict response: NR

Source Citation: Feiner and Maher 2010[125]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Median weeks seeking medical care: 20 (range 4 to 52)

Dose: Total ProLift, Anterior ProLift and Perigee, Apogee-Perigee

Frequency/Duration: Single administration

Response: Focal tenderness, Mesh contraction, Mesh erosion, Severe dyspareunia, Severe vaginal pain, Vaginal discharge/spotting, Vaginal shortening, Vaginal tightness

Patient characteristics (gender, mean age): 100% female, 54.9±11.7 years

Number per group: 17 with vaginal mesh contraction after POP repair.

Observations on adverse effects: Mesh erosion was noted in 53% of women with vaginal mesh contraction. Complications: 100% vaginal mesh contraction, 53% mesh erosion, 41% vaginal tightness, 29% vaginal shortening, 100% severe vaginal pain aggravated by movement, 100% severe dyspareunia, 100% focal tenderness over contracted portions of the mesh on vaginal examination, 18% vaginal discharge/spotting.

Timing of adverse effects: NR

Factors that predict response: The following material-related factors were noted as possible factors related to erosion: 1) excessive tension after shrinkage of the main body of the mesh against the serrated arms; 2) excessive tension on the fixation mesh arms; or 3) bunching of the mesh at implantation.

Source Citation: Heinonen et al. 2010[126]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 12-month follow-up

Dose: ProLift™

Frequency/Duration: Single administration

Response: Bacteriuria, De novo bowel symptoms, De novo LUTS, De novo pain/dyspareunia, De novo SUI, De novo urinary incontinence, Elevated CRP and/or mild fever, Feeling of tension, Hematoma, Mesh exposure, Sensation of bulge, Transient urinary retention

Patient characteristics (gender, mean age): 100% female, 65±10 years.

Number per group: 100 with recurrent vaginal prolapse or late primary POP with a paravaginal tissue defect.

Observations on adverse effects: 40 (40%) patients reported de novo symptoms including SUI in 20 patients. Early complications (at 2 months): 14 mesh exposure, 2 hematoma, 5 transient urinary retention, 15 bacteriuria, 7 elevated CRP and/or mild fever. Late complications (at 1 year): 20 de novo SUI, 15 de novo pain/dyspareunia, 9 de novo LUTS, 9 de novo bowel symptoms, 7 feeling of tension, 7 sensation of bulge, 10 de novo urinary incontinence.

Timing of adverse effects: Hematomas occurred during the post-operative hospital stay and at 3 weeks..

Factors that predict response: NR

Source Citation: Hollander et al. 2010[127]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median months follow-up: 20(range 1 to 43)

Dose: ProLift® , Gynecare

Frequency/Duration: Single administration 98%, repeat administration 2%

Response: De novo SUI, Dyspareunia, Fever, Mesh erosions, Pneumonia, Urge urinary incontinence,

Vaginal discharge

Patient characteristics (gender, mean age): 100% female, 64 years

Number per group: : 316 with prolapse ≥degree II.

Observations on adverse effects: A high rate of de novo SUI (17.3%) was reported. Early complications: 1 vaginal discharge due to fistula, 2 urge urinary incontinence, 56 (17.3%) de novo SUI, 5 (1.5%) dyspareunia, 4 (1.2%) fever, 3 pneumonia (0.9%).Late complications: 37 erosions (authors noted technique-related).

Timing of adverse effects: Fistula developed within 1 day.

Factors that predict response: NR

Source Citation: Lin et al. 2010[128]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Median months follow-up: 18 (range 12 to 26)

Dose: GYNEMESH

Frequency/Duration: Single administration

Response: Dyspareunia, Mesh erosion, Profuse vaginal discharge, Prolonged bladder drainage

Patient characteristics (gender, mean age): 100% female, 64.1 years.

Number per group: 39 with POP stage III or IV.

Observations on adverse effects: Rates of mesh erosion and dyspareunia were low (2.6%). Complications: 1 (2.6%) mesh erosion followed by profuse vaginal discharge 3 months until excision of mesh, 1 dyspareunia, 2 (5.1%) prolonged bladder drainage.

Timing of adverse effects: : Bladder drainage occurred >14 days postoperatively.

Factors that predict response: NR

Source Citation: Lopes et al. (2010)[129]

Study Design: RCT

Device or Material: PP mesh vs no mesh

Contact Duration: 1 year

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Erosion, Exposure

Patient characteristics (gender, mean age): all female, mean age 66

Number per group: 14

Observations on adverse effects (brief): Erosion 5 patients, exposure 3 patients.

Timing of adverse effects: Erosion 2-12 months, Exposure 3-12 months.

Factors that predict response: NR

Source Citation: Moore et al. 2010[130]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median months follow-up: 23.5

Dose: Perigee System® with IntePro®

Frequency/Duration: Single administration

Response: De novo dyspareunia, De novo urge/incontinence, Groin/pelvic/vaginal pain, Mesh extrusion

Patient characteristics (gender, mean age):): 100% female. 61.0 years.

Number per group: 114 with ≥ stage II cystocele.

Observations on adverse effects: Mesh extrusions in 12 (10.5%) patients were detected from 34 to 686 days. Complications: 12 (10.5%) mesh extrusion, 5 (4.4%) groin/pelvic/vaginal pain, 6/94 (6.4%) de novo dyspareunia, 4 (3.5%) de novo urge/incontinence.

Timing of adverse effects: Extrusions were detected from 34 to 686 days

Factors that predict response: NR

Source Citation: Ren et al. 2010[131]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean time to erosion: 9.1±7.6 months (range 1 to 24)

Dose: Prolene

Frequency/Duration: Single administration

Response: Bleeding, Foreign-body granuloma, Inflammation, Mesh erosion, Odynuria, Pain (vaginal, Abdominal, sexual), Purulent discharge, Rufous discharge, Urgency

Patient characteristics (gender, mean age): 100% female, 51.7±9.4 years with erosion, 54.7±13.4 without erosion.

Number per group: 128 with POP or SUI.

Observations on adverse effects: 7 vaginal mesh erosions occurred from 1 to 24 months postoperatively. Complications (follow-up 1.3 to 60 months): 7 (5.4%) vaginal mesh erosion, 2 vaginal pain, 1 lower abdominal pain, 1 sexual pain, 1 purulent discharge, 1 bleeding and rufous discharge, 1 odynuria and urgency, 1 multinucleated giant cell and foreign-body granuloma. Eroded tissue in all patients contained chronic inflammatory cells (lymphocyte, mononuclear macrophage, neutrophil granulocyte, plasmocyte).

Timing of adverse effects: : Erosion occurred at months 1, 3, 6, 8, 9, 13, and 24. Purulent discharge appeared at 1 month postoperatively.

Factors that predict response: NR

Source Citation: Cohen Tervaert JW 2018[47]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: >3-year follow-up

Dose: NR

Frequency/Duration: NR

Response: Allergy, Arthralgias/arthritis, ASIA, Autoantibody presence, Cognitive symptoms, Dry eyes/mouth, Elevated ACE, Elevated CK, Elevated CRP, Elevated IgE, Fatigue, IBS, Increased IgG/IgG subclasses, Livedo reticularis, Localized pain, Lymphadenopathy, Myalgia/muscle weakness, Pyrexia, Raynaud's, Stroke-like symptoms

Patient characteristics (gender, mean age): 80% female, 49.5 years (range 28 to 75

Number per group: 40 with mesh repair of hernia (18) SUI (4) and POP (18).

Observations on adverse effects: Of the 40 patients diagnosed with ASIA, 45% developed an autoimmune disease (e.g., RA) and 25% had immunodeficiencies (e.g., IgG subclass deficiency) detected >3 years follow-up. Abnormal laboratory findings were detected in most patients. Complications: ASIA symptoms: 98% fatigue, 95% myalgias/muscle weakness, 90% arthralgias/arthritis, 78% cognitive symptoms, 80% pyrexia, 85% dry eyes/dry mouth, 17% stroke-like symptoms. Additional symptoms: 78% localized pain, 30% Raynauds, 80% IBS, 75% allergy, 48% livedo reticularis, 75% lymphadenopathy. Laboratory findings: 33% elevated CRP, 24% elevated ACE, 26% elevated CK, 20% elevated IgE, 24% increased IgG or IgG subclasses, 38% autoantibodies (ANCA, ANA, or ACL).

Timing of adverse effects: <1 year (61%), 1-3 years (25%), >3 years (14%).

Factors that predict response: 7% with preexisting allergic disease. Note: 2 patients committed suicide due to intolerable severe weight loss from abdominal pain

Source Citation: Chugtai et al. 2017[132]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: 6 years exposed

Dose: NR

Frequency/Duration: NR

Response: SAID examined

Patient characteristics (gender, mean age): 100% female, 61.8±12.7 years.

Number per group: 2,102 with POP.

Observations on adverse effects: At 2- to 6-year follow-up, polypropylene mesh-based surgery was not associated with an increased risk of developing SAID.

Timing of adverse effects: n/a

Factors that predict response: n/a

Source Citation: De Landsheere et al. 2012[118]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Median months exposed, 13 (1 to 49)

Dose: ProLift

Frequency/Duration: Single administration

Response: Endometrial cancer

Patient characteristics (gender, mean age): 100% female, 64±10.1 years

Number per group: 524 with POP

Observations on adverse effects: 1 patient died of endometrial cancer 3 years after ProLift implantation. A negative Papanicolaou smear and no endometrial thickening were noted on pelvic ultrasound before diagnosis.

Timing of adverse effects: 3 years

Factors that predict response: Early cystocele stage (stage II) was significantly associated with mesh-related complications.

Source Citation: Ren et al. 2010[131]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 2 months

Dose: Prolene

Frequency/Duration: Single administration

Response: Anaphylactoid breakout

Patient characteristics (gender, mean age): 100% female, 51.7±9.4 with erosion

Number per group: 128 with POP or SUI.

Observations on adverse effects (includes timing): In a 71 year old woman, a wheal-like erythra with skin itch occurred at 2 months postoperatively, continued for >9 months and disappeared upon mesh removal.

Timing of adverse effects:

Factors that predict response: The inflammatory reaction to the mesh may have sensitized the patient to animal albumin which induced the erythra.

*Manufacturers and total number of devices causing complications included: AMS (9), Bard (3), Boston Scientific (6), Caldera (1), Coloplast (1), Gynecare (9), TOT hand cut prolene (1), TOT unspecified (10), n/a (2)

ACE: angiotensin converting enzyme; ACL: anti-cardiolipin antibodies; AMS: American Medical Systems; ANA: antinuclear antibodies; ANCA: anti-neutrophil cytoplasmic antibodies; ASIA: autoinflammatory/autoimmunity syndrome induced by adjuvants; BMI: body mass index; cm: centimeter; g/m^2: grams per square meter; CK: creatinine kinase; CRP: c-reactive protein; IBS: irritable bowel syndrome; IgE: immunoglobulin E; IgG: immunoglobulin G; IQR: interquartile range; IUU: urinary incontinence with urgency; LUTS: lower urinary tract symptoms; MMP-2: matrix metalloproteinase-2; MMP-9: matrix metalloproteinase-9; NA: not available; n/a: not applicable; NR: not reported; OR: odds ratio; PID: pelvic inflammatory disease; POP: pelvic organ prolapse; POP-Q: Pelvic Organ Prolapse Quantification score; PP: polypropylene; PVDF: polyvinylidene fluoride; RA: rheumatoid arthritis; SAID: systemic autoimmune inflammatory disorders; SIS: small intestine submucosa; SUI: stress urinary incontinence; TNF-*a*: tumor necrosis factor alpha; TVM: transvaginal mesh.

Table 12: Prolapse Mesh, Transvaginal – Health Effect (In Vivo) Animal Studies

Source citation: Ai et al. 2020[133]

Study Design: Nonrandomized controlled study

Device or Material: Titanized PP lightweight mesh (TiLOOP Mesh) to a conventional PP mesh (GYNEMESH PS)

Route: Vaginal implant

Dose: 1 implant

Frequency/Duration: 1 and 12 weeks

Response: Inflammation

Species (strain): Sheep

Gender: Female

Number per group: 6 for each group and time point

Observations on adverse effects (brief): One week after implantation, there was no significant difference in the inflammatory response between the two groups. Twelve weeks after implantation, the TiLOOP light mesh elicited a lower inflammatory response than was observed for the GYNEMESH PS. The messenger RNA expression levels of the inflammatory factors interleukin 10 and tumor necrosis factor α were lower in the TiLOOP Mesh group than in the Gynemesh PS group at both 1 and 12 weeks ($P < .05$)

Timing of adverse effects: NR

Factors that predict response: Titanized PP lightweight mesh induces slightly less tissue reactivity and has better in vivo biocompatibility.

Source citation: Hympánová et al. 2020[134]

Study Design: RCT

Device or Material: Simulated vaginal prolapse repair in a sheep model using three different materials: (1) ultra-lightweight PP non-degradable textile (Restorelle) mesh, (2) electrospun biodegradable ureidopyrimidinone-polycarbonate (UPy-PC), and (3) electrospun non-degradable polyurethane (PU) mesh in comparison with simulated native tissue repair (NTR)

Route: Posterior vaginal wall implant

Dose: 1 implant

Frequency/Duration: 60 and 100 days

Response: Inflammatory cell response

Species (strain): Sheep

Gender: Female

Number per group: 4 groups of 12

Observations on adverse effects (brief): No visible implant-related complications. The inflammatory response was mild with electrospun implants, inducing both more macrophages yet with relatively more type 2 macrophages present at an early stage than the PP mesh. The only slight difference seen was in the extent of the inflammatory response seen to the electrospun materials compared with that to the textile material, which could be explained by the higher surface area of the electrospun materials.

Timing of adverse effects: up to 100 days

Factors that predict response: Three very different materials were all well tolerated in the sheep vagina.

Data Quality: NR

Source citation: Lo et al. 2020[135]

Study Design: Nonrandomized controlled study

Device or Material: PP mesh: mesh-small [M-S], mesh-medium [M-M], mesh-large [M-L])

Route: Vaginal implant

Dose: 1 implant

Frequency/Duration: 7 and 30 days

Response: Inflammation

Species (strain): Sprague Dawley rats

Gender: Female

Number per group: NR

Observations on adverse effects (brief): significant increase in IL-1 and TNF-α immunoreactivity in the M-M and M-L groups on day 7 when compared with the sham group. M-L showed significantly higher immunoreactivity to TNF-α persisting until day 30. All study groups presented a significantly higher immunoreactivity toMMP-2 and NGF on day 7

Timing of adverse effects:

Factors that predict response: Mesh size is directly proportional to the inflammatory reaction in the host tissue. The prolonged inflammatory process leads to delayed tissue remodeling and angiogenesis, which could delay mesh–tissue integration.

Source citation: Lu et al. 2018[136]

Study Design: RCT

Device or Material: PP mesh with electro-mesh and dip-mesh membrane-coatings

Route: Subutaneous implant

Dose: 1 implant

Frequency/Duration: 2 and 4 weeks

Response: Adhesions

Species (strain): Wistar rats

Gender: Female

Number per group: 8 each for 2 groups

Observations on adverse effects (brief): After 2 weeks of implantation, the electro-mesh had medium adhesion, mesh adhered to the surrounding tissues tightly but separated without any damage. Dipmesh did not adhere to surrounding tissues, also without any tissue growth. By 4 weeks dipmesh had medium-adhesion. Histologic examination showed no lesions.

Timing of adverse effects: NR

Factors that predict response: NR

Source citation: Thomas et al. 2018[99]

Study Design: Systematic review

Device or Material: PP mesh

Route: Transvaginal implant

Dose: 1 implant

Frequency/Duration:

Response: Inflammation

Species (strain): Rabbits, ewes, rats, and mice

Gender: Female

Number per group: 547 total

Observations on adverse effects (brief): "Following the implantation of PP mesh transvaginally there is an immediate and persistent inflammatory response in both female animals and humans." Response was localized around or near the implant site and may be reduced over time but never disappears. No studies demonstrated any systemic changes.

Timing of adverse effects: NR

Factors that predict response: NR

Source citation: Lo et al. 2016[137]

Study Design: Nonrandomized controlled study

Device or Material: Avaulta Plus (C.R. Bard, Inc., Murray Hill, NJ, USA), a porcine collagen-coated macroporous PP mesh (MPC) and Perigee (AMS, Inc., Minnetonka, MN, USA), uncoated macroporous PP mesh (MP)

Route: Pelvic wall implant

Dose: 1 implant

Frequency/Duration: 7 and 30 days

Response: Inflammation

Species (strain): Sprague Dawley rat

Gender: Female

Number per group: 7 groups of 6

Observations on adverse effects (brief): Results showed intense inflammatory reaction on day 7 in the study groups which decreased on day 30. IL-1, TNF-α, MMP-2 and CD31 were observed to decrease from day 7 to day 30. The reaction was significantly more intense in the mesh group than the sham and normal groups, where MPC showed a larger area of inflammation as compared to MP with $p < 0.001$.

Timing of adverse effects: 7 and 30 days

Source citation: Barbosa et al. 2015[138]

Study Design: Case series

Device or Material: Synthetic PP mesh-1

Route: Posterior vaginal implantation

Dose: 1 implant

Frequency/Duration: 3 and 6 months

Response: Inflammation / foreign body reaction

Species (strain): Sheep

Gender: Female

Number per group: 4 at each time point

Observations on adverse effects (brief): Inflammatory reaction was also very low in the main study, being almost non-existent in the explants examined at 6 months post implantation.

Timing of adverse effects: NR.

Factors that predict response: NR.

Source citation: Endo et al. 2015[139]

Study Design: Nonrandomized controlled study

Device or Material: Cross-linked acellular collagen matrix (ACM), pretreated by the anti-calcification procedure ADAPT® compared with PP mesh control

Route: Simultaneous vaginal and abdominal implantation

Dose: 1 implant at each site

Frequency/Duration: 180 days

Response: Inflammation

Species (strain): Sheep

Gender: Female

Number per group: 10 experimental and 6 control

Observations on adverse effects (brief): Histology of vaginal explants with PP differed completely from those with recognizable ACM. PP induced a mild inflammation, with few cells, nearly all macrophages or foreign body giant cell, and less collagen deposition.

Timing of adverse effects: NA

Factors that predict response: NR

Source citation: Feola et al. 2015[140]

Study Design: RCT

Device or Material: Macroporous mesh: (1) Avaulta Solo (plain PP mesh; Bard Medical, Covington, GA), (2) Avaulta Plus (Bard Medical), Avaulta Solo with a sheet of hydrophilic crosslinked porcine acellular collagen matrix (ACM), and (3) Ugytex (Sofradim International, Trevoux, France) PP filaments coated with atelocollagen, poly-ethylene glycol, and glycerol

Route: Abdominal and vaginal mesh implantation

Dose: 1 implant at each site

Frequency/Duration: 60 and 180 days

Response: Inflammation

Species (strain): Sheep

Gender: Female

Number per group: 12 sheep each in 3 experimental groups and 6 sheep in a control group

Observations on adverse effects (brief): For PP, surrounded by connective tissue and a mild inflammatory infiltrate. We observed progressively more mature collagen around the vaginal and abdominal explants between 60 and 180 days. There was a marked increase in collagen content ($p = 0.009$) and collagen organization ($p = 0.024$), along with a higher number of FBGCs ($p = 0.006$) in abdominal explants compared with vaginal explants (180 days).

Timing of adverse effects: NA

Factors that predict response: We found no measurable changes in the exposures, contraction, stiffness, or histologic condition with the addition of collagen

Data Quality: NR

Source citation: Fan et al. 2014[63]

Study Design: RCT

Device or Material: PP mesh

Route: Implanted in vagina and abdomen

Dose: Gynemesh

Frequency/Duration: Single administration, 12 weeks indwelling

Response: erosion, inflammation degree, necrosis

Species (strain): New Zealand white

Gender: Female

Number per group: 20

Observations on adverse effects (brief): Placement of vaginal PP resulted in a moderate-to-severe inflammatory response (including necrosis) and higher inflammation scores vs. other subgroups (vaginal cUBM, abdomen cUBM, abdomen PP). Erosion occurred in 8/12 (67%) rats with vaginal Gynemesh.

Timing of adverse effects: NR

Factors that predict response: NR

Source citation: Karabulut et al. 2014[66]

Study Design: Case control

Device or Material: PP mesh

Route: Implanted in vagina and abdomen

Dose: Atrium®

Frequency/Duration: Single administration, 9 weeks indwelling

Response: fibrosis, foreign body type reaction, granulocyte, inflammation degree, lymphocyte, macrophages, mast cells, necrosis

Species (strain): Wistar albino rats

Gender: Female

Number per group: 37 (10 each control, menopause, steroid + menopause; 7 DM plus menopause)

Observations on adverse effects (brief): Mesh at the abdominal region had more intense granulocyte infiltration while mesh at the vaginal region showed more prominent inflammation and necrosis.

Timing of adverse effects: NR

Factors that predict response: Menopause increased tissue response, while steroid use reduced the response

Data Quality: NR

CD31 = cluster of differentiation 31; cUBM = cross-linked urinary bladder matrix ; DM = diabetes mellitus; FBGC = foreign body giant cell; IL-1 = interleukin 1; MMP-2 = matrix metalloproteinase-2; NA = not applicable; NR = not reported; PP = polypropylene; TNF-α = tumor necrosis factor α

Table 13: Prolapse Mesh, Transabdominal Apical and Uterine – Health Effect (In Vivo) Human Studies

Source citation: Akyol et al. (2014)[141]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 1 to 5.6 years

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure

Patient characteristics (gender, mean age): All female, mean 60

Number per group: 292

Observations on adverse effects (brief): Exposure (19 patients)

Timing of adverse effects: Exposure 3-56 months

Factors that predict response: obesity, parity, menopause, hormone therapy, diabetes, smoking, prior prolapse surgery

Source citation: Heinonen et al. (2011)[126]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 2 -12 months

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure, Pain/dyspareunia

Patient characteristics (gender, mean age): all female mean age 65

Number per group: 100

Observations on adverse effects (brief): Exposure 14, Pain/dyspareunia 15

Timing of adverse effects: Exposure 2 months, Pain/dyspareunia 1 year

Factors that predict response: NR

Source citation: Adedipe et al. (2010)[142]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: 3-12 months

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure, Erosion

Patient characteristics (gender, mean age): all female mean 62

Number per group: 27

Observations on adverse effects (brief): exposure 2, erosion 1

Timing of adverse effects: Exposures 3 months, erosion 12 months

Factors that predict response: NA

Source citation: Clavé et al. 2010[143]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: Mean contact: 790.6 days (range 16 to 3295)

Dose: ≤50-60 g/m2 (28) ≥60 g/m2 (31), NR (4)

Frequency/Duration: NR

Response: chronic inflammation, degradation, exposure, fibrosis, pain, sclerosis, shrinkage

Patient characteristics (gender, mean age): 100% female, NR

Number per group: 84 PFD-related explants (63 PP, 8 composite, 13 PET)

Observations on adverse effects (brief): Degradation was highest with NKNW (100%) and PP multifilament (75%) and lowest with LDPPMF (21%). Complications: Chronic inflammation, pronounced fibrosis (significantly more sclerosis with PPMP vs. other PP and composite implants), degradation by PP type: 21.43% LDPPMF, 47.83% HDPPMF, 33.3% PPMP, 100% NKNW, 75% PP multifilament)

Timing of adverse effects: 16 to 3,295 days. Degradation was detected after 3 months in all types of PP implants

Factors that predict response: NR

Source citation: Nieminen et al. (2010)[144]

Study Design: RCT

Device or Material: PP mesh vs no mesh

Contact Duration: 0-3 years

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure

Patient characteristics (gender, mean age): All female, mean age 66

Number per group: 95

Observations on adverse effects (brief): Exposure (20 patients)

Timing of adverse effects: 0-3 years

Factors that predict response: NR

HDPPMF: high density monofilament; LDPPMF: low density monofilament; NKNW: non-knitted nonwoven; NR: not reported; PET: polyethylene terephthalate; PFD: pelvic floor disorder; PP: polypropylene; PPMP: PP monofilament

Table 14: Prolapse Mesh, Transabdominal Apical and Uterine – Health Effect (In Vivo) Animal Studies

Source citation: Gokmen-Karasu et al. (2017)[145]

Study Design: RCT

Device or Material: PP mesh vs composite polyester

Route: Midline incision to enter the abdominal cavity

Dose: NA

Frequency/Duration: 1 mesh implant

Response: Exposure, Erosion, Inflammatory response.

Species (strain): rabbits, New Zealand white

Gender: All female

Number per group: 292

Observed on adverse effects (brief): Exposure 3. PP mesh reduced vaginal smooth muscle thickness by 17% compared to sham, and also reduced vaginal muscle contractility by 40%-50%

Timing of adverse effects: Exposure 3-56 months. Prolapse stage, concomitant hysterectomy, 3+ concomitant procedures had associations with exposure. No associations between exposure and 7 other factors: obesity, parity, menopause, hormone therapy, diabetes, smoking, prior prolapse surgery.

NA: not applicable; NR: not reported; PP: polypropylene; RCT: randomized controlled trial.

Table 15: Female SUI Mesh, Synthetic – Health Effect (In Vivo) Human Studies

Source citation: Sabadell et al. 2016[147]

Study Design: Cohort

Device or Material: P sling (amid type-I polypropylene)

Contact Duration: Median months follow-up: 24.6, IQR 12.6-39.5

Dose: n/a

Frequency/Duration: Single administration

Response: cystitis, de novo urgency, repeated cystitis, tape erosion, temporary elevated PVRV, transient groin pain, urethrolysis, urinary obstruction, voiding difficulty requiring ISC

Patient characteristics (gender, mean age): 100% female, 63.8 years

Number per group: 115 (92 PP sling, 23 PVDF)

Observations on adverse effects (brief): Temporary elevated PVRV, de novo urgency, and urethrolysis were higher with PP. Early postoperative complications: 28 (30%) PP, 3 (13%) PVDF: Of 25 temporary elevated PVRV, 22 occurred with PP. 2 cystitis and 4 voiding difficulty requiring ISC occurred with PP. Late postoperative complications: 6 (6.5%) PP, 0 PVFD: 1 repeated cystitis, 4 urinary obstruction, 1 transient groin pain; De novo urgency: 13 (14.1%) PP, 1 (4.3%) PVFD.

Timing of adverse effects: NR

Factors that predict response: NR

Source citation: Bozkurt et al. 2015[148]

Study Design: Case series

Device or Material: PP sling

Contact Duration: Mean months follow-up: 30.3±.4

Dose: n/a

Frequency/Duration: Single administration

Response: de novo urge incontinence, dyspareunia, inguinal pain extending to legs, perineal pain, urinary retention, vaginal erosion, worsening urgency

Patient characteristics (gender, age): 100% female, 48.43±6.24 years

Number per group: 156 for TVT-O

Observations on adverse effects (brief): De novo urge incontinence and worsening urgency occurred in 8.9% of patients. Dyspareunia occurred in 7.1% of patients. Early postoperative complications:5 (3.2%) urinary retention, 48 (30.7%) inguinal pain extending to legs. Late postoperative complications: 8 (7.1%) dyspareunia, 14 (8.9%) de novo urge incontinence, 14 (8.9%) worsening urgency, 7 (4.4%) vaginal erosion, 7 (4.4%) perineal pain.

Timing of adverse effects: Follow-up visits at 2 months, 6 months, 1 year, 2 years, up to 42 months

Factors that predict response: NR

Source citation: ElSheemy et al. 2015[149]

Study Design: Case series

Device or Material: PP tape

Contact Duration: Mean months follow-up: 61.67±7.39

Dose: Tailored 11 x 1.5 cm from 11x6 cm Prolene®

Frequency/Duration: Single administration

Response: dyspareunia, groin/thigh pain, obstructive urinary symptoms, UTI, vaginal discharge

Patient characteristics (gender, age): 100% female, 47.47±8.52 years

Number per group: 59 undergoing TVT-O

Observations on adverse effects (brief): No cases of erosion, mesh exposure or de novo urgency were reported. Pain or discomfort in the thigh or groin were observed in 12 (20%) patients directly post-operative. Complications: 4 (6%) vaginal discharge, 12 (20%) pain/discomfort in the thigh folds and groin, 1 (1%) obstructive urinary symptoms, 1 (1%) dyspareunia, 2 (3%) UTI

Timing of adverse effects: pain/discomfort directly post-op

Factors that predict response: NR

Source citation: Zargham et al. 2013[150]

Study Design: RCT

Device or Material: PP mesh

Contact Duration: Median months follow-up: 18

Dose: NR (T-sling mesh kit)

Frequency/Duration: Single administration

Response: bladder penetration, chronic urinary retention, cystitis, de nova urgency, hematoma, SUI recurrence, vaginal bleeding, vaginal erosion

Patient characteristics (gender, age): 100% female, mean 54.1±4.1 years T-Sling, 55.9±4.1 years AVWS

Number per group: 56: 26 AVWS, 30 T-Sling with PP mesh

Observations on adverse effects (brief): Chronic urinary retention was significantly higher with T-Sling (16% vs. 0%). Vaginal erosion and de nova urgency occurred in 8% of individuals with T-Sling (vs 0% with AVWS). Early postoperative complications (≤1 month)(n=50, 25 each arm): vaginal bleeding (12% T-Sling, 21% AVWS), hematoma (8% T-Sling), bladder penetration (8% T-Sling, 4% AVWS). Late postoperative complications (>1 month)(n=50, 25 each arm): cystitis (12% T-Sling, 12% AVWS), vaginal erosion (8% T-Sling), de nova urgency (8% T-Sling), SUI recurrence (8% T-Sling, 32% AVWS), chronic urinary retention (16% T-Sling).

Timing of adverse effects: Vaginal bleeding, hematoma, and bladder penetration occurred ≤1 month. Remaining complications occurred >1 month

Factors that predict response: NR for T-Sling

Source citation: Da Fonseca et al. 2013[151]

Study Design: Case series

Device or Material: PP mesh sling

Contact Duration: Follow-up at 1 month, 6 months, and 1 year post-op

Dose: NR (Polyform® Synthetic Mesh)

Frequency/Duration: Single administration

Response: vaginal discharge, mesh erosion

Patient characteristics (gender, age): 100% female, mean 52.8±1.3 years

Number per group: 69

Observations on adverse effects (brief): Mesh erosion occurred in 5 (7.2%) patients; 80% occurring within 12 weeks of surgery. Early postoperative complications: 4 (5.7%) odorless vaginal discharge. Late postoperative complications (>1 month): 5 (7.2%) mesh erosion.

Timing of adverse effects: 4 mesh erosions ≤12 weeks, 1 mesh erosion at 8 months post-op.

Factors that predict response: Previous surgery for SUI and perioperative inadvertent vaginal transfixation were significantly associated with vaginal mesh erosion.

Source citation: Ascher-Walsh et al. 2010[152]

Study Design: Chart review

Device or Material: PP mesh sling

Contact Duration: Follow-up median months: 2.1 synthetic (n=15), 2.2 fascia lata (n=96), 2.62 rectus (n=16)

Dose: NR (Gynecare)

Frequency/Duration: Single administration

Response: de novo fistula, erosion, SUI recurrence

Patient characteristics (gender, age): 100% female, 25.2±6.3 years synthetic sling, 27.7±8.4 fascia lata sling, 27.2±7.5 rectus sling

Number per group: 19 synthetic polypropylene mesh sling (Gynecare), 104 fascia lata sling, 17 rectus sling. All patients had SUI after fistula repair

Observations on adverse effects (brief): Erosion was significantly higher with synthetic sling (20% vs 0% with other slings). De novo fistula occurred in 2 (13.3%) patients with synthetic sling. Complications: Erosion occurred in 3 (20%) individuals with synthetic sling. De novo fistula occurred in 18 (18.7%) fascia lata sling, 2 (13.3%) synthetic sling, and 2 (12.5%) rectus sling. SUI recurrence occurred in 34 (35.4%) fascia lata sling, 4 (26.7%) synthetic sling, and 8 (50%) rectus sling.

Timing of adverse effects: NR

Factors that predict response: Pelvis type may be a factor

Source citation: Clavé et al. 2010[143]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: mean contact: 790.6 days (range 16 to 3295)

Dose: ≤50-60 g/m2 (28) ≥60 g/m2 (31), NR (4)

Frequency/Duration: NR

Response: chronic inflammation, degradation, exposure, fibrosis, pain, sclerosis, shrinkage

Patient characteristics (gender, age): 100% female. NR

Number per group: 84 PFD-related explants (63 PP, 8 composite, 13 PET)

Observations on adverse effects (brief): Degradation was highest with NKNW (100%) and PP multifilament (75%) and lowest with LDPPMF (21%). Poly(ethylene terephtahlate) explants appeared to sustain less degradation in vivo than the PP explants. Complications: chronic inflammation, pronounced fibrosis (significantly more sclerosis with PPMP vs. other PP and composite implants), degradation by PP type: 21.4% LDPPMF, 47.8% HDPPMF, 33.3% PPMP, 100% NKNW, 75% PP multifilament).

Timing of adverse effects: 16 to 3295 days. Degradation was detected after 3 months in all types of PP implants

Factors that predict response: NR

Source citation: Ren et al. 2010[131]

Study Design: Case series

Device or Material: PP mesh

Contact Duration: Mean time to erosion: 9.1±7.6 months (range 1 to 24)

Dose: Prolene

Frequency/Duration: Single administration

Response: bleeding, foreign-body granuloma, inflammation, mesh erosion, odynuria, pain (vaginal, abdominal, sexual), purulent discharge, rufous discharge, urgency

Patient characteristics (gender, age): 100% female. 51.7±9.4 years with erosion, 54.7±13.4 without erosion

Number per group: 128 with POP or SUI

Observations on adverse effects (brief): 7 vaginal mesh erosions occurred from 1 to 24 months postoperatively. Complications (follow-up 1.3 to 60 months): 7 (5.4%) vaginal mesh erosion, 2 vaginal pain, 1 lower abdominal pain, 1 sexual pain, 1 purulent discharge, 1 bleeding and rufous discharge, 1 odynuria and urgency, 1 multinucleated giant cell and foreign-body granuloma. Eroded tissue in all patients contained chronic inflammatory cells (lymphocyte, mononuclear macrophage, neutrophil granulocyte, plasmocyte).

Timing of adverse effects: Erosion occurred at months 1, 3, 6, 8, 9, 13, and 24. Purulent discharge appeared at 1 month postoperatively

Factors that predict response: NR

CompSource citation: Cohen Tervaert JW 2018[47]

Study Design: Cohort

Device or Material: PP mesh

Contact Duration: >3 year follow-up

Dose: NR

Frequency/Duration: NR

Response: allergy, arthralgias/arthritis, ASIA, autoantibody presence, cognitive symptoms, dry eyes/mouth, elevated ACE, elevated CK, elevated CRP, elevated IgE, fatigue, IBS, increased IgG/IgG subclasses, livedo reticularis, localized pain, lymphadenopathy, myalgia/muscle weakness, pyrexia, Raynauds, stroke-like symptoms

Patient characteristics (gender, age): 80% female, 49.5 years (range 28 to 75)

Number per group: 40 with mesh repair of hernia (18) SUI (4) and POP (18)

Observations on adverse effects (brief): Of the 40 patients diagnosed with ASIA, 45% developed an autoimmune disease (e.g., RA) and 25% had immunodeficiencies (e.g. IgG subclass deficiency) detected >3 years follow-up. Abnormal laboratory findings were detected in most patients. Complications: ASIA symptoms: 98% fatigue, 95% myalgias/muscle weakness, 90% arthralgias/arthritis, 78% cognitive symptoms, 80% pyrexia, 85% dry eyes/dry mouth, 17% stroke-like symptoms. Additional symptoms: 78% localized pain, 30% Raynaud's, 80% IBS, 75% allergy, 48% livedo reticularis, 75% lymphadenopathy. Laboratory findings: 33% elevated CRP, 24% elevated ACE, 26% elevated CK, 20% elevated IgE, 24% increased IgG or IgG subclasses, 38% autoantibodies (ANCA, ANA. or ACL).

Timing of adverse effects: <1 year (61%), 1-3 years (25%), >3 years (14%)

Factors that predict response: 7% with preexisting allergic disease. Note: 2 patients committed suicide due to intolerable severe weight loss from abdominal pain.

ACL: anticardiolipin antibodies; ANA: antinuclear antibodies; ANCA: antineutrophil cytoplasmic antibodies; ASIA: autoinflammatory syndrome induced by adjuvants; AVWS: anterior vaginal wall sling; CK; creatinine kinase; IQR: interquartile range; ISC: intermittent self-catherization; N/A: not available; NKNW: non-knitted non-woven polypropylene; NR: not reported: LDPPMF: low density polypropylene monofilament; PFD: pelvic floor disorder; PP: polypropylene; POP: pelvic organ prolapse; PVDF: polyvinylidene fluoride; PVRV: post-void residual urine volume; SUI: stress urinary incontinence; TVT-O: transobturator vaginal tape inside-out technique; UTI: urinary tract infection.

Table 16: Female SUI Mesh, Synthetic – Health Effect (In Vivo) Animal Studies

Source citation: Roman et al. 2016[153]

Study Design: Comparative

Device or Material: polypropylene mesh

Route: 2 upper quadrants of the abdominal wall parallel to the midline

Dose: Two 20 x 5 mm defects

Frequency/Duration: Singe administration

Response: adhesions, fibrosis, inflammation, mesh exposure

Species (strain): Rabbits (New Zealand)

Gender: Male

Number per group: 40; 8 each polypropylene (PPL), polyurethane (PU), polyvinylidene fluoride (PVDF), poly-L-lactic acid (PLA), and sham

Observed adverse effects: PPL and PVDF mesh demonstrated a sustained chronic inflammatory response profile (M1 response) vs PLA and PU groups (M2 response). Excessive fibrotic tissue formation by 90 days was noted in PPL and PVDF arms. Complications: 5 mesh exposure at 30 days (3 PPL, 2 PVDF), 6 adhesions at day 30 (1 PPL, 3 PU, 2 sham), 6 adhesions at day 90 (1 PPL, 5 PLA).

Timing of adverse effects: 30 and 90 days

Factors that predict response: NR

NR: not reported

Table 17: Female SUI Mini-Sling, Transvaginal – Health Effect (In Vivo) Human Studies

Source citation: Nalliah et al. (2018)[154]

Design: SR (5 human studies, 4 of which used PP

Device or Material: Intravaginal sling

Contact Duration: NA

Dose: NA

Frequency/ Duration: 1 mesh implant

Response: Erosion

Patient characteristics (gender, age): All female, NR

Number per group: 1674

Observations on adverse effects (brief): Erosion rate ranges from 3.5% to 17%.

Timing of adverse effects: 1 month to 37 months.

Factors that predict response: No erosion differences between monofilament vs multifilament.

Source citation: Nolfi et al. 2016[101]

Design: Case control

Device or Material: Polypropylene mesh

Contact Duration: mean months implanted: 36.9±30.3 mesh exposure (n=15), 30.9±18 pain (n=12)

Dose: AMS, Bard, Boston Scientific, Caldera, Coloplast, and Ethicon

Frequency/ Duration: NR

Response: Degradation, Exposure, Fibrosis, Inflammation, Pain

Patient characteristics (gender, age): 100% female. 52 to 56 years

Number per group: 27 mesh (15 incontinence mild urethral slings, 12 prolapse); 30 mesh naïve with stage II or III prolapse

Observations on adverse effects (brief): Mesh explants contained significantly higher cytokines/chemokines (including M1, M2, TNF-a, Interleukin-4), and MMP-9 (pro- and active) and MMP-2 (active) proteolytic enzymes vs. mesh-naïve explants

Timing of adverse effects: 4.5 to 93 months

Factors that predict response: NR

Source citation: Surkont et al. (2015)[156]

Design: Case series

Device or Material: IVS

Contact Duration: 1-12 months

Dose: NA

Frequency/ Duration: 1 mesh implant

Response: Erosion, Protrusion, Abdominal abscess

Patient characteristics (gender, age): all female, mean age 60

Number per group: 72

Observations on adverse effects (brief): Erosion 6, Protrusion 2, Abdominal abscess 4

Timing of adverse effects: Erosion 9 months to 2 yrs, Protrusion 2-3 yrs, Abdominal abscess 2-6 yrs.

Factors that predict response: NR

Source citation: Wu et al. (2013)[157]

Design: Cohort study

Device or Material: IVS

Contact Duration: 12-50 months

Dose: NA

Frequency/ Duration: 1 mesh implant

Response: Erosion, Exposure

Patient characteristics (gender, age): All female mean age 66

Number per group: 89

Observations on adverse effects (brief): Erosion 5, exposure 5

Timing of adverse effects: NR

Factors that predict response: NR

Source citation: Ren et al. 2010[131]

Design: Case series

Device or Material: Polypropylene mesh

Contact Duration: mean time to erosion: 9.1±7.6 months (range 1 to 24)

Dose: Prolene

Frequency/ Duration: Single administration

Response: Bleeding, foreign-body granuloma, inflammation, mesh erosion, odynuria, pain (vaginal, abdominal, sexual), purulent discharge, rufous discharge, urgency

Patient characteristics (gender, age): 100% female, 51.7±9.4 years with erosion, 54.7±13.4 without erosion

Number per group: 128 with POP or SUI

Observations on adverse effects (brief): 7 vaginal mesh erosions occurred from 1 to 24 months postoperatively. Complications (follow-up 1.3 to 60 months): 7 (5.4%) vaginal mesh erosion, 2 vaginal pain, 1 lower abdominal pain, 1 sexual pain, 1 purulent discharge, 1 bleeding and rufous discharge, 1 odynuria and urgency, 1 multinucleated giant cell and foreign-body granuloma. Eroded tissue in all patients contained chronic inflammatory cells (lymphocyte, mononuclear macrophage, neutrophil granulocyte, plasmocyte)

Timing of adverse effects: Erosion occurred at months 1, 3, 6, 8, 9, 13, and 24. Purulent discharge appeared at 1 month postoperatively

Factors that predict response: NR

Source citation: Adel et al. (2017)[155]

Design: SR (10 human studies)

Device or Material: Intravaginal sling

Contact Duration: Mean follow-up in 2 largest studies: 42 to 60 months

Dose: NA

Frequency/ Duration: 1 mesh implant

Response: Cancer not associated with mesh

Patient characteristics (gender, mean age): all female, age NR

Number per group: 4835

Observations on adverse effects (brief): Cancer not associated with mesh

Timing of adverse effects: NA

Factors that predict response: Authors stated "there have been no studies linking exposure to tumor formation."

Source citation: Ren et al. 2010[131]

Design: Case series

Device or Material: Polypropylene mesh

Contact Duration: Time to erosion: 1 month

Dose: Prolene

Frequency/ Duration: Single administration

Response: anaphylactoid breakout

Patient characteristics (gender, mean age): 100% female, 51.7±9.4 with erosion

Number per group: 128 with POP or SUI

Observations on adverse effects (including timing): In a 71 year old woman, a wheal-like erythra with skin itch occurred at 2 months postoperatively, continued for >9 months and disappeared upon mesh removal

Factors that predict response: The inflammatory reaction to the mesh may have sensitized the patient to animal albumin which induced the erythra.

AMS: American Medical Systems; MMP-2: matrix metalloproteinase-2; MMP-9: matrix metalloproteinase-9; NR: not reported; POP: pelvic organ prolapse; SUI: stress urinary incontinence.

Table 18: Female SUI Mini-Sling, Transvaginal – Health Effect (In Vivo) Animal Studies

Source citation: Przydacz et al. 2017[158]

Study Design: RCT

Device or Material: Polypropylene mesh

Route: Implant

Dose: Gynecare TVT-Obturator tape®, I-STOP®, 20 x 10 mm strips

Frequency/ Duration: Single administration, 6 to 12 month indwelling

Response: eosinophils, fibrosis, foreign body giant cell reaction, inflammation, lymphocytes, plasmocytes

Species (strain): Sprague-Dawley rats.

Gender: 100% female.

Number per group: 6 rats per 5 groups based on dwelling time.

Observed adverse effects: No significant difference in acute inflammation (rare eosinophils), chronic inflammation (lymphocytes and plasmocytes), or fibrosis.

Timing of adverse effects: Mild foreign body giant cell reactions (graded 1) were detected in all specimens from 6 weeks to 12 months. Acute inflammation was noted at 3 months. Chronic inflammation was noted at 6, 9, and 12 months. Fibrosis at 6 weeks, 9 months and 12 months.

Factors that predict response: NR.

NR: not reported; RCT: randomized controlled trial; TVT: transvaginal tape.

Appendix E. References

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Appendix F. Surveillance Event Reports – PSO and Accident Investigation

Provided with this report as separate Excel spreadsheet.

Appendix G. Regulatory and Manufacturer Safety Alerts

Specific search terms are provided here. The associated alerts are provided with this report as a separate PDF.

Search terms*:* Apogee, Perigee, Large Pore Polypropylene Mesh, Pinnacle Lite, Uphold Lite, Ascend, Exair, Avaulta Solo/Avaulta Plus Gynecare, Prolift +M Gynecare, Prosima, Novasilk, Restorelle, Minimesh, Sure lift, Parietene Duo/Parietene Quadra, Male Transobturator Sling System, Advance XP, I-Stop, Virtue, Male Remeex System, Sparc, Monarc, Retroarc, Intermesh, Bioarc, Blue Sui, Trelex, Desara TV, Desara Blue, I-Stop Mid-Urethral Sling, Supris, Align/Align To, Gynecare TVT, Gynecare TVT Abbrevo, Gynecare TVT Exact, GMD Universal, Gynecare Tension-Free Vaginal Tape, Sling, Triangle, In-Sling, Ibibol, Aris , Obtape, Omnisure, Minitape Extra, Kim, Safyre VS/Safyre T, Uretex, Remex System for Urinary Incontinence, SIIS#1, Arctv, Miniarc, Boston Scientific Surgical Mesh, Desara One, Desara Mini, Altis, Ajust Helical, Gynecare TVT , Secur, Gyne Ideas Minitape, T-Sling, Minitape Extra, Ophira, Needleless Sling, Large Pore Polypropylene Mesh, Polyform, Upsylon, Vertessa Lite, Restorelle Y/Restorelle M/Restorelle XL/Restorelle L, Novasilk, Alyte, Bard Sacrocolpopexy Graft, Artisyn, Gynecare Gynemesh, Prolene, Endofast Reliant, Minimesh, Parietene Duo/Parietene Quadra, Ugytex Sual, Tephaflex, Prolex Mesh, Optilene, Alacer Surgical Scaffold, Refine, PFR Sling, Topas, Triangle, Repol, Angimesh, Inclose, Witmann Patch, Endoform Restella, Endoform Topical, Sportmesh or Artelon, SURGIMESH Xb, C-Qur, Prolite/Prolite Ultra, Atrium Centrilfx, Atrium Lite, Tio2mesh, Biomerix, Ventral Hernia Repair System, Assure, Covamesh, Biosil, Glucamesh/Glucatex, Flurotex, Popmesh, Biodesign Parastomal Hernial Repair, Surgisis Gold, Gianturco-Helfrich Hernisa Mesh, Premium,Biomesh Ca.b.s.,4ddome, IVS Tunneller Devices, 3dma, Phasix, Ventralight, Perfix Light, Onflex, Ventrale, Composix, Ventrio, Bard Large Pore Soft Mesh/Soft Mesh Preshaped, Ventralex Patch, Crurasoft, Sperma-Tex,Visilex,Marlex Mesh,Curaseal Percutaneous Intraluminal Closure system, Tigerpaw Pro, Polypropylene Mesh, Usher's Marlex Tubular Mesh, T-Line, Kugel Hernia Patch, Vicryl Mesh, Prolene 3D Patch, ULTRAPRO Mesh/ULTRAPRO Advanced, Prolene Soft, Physiomesh, Proceed, Vypro Mesh, FRM, Exogenesis Hernia Mesh, Dynamesh, Rapiseal Patch, Xlr8, Universal Surgical Mesh, Focalseal-L, Sepramesh, Timesh, Glycar Staple Strips, Glycar Tissue Repair Patch, Relimesh, Reperen, Implantech Eptefe sheeting, Biosling, Insightra Freedom, Flexband Plus, AFB, Abthera, Kensey Nash Macropore Shield, VAC Abdominal Dressing, LTM-T, Macropore Surgi-Wrap Mast Bioresorbable Sheet, Pelvimesh/Hermesh, Ortho-Wrap Bioresorbable Sheet, Surgi-Wrap Mast, Tendon Sheet, Surgi-Wrap Mast Bioresorbable Sheet, Invia, Medlinx Surgical Mesh, Tyrx Neuro, Tyrx Absorbable Antibacterial Envelope, Mentor Suspend, Hydrofix, Rebound, Tigr Matrix/Tigr Surgical Mesh, Nuvasive Surgical Mesh System, Immix Plastifilm, Xtac, Star, Orthadapt, Vivosorb, Medpor, Hydrocoat Mesh, Minisling, Zippere, Vitamesh, Motifmesh, Supramesh Extra, SIS Hernia Repair Device, Seriscaffold, Shelhigh No-React Biocuff, Renasys, X-Repair, Dextile, Parietex, Duatene, Parietene DS, Versatex, Progrip, Parietene Macroporous Mesh, Symbotex, Prevadh, Ugytex, Polydioxanone Surgical Scaffold, Surgicraft Surgical Mesh System, Trulene, Proseries Bioimplants, Synthasome X-Repair, Synthes Porous Polyethylene Implants, Sil-Tec, Orthomend, Tissue Fixation System, Permacol Softform, STAT, Biofiber, Aigis, Pivit A/B, Surgipro Mesh, Gore Syneco, Gore Bio-A, Gore Infinit, Gore Seamguard, Gore Dualmesh Plus/Mycromesh Plus, Dualmesh Emerge Plus