

Pathogenesis, consequences, and control of peritoneal adhesions in gynecologic surgery: a committee opinion

Practice Committee of the American Society for Reproductive Medicine in collaboration with the Society of Reproductive Surgeons

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Postoperative adhesions are a natural consequence of surgical tissue trauma and healing and may result in infertility, pain, and bowel obstruction. Adherence to microsurgical principles and minimally invasive surgery may help to decrease postoperative adhesions. Some surgical barriers have been demonstrated effective for reducing postoperative adhesions, but there is no substantial evidence that their use improves fertility, decreases pain, or reduces the incidence of postoperative bowel obstruction. This document replaces the document of the same name last published in 2008 (Fertil Steril 2008;90[5 Suppl]:S144-9). (Fertil Steril® 2013;99:1550-5. ©2013 by American Society for Reproductive Medicine.)

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Postoperative adhesions are a natural consequence of surgical tissue trauma and healing. Peritoneal adhesions may result in infertility, pain, or bowel obstruction and may increase the technical difficulty of subsequent abdominal or pelvic surgery. The purpose of this document is to review the epidemiology, pathogenesis, and clinical consequences of adhesion formation and to summarize available evidence regarding the effectiveness of various strategies for reducing postoperative adhesion formation.

EPIDEMIOLOGY AND IMPACT OF POSTOPERATIVE ADHESIONS

Studies conducted by the Surgical and Clinical Adhesions Research (SCAR)

Group have analyzed the records of surgical patients in Scottish National Health Service hospitals and helped to define the epidemiology and impact of postoperative adhesions (1, 2). Overall, approximately one-third of patients who underwent open abdominal or pelvic surgery were readmitted an average of 2 times over the subsequent 10 years for conditions directly or possibly related to adhesions or for further surgery that could be complicated potentially by adhesions; more than 20% of all such readmissions occurred during the first year after the initial surgery and 4.5% of readmissions were for small bowel obstruction (1, 2). Among open gynecologic procedures, ovarian surgery had the highest rate of readmissions directly related to adhesions (7.5/100 initial

operations) (2). In the Scottish experience, excepting laparoscopic sterilization procedures, open and laparoscopic gynecologic surgery was associated with comparable risk for adhesion-related hospital readmission (3). Another retrospective study of Canadian women admitted to the hospital with a diagnosis of small bowel obstruction after gynecologic procedures found that hysterectomy was a significant cause of adhesion-related small bowel obstruction and that laparoscopic supracervical hysterectomy was associated with a lower risk compared to abdominal hysterectomy (4). In two studies, the incidence of small bowel obstruction after abdominal hysterectomy ranged between 13.6 and 16.3 per 1,000 procedures (4, 5).

Postoperative adhesions increase operating times (6, 7) and the risk of bowel injury during subsequent surgery (8). Adhesions also have major financial implications. In the United States, adhesion-related health care costs exceed one billion dollars annually (9).

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PATHOGENESIS

Adhesions are the consequence of tissue trauma that may result from sharp, mechanical, or thermal injury; infection; radiation; ischemia; desiccation; abrasion; or foreign-body reaction. Such trauma triggers a cascade of events that begins with the disruption of stromal mast cells, which releases vasoactive substances such as histamine and kinins that increase vascular permeability. Fibrin deposits then form, containing exudates of cells, leukocytes, and macrophages (10). Healing occurs by a combination of fibrosis and mesothelial regeneration (11). Unlike skin wounds, which heal from the edges, the repair of peritoneal defects occurs from the underlying mesenchyme. As a result, both large and small peritoneal defects heal relatively quickly. Fibrinous exudates form within 3 hours after injury. Most fibrinous exudates are transient and are broken down by fibrinolysis within 72 hours. Trauma-induced local suppression of peritoneal fibrinolysis leads to early fibrinous adhesions (10) (Fig. 1). The invasion of fibroblasts and blood vessels soon follows, resulting in permanent vascular adhesions (10) (Fig. 1).

CONSEQUENCES OF ADHESION FORMATION

The most important potential consequences of adhesion formation are infertility, bowel obstruction, and abdominal/pelvic pain.

Infertility

Adhesions may affect fertility adversely by distorting adnexal anatomy and interfering with gamete and embryo transport. The only study to assess adhesiolysis and infertility was a small retrospective review. Among infertile women with otherwise unexplained infertility diagnosed with adnexal adhesions at laparoscopy, pregnancy rates (PR) were 32% at 12 months and 45% at 24 months after subsequent

adhesiolysis by laparotomy compared with 11% at 12 months and 16% at 24 months in women left untreated (12). In women followed for an average of 49 months after tubal surgery, term PRs were inversely correlated with adhesion scores as assigned using the American Society for Reproductive Medicine classification system for adnexal adhesions (13).

Bowel Obstruction

Adhesions are the most common cause of postoperative small bowel obstruction (5). In a series of 552 patients with bowel obstruction, intra-abdominal adhesions were judged responsible in 74% of cases (14).

Abdominal/Pelvic Pain

The relationship between adhesions and pelvic pain is unclear. Although nerve fibers have been identified in pelvic adhesions, their prevalence is no greater in patients with pelvic pain than in those without pelvic pain (15). Moreover, there is no relationship between the extent of adhesions and the severity of pain. It generally is accepted that adhesions may cause visceral pain by impairing organ mobility (16, 17). A study of patients with chronic pelvic pain randomized to laparotomy with adhesiolysis or laparotomy alone found that adhesiolysis was effective only in those having dense adhesions involving the bowel (18). A randomized, controlled multicenter trial observed that laparoscopic lysis of mild abdominal adhesions relieved abdominal or pelvic pain, but to no greater extent than sham surgery (19). Clearly, the impact that lysis of bowel or adnexal adhesions may have on abdominal and pelvic pain cannot be confidently predicted.

REDUCTION IN ADHESION FORMATION

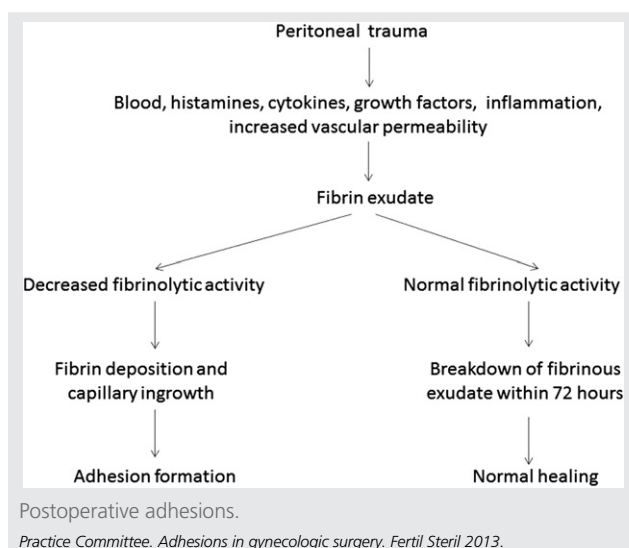
All surgeons must be familiar with the risks and consequences of postoperative adhesions. Theoretically, formation of adhesions might be reduced by minimizing peritoneal injury during surgery, by preventing the introduction of reactive foreign bodies, by reducing the local inflammatory response, by inhibiting the coagulation cascade and promoting fibrinolysis, or by placing barriers between damaged tissues.

Surgical Technique

Formation of postoperative adhesions often may be minimized by careful surgical technique with adherence to microsurgical principles, which includes gentle tissue handling; meticulous hemostasis; excision of necrotic tissue; minimizing ischemia and desiccation; the use of fine, nonreactive suture materials; and prevention of foreign-body reaction and infection (20, 21).

Postoperative adhesions have been observed in up to 94% of patients after laparotomy (22, 23). Laparoscopy does not necessarily result in fewer adhesions than laparotomy; the extent of tissue injury, not the surgical approach, is the determining factor (24, 25). Risk for the development of de novo anterior abdominal wall adhesions likely is lower after

FIGURE 1



laparoscopy than after laparotomy because the risk relates to the length of the abdominal incision(s) (25). Minimally invasive endoscopic surgery also may result in less tissue and organ handling and trauma, avoids contamination with foreign bodies such as surgical glove powder and lint from laparotomy pads, and facilitates more precise tissue manipulation, all of which may help to reduce risk for postoperative adhesion formation. The incidence of postoperative infection, another risk factor for adhesion formation, is lower after laparoscopy than after laparotomy. Pneumoperitoneum has a tamponade effect that may help to facilitate hemostasis during laparoscopy. However, as most commonly performed using standard insufflators, laparoscopy also can desiccate the peritoneum and, thus, may increase the risk for adhesion formation (26). In animals, adhesion risk increases with both time and insufflation pressure (27, 28). The use of warmed humidified CO₂ has been shown to decrease adhesions in a mouse model (29).

Regardless of the surgical approach selected, procedures such as myomectomy often result in adhesions. The prevalence of adhesions after open abdominal myomectomy is greater than 90% but is still at least 70% after laparoscopic myomectomy (30–32).

Whether parietal peritoneal closure is necessary or advisable remains controversial (33–36). Evidence suggests that the incidence of adhesions at the site of closure after laparotomy is approximately 22% with peritoneal closure and 16% without peritoneal closure (33, 34). In women with ovarian cancer, closure of pelvic and periaortic peritoneum appears to result in greater adhesion formation than is observed when the dissected areas are left open (35). However, parietal peritoneal closure at primary cesarean delivery has been observed to yield significantly fewer dense and filmy adhesions (36).

Adjuncts to Surgical Technique

Three types of adjuncts to surgical technique have been used in attempts to reduce postoperative adhesions: anti-inflammatory agents, peritoneal instillates, and surgical adhesion barriers.

Anti-inflammatory agents. A number of local and systemic anti-inflammatory drugs and adhesion-reducing substances, including dexamethasone and promethazine, have been evaluated, but none has been found effective for reducing postoperative adhesions (37–39).

Peritoneal instillates. Antibiotic solutions for peritoneal lavage and prevention of postoperative infection do not reduce adhesions, and some may promote adhesion formation (40).

Thirty-two percent dextran 70 and crystalloid solution instillates, such as normal saline and Ringer's lactate with or without heparin or corticosteroids, have been used to separate adjacent peritoneal surfaces via "hydroflotation" (41, 42), but none has been demonstrated effective for reducing adhesion formation (42).

Icodextrin 4% solution (Adept Adhesion Reduction Solution, Baxter Healthcare Corp.) is a water-soluble, high

molecular weight, alpha (1,4)-linked glucose polymer in an electrolyte solution. When used as a peritoneal instillate (1–1.5 L), 4% icodextrin functions as a colloid osmotic agent to retain fluid within the peritoneal cavity for an interval of 3–4 days. Icodextrin is transferred into the systemic circulation via peritoneal lymphatic drainage and metabolized by alpha-amylase to lower molecular weight oligosaccharides that are eliminated by renal excretion. Although a preliminary randomized, controlled pilot study observed that icodextrin 4% reduced adhesion formation (43), a systematic review concluded that there is insufficient evidence for its use as an adhesion-preventing agent (42). Icodextrin 4% has been approved by the US Food and Drug Administration (FDA) for use in the United States as an adjunct to good surgical technique for the reduction of postoperative adhesions in patients undergoing gynecologic laparoscopic adhesiolysis.

Heparin has been suggested as a means to decrease adhesion formation via inhibition of the coagulation cascade and the promotion of fibrinolysis (44, 45). However, in the only clinical trial, peritoneal irrigation with heparin solution did not appear to reduce peritoneal adhesions after pelvic surgery (45).

Surgical adhesion barriers. Surgical barriers may help to decrease postoperative adhesion formation but cannot compensate for poor surgical technique.

Sodium hyaluronic acid (HA) and carboxymethyl cellulose (CMC) are combined in a bioresorbable membrane (Seprafilm, Genzyme Corp.) that has been modified to prolong its retention time in the body. CMC is nontoxic and is used commonly as filler in food, cosmetics, and pharmaceuticals. The HA film is a transparent and absorbable membrane that acts to separate opposing tissue surfaces and lasts for 7 days (46, 47). In one study involving 127 patients undergoing open abdominal myomectomy, women randomized to receive HA film were observed to have fewer adhesions than untreated controls (48). Although use of HA film may reduce midline adhesions (22), a systematic review concluded that there is limited evidence for its effectiveness for preventing adhesion formation after myomectomy (49). A large multicenter trial involving 1,701 patients randomized to treatment with HA film or no treatment at time of intestinal resection observed no overall difference in the incidence of postoperative small bowel obstruction between the two groups (50). The HA film is limited largely to use during laparotomy because it fragments easily if not handled gently. The HA film has been approved by the FDA for use in the United States.

Oxidized regenerated cellulose (Interceed, ETHICON Women's Health and Urology) is an absorbable adhesion barrier that requires no suturing. It is degraded into monosaccharides and absorbed within 2 weeks after application. The product has been shown to reduce adhesion formation in randomized controlled clinical trials (51–55), all of which have demonstrated benefit for reducing the incidence and extent of new and recurrent adhesions by 50%–60% after both laparoscopic and open abdominal surgical procedures (49). However, there is scant evidence

that the reduction in adhesions resulting from use of oxidized regenerated cellulose improves fertility. In one small retrospective study involving 38 infertile women who required pelvic reconstructive surgery, the postoperative PR was higher among those treated with oxidized regenerated cellulose than among women not treated with the adhesion barrier (56).

Complete hemostasis must be achieved, as the product is rendered ineffective when saturated with blood. A study in humans (in contrast to the results from animal studies) found that adding heparin to oxidized regenerated cellulose provided no additional benefit (57). Oxidized regenerated cellulose (in the form of Interceed) has been approved by the FDA for use in the United States for reducing adhesions.

Expanded polytetrafluoroethylene (ePTFE, Gore-Tex Surgical Membrane, W.L. Gore and Associates) is a nonabsorbable adhesion barrier produced in thin sheets (0.1 mm thick) with an average pore size of less than 1 mm. ePTFE has been approved by the FDA for use in the United States for peritoneal repair. Unlike oxidized regenerated cellulose and HA film, ePTFE must be sutured to tissue. The product can help to prevent adhesion formation and reformation regardless of the type of injury or whether complete hemostasis has been achieved (58). In a small randomized trial, ePTFE was found to decrease post myomectomy adhesions (59). ePTFE was found to be more effective than oxidized regenerated cellulose in preventing adhesion formation after adnexal surgery in a randomized clinical study (60). Its use has been limited by the need for suturing and later reoperation for removal (49). It is questionable whether it needs to be removed as ePTFE has been used as a pericardial graft for many years.

Hyaluronic acid solution (Sepracat, Genzyme Corp.) is a natural bioabsorbable component of the extracellular matrix and is cleared in less than 5 days. Women undergoing open gynecologic procedures treated with HA solution have been observed to have fewer new adhesions, particularly in areas of indirect trauma, and a greater likelihood of having at least one adhesion-free ovary compared with women treated with placebo in a randomized multicenter study (61). The HA solution is not approved by the FDA for adhesion reduction in the United States.

Polyethylene glycol (PEG) (SprayGel, Confluent Surgical Inc.) is a two-component system consisting of two PEG-based liquids. The delivery system consists of an air pump and spray applicator and dispenses blue-colored PEG to cover the serosal defects. Within seconds after application, PEG becomes a gel that adheres to tissue. PEG has shown efficacy in early clinical trials (62), but larger studies are needed to better evaluate its effectiveness. PEG has not been approved by the FDA for use in the United States.

Fibrin sealant (Tisseel VH, Baxter Healthcare Corp.) also has been used as an adhesion-reducing substance. In animal studies, treatment of peritoneal defects with fibrin sealant has been observed to decrease intra-abdominal adhesion formation and reformation (63). Clinical data regarding the use of fibrin sealant in prevention of adhesions are limited. The product has been reported to decrease formation of adhesions after salpingostomy, salpingolysis, and ovariolysis,

but not after tubal anastomosis (64, 65), probably because the extent of adhesion formation after anastomosis is typically only minimal or mild. Fibrin sealant is a biological product derived from human blood donors and therefore poses a theoretical risk for transmission of infectious agents. Fibrin sealant has been approved by the FDA for use in the United States as an adjunct to hemostasis in cardiothoracic surgery and the surgical treatment of splenic injuries and as an adjunct for the closure of colostomies.

SUMMARY

- Postoperative adhesions are a natural consequence of tissue trauma and healing.
- Postoperative pelvic adhesions may result in infertility, pain, and bowel obstruction.
- Adherence to microsurgical principles and minimally invasive techniques may help to reduce postoperative adhesions.

CONCLUSIONS

- There is no evidence that anti-inflammatory agents reduce postoperative adhesions.
- There is insufficient evidence to recommend peritoneal instillates such as icodextrin to reduce adhesions.
- The FDA-approved surgical barriers Sefrafilm, Interceed, and the Gore-Tex Surgical Membrane have been demonstrated effective for reducing postoperative adhesions. However, there is no substantial evidence that their use improves fertility, decreases pain, or reduces the incidence of postoperative bowel obstruction.

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