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A study on the impact of postoperative peritoneal adhesions on adults

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Abstract
Introduction: Postoperative adhesions are a significant health problem with major implications on quality of life and health care expenses. The purpose of this review was to investigate the efficacy of preventative techniques and adhesion barriers and identify those patients who are most likely to benefit from these strategies.
Methods: The National Library of Medicine, Medline, Embase, and Cochrane databases were used to identify articles related to postoperative adhesions.
Results: Ileal pouch–anal anastomosis, open colectomy, and open gynecologic procedures are associated with the highest risk of adhesive small-bowel obstruction (class I evidence). Based on expert opinion (class III evidence) intraoperative preventative principles, such as meticulous hemostasis, avoiding excessive tissue dissection and ischemia, and reducing remaining surgical material have been published.
Laparoscopic techniques, with the exception of appendicitis, result in fewer adhesions than open techniques (class I evidence). Available bioabsorbable barriers, such as hyaluronic acid/carboxymethylcellulose and icodextrin 4% solution, have been shown to reduce adhesions (class I evidence).
Conclusions: Postoperative adhesions are a significant health problem with major implications on quality of life and health care. General intraoperative preventative techniques, laparoscopic techniques, and the use of bioabsorbable mechanical barriers in the appropriate cases reduce the incidence and severity of peritoneal adhesions.

Keywords: peritoneal, adhesions, adults

Introduction
Patients undergoing laparotomy for various reasons have a 90% risk of developing intraperitoneal adhesions [1, 2] and the incidence of re-admissions directly related to adhesions varies from 5% to 20% [3-6]. It is estimated that in the United States there are 117 hospitalizations for adhesion-related problems per 100,000 people and the total cost for hospital and surgeon expenditures is about $1.3 billion [7]. In some European countries the direct medical costs for adhesionrelated problems were more than the surgical expenditure for gastric cancer and almost as much as for rectal cancer [8, 9] In view of the magnitude of the health problems and financial burden related to adhesions, prevention or reduction of postoperative adhesions is an important priority. Numerous articles on the prevention of postoperative adhesions have been published but several controversies such as the effectiveness of available agents and their indication in general surgical patients still exist. Most of the available literature is based on gynecologic patients. For general surgical patients no recommendations or guidelines exist. The purpose of this literature review was to assess the efficacy of various described adhesion prevention strategies after emergency and elective general surgery and to identify those patients who are most likely to benefit from these various prevention strategies.

Methods
Case reports, letters to editors, and review articles were excluded. To specifically identify preventative measures for the development of adhesive morbidity, we used the search terms “abdominal adhesion AND prevention” and “adhesive small bowel obstruction AND prevention.” In addition, specific names of mechanical barriers were entered to identify all studies assessing their ability to prevent postoperative intestinal adhesions and obstruction. The titles and abstracts when available were scrutinized to select relevant controlled studies addressing the safety and efficacy of the use of these agents in abdominal surgery. A total of 39 studies and meta-analyses investigating different mechanical barriers were selected and further evaluated. Of those, 19 prospective randomized trials and 3 meta-analyses were identified and are discussed here in detail.

Pathophysiology
Peritoneal tissue repair is a complex process that involves several different cell types, cytokines, coagulation factors, and proteases, all acting together to restore tissue integrity. A complex interaction of biochemical events involved in inflammation, angiogenesis, and tissue repair control the adhesion formation process. It is widely accepted that the fibrinolytic system plays a central role in postoperative peritoneal healing. Immediately after surgical injury to the peritoneum there is bleeding and an increase in vascular permeability with extravasation of fibrinogen-rich fluid from the injured surfaces [5] Almost simultaneously, an inflammatory response occurs, with migration of inflammatory cells, release of cytokines, and activation of the coagulation cascade [3]. The activation of the coagulation system results in thrombin formation, which is necessary for the conversion of fibrinogen to fibrin. Fibrinolysis is a key factor in determining the amount of adhesion formation. Early fibrinolysis, within 5 days, encourages healing of the peritoneum without adhesion to the adjunct tissues. However, if fibrinolysis does not occur

within 5 to 7 days of the peritoneal injury, the temporary fibrin matrix persists and gradually becomes more organized as collagen-secreting fibroblasts and leads to adhesion formation. There are 2 major activators in the fibrinolytic system: tissue plasminogen activator and urokinase-like plasminogen activator. They are the main factors that convert plasminogen into active plasmin, a broad-range protease capable of degrading fibrin.

Plasminogen activator inhibitors inhibit fibrinolysis and encourage adhesion formation (Fig. 1). Inflammatory mediators also may play an important role in adhesion formation. There is experimental evidence that certain mediators, such as transforming growth factor- and interleukins, decrease the fibrinolytic capacity of the peritoneum and increase the formation of adhesions.

Clinical relevance of adhesion-related complications

Abdominal adhesions pose a significant health problem with major adverse effects on quality of life, use of health care resources, and financial costs. The most common adhesion-related problem is small-bowel obstruction (SBO). Adhesions are the most frequent cause of SBO in the developed world and are responsible for 60% to 70% of SBO. In addition, adhesions have been implicated as a major cause of secondary infertility. Pelvic adhesions were found to be responsible in 15% to 40% of infertilities. It has been suggested that these adhesions may interfere with the ovum pick-up mechanism and gamete transportation. Furthermore, some investigators reported that adhesions are responsible for many cases of chronic abdominal pain although this concept remains a controversial issue. Finally, the presence of adhesions makes reoperation more difficult, adds an average of 24 minutes to the surgery, increases the risk of iatrogenic bowel injury, and makes future laparoscopic surgery more difficult or even not possible.

Risk factors for adhesion-related problems

The identification of high-risk patients may help in the development and use of adhesion-preventing strategies and advice them on the risk of adhesive SBO before an elective surgery. Review of the literature shows clearly that the most important risk factor for adhesive SBO is the type of surgery and extent of peritoneal damage. Surgeries of the colon and rectum are associated with a higher risk of adhesion-related problems than surgeries to the small bowel, appendix, or gallbladder.

Total colectomy with ileal pouch–anal anastomosis is the procedure with the highest incidence for adhesion-related problems with an overall incidence of SBO of 19.3%. Other highrisk procedures include gynecologic surgeries (11.1%) and open colectomy (9.5%). Table 1 shows the incidence of adhesion-related re-admission after various abdominal surgical procedures. In general, open procedures, with the exception of appendectomy, have a higher risk for the development of adhesions than a laparoscopic intervention. Other possible risk factors include age younger than 60 years, previous laparotomy within 5 years, peritonitis, multiple laparotomies, emergency surgery, omental resection, and penetrating abdominal trauma, especially gunshot wounds.

Some studies examined possible risk factors for recurrence of SBO. There is evidence that with growing numbers of previous episodes of SBO requiring adhesiolysis, the risk for future re-admission for SBO increases.

The same studies identified nonsurgical management of the initial episode as a risk factor for recurrence. A multicenter prospective study of 286 patients with adhesive SBO and a 5-year follow-up period identified age younger than 40 years, the presence of matted adhesions, and surgical complications during the surgical management of the first episode as independent risks for recurrence.

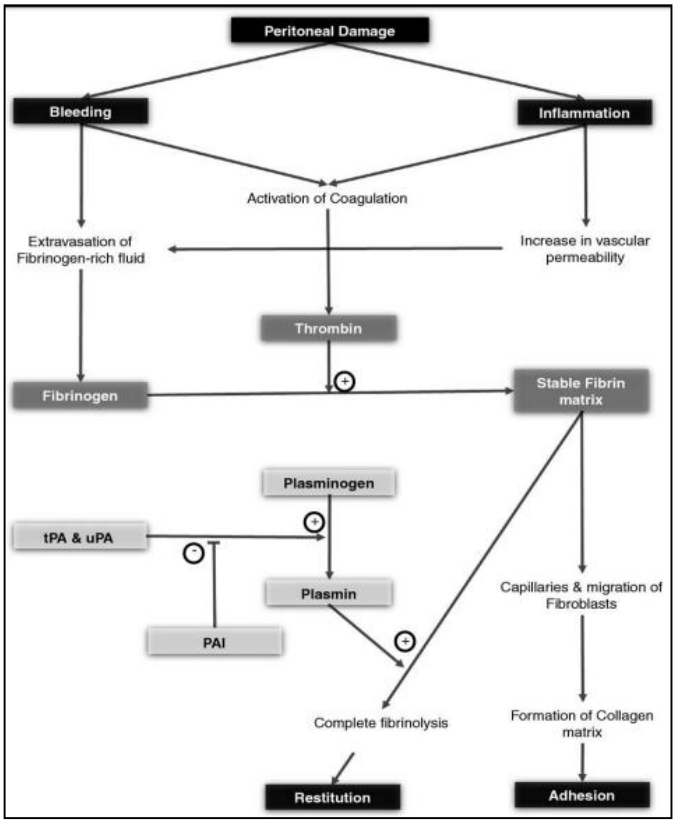

Fig 1: Pathophysiology of peritoneal adhesions. tPA= tissue plasminogen activator; uPA= Urokinase-like plasminogen activator; PAI= plasminogen activator inhibitor.

Table 1: Incidence of adhesion-related re-admissions according to surgical procedure

Surgery	Total number of patients	Adhesion-related re-admission	References
Open appendectomy	266,695	3,663 (1.4%)	4,6,8,64,98–119
Laparoscopic appendectomy	4,445	57 (1.3%)	41,42,54,100,102,105–107,109–114,118,120
Open cholecystectomy	141	10 (7.1%)	121,122
Laparoscopic cholecystectomy	7,103	11 (.2%)	121–123
Open colectomy	121,085	11,491 (9.5%)	4–6,64,124–128
Laparoscopic colectomy	930	40 (4.3%)	123,128,129
Ileal pouch–anal anastomosis	5,268	1,018 (19.3%)	17,115,130–142
Gynecologic procedures	38,751	4297 (11.1%)	
Open hysterectomy	20,377	3,182 (15.6%)	143–145
Laparoscopic hysterectomy	303	0 (.0%)	6,145
Open adnexal surgery	4621	1,105 (23.9%)	143–145
Laparoscopic adnexal surgery	470	0 (.0%)	144,145
Cesarean section	12,980	10 (.1%)	143–145
Overall incidence	446,331	20,635 (4.6%)	

Prevention

In view of the magnitude of the medical problems and financial burden related to adhesions, prevention or reduction of postoperative adhesions in an important priority. Some groups have recognized the importance of the problem and have attempted to educate physicians on this issue. Numerous articles on adhesion barriers have been published but several controversies such as the effectiveness of available agents and their indication in general surgical patients still exist.

Most of the available literature is based on gynecologic patients. For general surgical patients no recommendations or guidelines exist. Any prevention strategy should be safe, effective, practical, and cost effective. A combination of prevention strategies might be more effective but our knowledge on this topic is fairly limited. The prevention strategies can be grouped into 4 categories: general principles, surgical techniques, mechanical barriers, and chemical agents. Azziz [19] in a prospective randomized study of 134 women undergoing adhesiolysis by laparotomy (268 pelvic sidewalls), applied Interceed on one sidewall and left the opposite side uncovered. The incidence and severity of adhesions were evaluated at a second-look laparoscopy 10 days to 14 weeks after surgery. Interceed significantly reduced the incidence and extent of adhesions. Larsson *et al* [20] of the Nordic Adhesion Prevention Study group in a multicenter, prospective, randomized, blinded study of 66 women undergoing adhesiolysis of 132 ovaries used Interceed around the adnexa on one side and left the other side uncovered.

The incidence and severity of adhesions were assessed at a second-look laparoscopy 4 to 10 weeks after the initial surgery. The study showed that Interceed significantly reduced the incidence, extent, and severity of adhesions. Other smaller, prospective, randomized studies using the same methodology showed similar efficacy of Interceed application in laparoscopic or open surgery.

A metaanalysis of 7 randomized studies showed that Interceed decreased the incidence of adhesions by 24.2%

3.3% (P. 001) when compared with untreated sites. A more recent meta-analysis also concluded that Interceed reduced the incidence and severity of adhesions after open or laparoscopic gynecologic surgery

Fluid agents

Fluid agents have the theoretical advantage of covering more potential sites of adhesion formation than mechanical barriers. However, the experience is still limited and much more work is needed to show their efficacy. The most widely studied and the only Food and Drug Administration–approved adhesion-prevention fluid agent in laparoscopic surgery is Adept (Baxter Healthcare, Deer- field, IL). Adept (icodextrin 4% solution) is used as an irrigant fluid throughout surgery and at the end of surgery 1,000 mL is instilled and left in the peritoneal cavity.

The fluid remains in the peritoneal cavity for several days and separates the damaged surfaces during the critical period of adhesion formation. A large multicenter, prospective, randomized, double-blind study by Brown *et al* 30 compared Adept (N 203) with lactated Ringer's solution (N 199), in women undergoing laparoscopic gynecologic surgery for adhesiolysis. The study patients returned for a second laparoscopy within 4 to 8 weeks. Adept was significantly more likely to reduce adhesions and improve fertility scores than lactated Ringer's solution. There was a higher incidence of labial swelling in the treatment group (6% vs. 4%; P. 002). Intergel solution (Lifecore Biomedical, Inc, Chaska, MN), which contains. 5% ferric hyaluronate, is another solution used for adhesion prevention. In preliminary studies it has been shown to reduce the number, severity, and extent of adhesions in peritoneal surgery. However, the use of Intergel in abdominal surgery in which the gastrointestinal tract was opened led to an unacceptably high rate of postoperative complications.

Conclusions

Postoperative adhesions are a significant health problem with major implications on quality of life and health care expenses. General intraoperative preventative techniques, such as starch-free gloves, avoiding unnecessary peritoneal dissection, avoiding spillage of intestinal contents or gallstones, and reducing remaining surgical material, may reduce the risk of adhesions and should be applied in every patient. Laparoscopic techniques are preferable to open techniques whenever possible. In high-risk procedures the use of bioabsorbable mechanical barriers should be considered.

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