REVIEW

Port site infection in laparoscopic surgery: A review of its management

Prakash K Sasmal, Tushar S Mishra, Satyajit Rath, Susanta Meher, Dipti Mohapatra

Prakash K Sasmal, Tushar S Mishra, Satyajit Rath, Susanta Meher, Department of Surgery, All India Institute of Medical Sciences, Bhubaneswar, Odisha 751019, India

Dipti Mohapatra, Department of Physiology, IMS and SUM Hospital, Bhubaneswar, Odisha 751030, India

Correspondence to: Dr. Prakash K Sasmal, MS (Surgery), FNB (Min. Access Surgery), FAIS, Assistant Professor, Department of Surgery, All India Institute of Medical Sciences, Room No. 402, 4th floor Academic Block, Bhubaneswar, Odisha 751019, India. drpksasmal@gmail.com
Telephone: +91-94-38884255

Abstract

Laparoscopic surgery (LS), also termed minimal access surgery, has brought a paradigm shift in the approach to modern surgical care. Early postoperative recovery, less pain, improved aesthesis and early return to work have led to its popularity both amongst surgeons and patients. Its application has progressed from cholecystectomies and appendectomies to various other fields including gastrointestinal surgery, urology, gynecology and oncosurgery. However, LS has its own package of complications. Port site infection (PSI), although infrequent, is one of the bothersome complications which undermine the benefits of minimal invasive surgery. Not only does it add to the morbidity of the patient but also spoils the reputation of the surgeon. Despite the advances in the field of antimicrobial agents, sterilization techniques, surgical techniques, operating room ventilation, PSIs still prevail. The emergence of rapid growing atypical mycobacteria with multidrug resistance, which are the causative organism in most of the cases, has further compounded the problem. PSIs are preventable if appropriate measures are taken preoperatively, intraoperatively and postoperatively. PSIs can often be treated non-surgically, with early identification and appropriate management. Macrolides, quinolones and aminoglycosides antibiotics do show promising activity against the atypical mycobacteria. This review article highlights the clinical burden, presentations and management of PSIs in LS as shared by various authors in the literature. We have given emphasis to atypical mycobacteria, which are emerging as a common etiological agent for PSIs in LS. Although the existing literature lacks consensus regarding PSI management, the complication can be best avoided by strictly abiding by the commandments of sterilization techniques of the laparoscopic instruments with appropriate sterilizing agent.

Core tip: Laparoscopic surgery has brought about a paradigm shift in the approach to various surgical diseases. Port site infection, although infrequent, is a complication which can undermine the benefits of the surgery. The complication is not life threatening, but definitely adds a lot to the morbidity, affects the postoperative quality of life, and spoils the aesthesis of the surgery. Leaving aside the bacterial causes, the rapidly emerging multidrug resistant atypical mycobacteria are a constant threat. By doing a thorough review of this topic, this paper aims to present the relevant literature regarding the diagnosis, currently available treatment options and commandments to prevent the occurrence of this somewhat preventable complication.

INTRODUCTION

Rapid growths in health care technology have given the surgeon the power of not only treating diseases surgically but also limiting surgical invasiveness. The greatest example is minimal access surgery (MAS) also commonly termed laparoscopic surgery (LS) or keyhole surgery, which has caused a paradigm shift in the approach to modern surgery, by limiting the access related morbidities.

LS involves the use of reusable metallic or disposable plastic trocars inserted through small skin incisions or ports made on the skin away from the site of surgery. This ports form the portal of entry to perform the surgical procedure by means of specially devised instruments and telescope. It has gained popularity due to better aesthesis, lesser pain, early ambulation and discharge from the hospital with early return to work, minimizing the financial burden to the patient. Ever since Philips Mouret reported the first laparoscopic cholecystectomy in 1987, the approach has been adopted for many other surgical procedures including appendectomy, herniorrhaphy, colonic surgery, gastric surgery, urological and gynaecological surgery[1-5]. This is because of the combination of advancement in technology with the increasing acceptance of MAS by patients, which has led to the expansion of the horizon of LS.

LS, however, has its package of unique complications. One such complication, which is preventable although, is the port site infection (PSI). PSI soon erodes the advantages of LS, with the patient becoming worried with the indolent and nagging infection and losing confidence on the operating surgeon. There

occurs a significant increase in the morbidity, hospital stay and financial loss to the patient. The whole purpose of MAS to achieve utmost cosmesis is turned into an unsightly wound, and the quality of life of patients is seriously affected.

In this article we review the current literature regarding the incidence, clinical presentation, etiopathogenesis, management and methods of prevention of PSI in LS. We emphasize on the management of PSI due to the emerging rapid growing atypical mycobacteria that do not respond to the standard anti-tubercular drugs.

Incidence of PSIs

No surgical wound is completely immune to infections. Despite the advances in the fields of antimicrobial agents, sterilization techniques, surgical techniques, and operating room ventilation, PSIs still prevail. Incidence of SSI after elective laparoscopic cholecystectomy is less than that after open elective cholecystectomy due to shorter length of incision[6]. The technique of primary port entry to the peritoneum does not show any difference in umbilical PSIs in patients undergoing laparoscopic cholecystectomy[7]. The umbilical PSI rate in LS has been reported to be 8% with 89% of the infections occurring after laparoscopic cholecystectomy, whereas 11% after laparoscopic appendectomy[8]. Francis *et al*[9] studied the factors predicting 30-d readmission after laparoscopic colorectal cancer surgery. Out of 268 patients in their study who underwent laparoscopic colorectal surgery, 48 (18%) were readmitted with surgical site infection (SSI)[9]. Several other authors have found that SSI rate is much higher in conventional surgical procedures than in MAS[10-12]. The immune functions are less affected in LS as compared to open surgery[13]. The incidences of PSI in laparoscopic cholecystectomy as per various studies[14-22] are illustrated in Table 1.

SSIs and PSIs

SSIs are infections consequent to the surgery that are present within a month of the operative procedure. Surveillance in surgeries, such as breast, cardiac, cranial, spinal and bone surgeries, with use of prosthetic material, extends to 90 d after surgery[23-25].

PSI is a type of SSI but limited to LS. The same criteria for SSIs are applicable to PSIs, but the infections are limited to superficial and deep surgical sites only as detailed below.

According to the definitions developed by the United States Centre for Disease Control (CDC), SSIs were categorized into[25]: (1) Superficial SSIs which involve skin and subcutaneous tissue; (2) Deep SSIs which involve fascia and muscle layers; and (3) Organ/Space SSIs.

Wounds are classified as (as per CDC criteria for SSI 2015)[25]: (1) Clean: A surgical wound that is neither exposed to any inflamed tissue nor has breached the gastrointestinal, respiratory, genital, or uninfected

Table 1 Studies showing frequency of port site infection following laparoscopic cholecystectomy

No.	Ref.	Year of publication	Type of study	Total number of patients	Frequency of infection
1	Karthik *et al*[14]	2013	Prospective	570	10 (1.8%)
2	Mir *et al*[15]	2013	Prospective	675	45 (6.7%)
3	Yanni *et al*[16]	2013	Prospective	100	4 (4%)
4	Taj *et al*[17]	2012	Observational	492	27 (5.48%)
5	Yi *et al*[18]	2012	NA	400	11 (2.75%)
6	Triantafyllidis *et al*[19]	2009	Retrospective	1009	14 (1.39%)
7	Chuang *et al*[20]	2004	NA	420	6 (1.4%)
8	Shindholimath *et al*[21]	2003	Prospective	113	7 (6.3%)
9	den Hoed *et al*[22]	1998	Prospective	189	10 (5.3%)

NA: Not available.

urinary tract; (2) Clean-Contaminated: Surgical wounds where there is controlled entry into the gastrointestinal, respiratory, genital, or uninfected urinary tract with minimal contamination; (3) Contaminated: Fresh wounds related to trauma, surgical wounds with major breach in sterile technique or gross contamination from the gastrointestinal tract, and incisions through nonpurulent inflammatory tissues; and (4) Dirty or Infected: Old wounds following trauma having devitalized tissue and surgical procedure performed in the presence of active infection or visceral perforation.

Most of the surgical procedures done by laparoscopy belong to Classes 1 and 2 wounds. The human body hosts a variety of microbes which can cause infections. When the host systemic immunity is suppressed due to any disease, medications or disruptions of the integrity of the skin or mucous membranes secondary to surgical insult, patients' own commensal microbial flora may cause infection. The PSIs in LS manifest in the form of seropurulent discharge from the port sites with surrounding skin inflammation or symptoms related to the organ/space infection.

The active surveillance for PSIs in LS remains a challenge, due to the early discharge and day care setting[10,12]. In the absence of post-discharge surveillance, it is estimated that a third of all SSIs will be missed[26]. The reported incidence of SSIs varies in various regions of the world. The reported incidence of SSIs in a recent article from Turkey was higher than the CDC National Healthcare Safety Network (NHSN) rates[27]. Hence, the actual incidence of the PSIs may be much higher than revealed.

There is a higher incidence of superficial incisional SSIs as compared to that of deep incisional SSIs in LS[12]. The PSI after a LS should be promptly diagnosed and treated appropriately. Although it may not be possible to achieve zero percent PSI, every attempt should be made to prevent it. Insight into the pathophysiology of incision site infections, pathogens involved and knowledge of the appropriate antibiotic is essential for successful management of PSI in LS.

Risk factors for PSIs
A number of contributing factors are somewhat responsible for the emergence of postoperative PSIs.

Antibiotics always may not be the answer to this problem. Thus, using them irrationally, as is often done will only result in the emergence of multidrug resistant microbes. The majority of the reports of postoperative wound infection are of SSIs. PSIs following LS have been less reported. The risk factors for SSIs, however, may be applicable to PSIs.

Preoperative stay in hospital: Lilani *et al*[10] reported a significant increase in the incidence of SSIs with preoperative stay of more than 2 d for open surgical procedures.

Duration of operation: The study by Lilani *et al*[10] reported a nil infection rate in surgeries of less than 30 min duration. There was a significant increase in SSIs for operations of prolonged duration for two hours or more.

Other factors: Obesity, prophylactic antibiotics, and drains have no effect on the rate of SSIs following laparoscopic cholecystectomy[28]. Factors like emergency/multi-procedure surgery and surgery in acutely inflamed organs adversely affect the rate of SSIs[20,22]. The risk of SSIs increases in patients with a history of nicotine or steroid usage, diabetes, malnutrition, long preoperative hospital stay, preoperative colonization of nares with *Staphylococcus aureus*, or perioperative blood transfusion[29,30].

PSIs are more common in the umbilical port[12]; the infection rate may depend upon the port through which the specimen is extracted. The infected specimen should be removed in an endobag in order to prevent wound infection and accidental spillage of contents or occult malignant cells. An improvised endobag can be prepared from a simple surgical glove which is easy to make, cheap, readily available and disposable[17].

Microbial flora causing PSIs in LS
PSIs occur due to exposure of surgical wound to microbes which may be from an endogenous or exogenous source. The source of endogenous flora usually is from the patient's skin, mucous membranes or any of the viscera. The exogenous flora may be from any contaminated sources present in the sterile surgical

field including surgeon and team, instruments, room air, *etc*[31].

The pathogenic organisms causing SSIs differ with the surgical procedure performed. Clean surgical wounds usually harbor *Staphylococcus aureus* which may have an exogenous origin or may be from the patient's native flora. Infections in clean-contaminated, contaminated and dirty surgical wounds are poly-microbial, resembling the endogenous flora of the target organ[32].

PSIs are of two broad varieties based on the timing when they are present. The more common type manifests early, within a week of the surgical procedure. Gram positive or negative bacteria are the usual offending organisms which are contracted from the native skin or infected surgical site. They usually respond well to the commonly used antimicrobial agents. The other variety is caused by rapid growing atypical mycobacterium species, which has an incubation period of 3 to 4 wk. They show a poor response to the usual antimicrobial agents[33].

Non-mycobacterial isolates: Kownhar *et al*[34] reported superficial SSIs as the most common in both MAS and open surgical procedures, with *Staphylococcus aureus* as the most common isolate. They studied the SSIs and found various common bacteria isolated as *Staphylococcus aureus* (37%) and *Pseudomonas aeruginosa* (37%), followed by *Klebsiella pneumonia* (8%), *Acinetobacter spp*. (3.2%), *Proteus spp*. (4.8%), *Escherichia coli* (4.8%), *Citrobacter freundii* (1.6%), *Edwardsiella tarda* (1.6%) and *Enterococcus faecalis* (1.6%). *Klebsiella sp.* is the most common offending organism in deep SSIs irrespective of the surgical approach[34]. Usually hospital acquired skin flora cause superficial SSIs. Organisms causing deep SSIs usually are endogenous in origin or may be the skin commensals which reach the fascia or muscle layers through surgical incision[23]. *Bacteroides sp.* was the predominant flora (60%) causing SSIs, in a study reported by Wolcott *et al*[35]. *Bacterioides fragilis* may originate from intraoperative visceral spillage. Mir *et al*[15] in their series found pseudomonas (42.2%) as the common offending organism in PSIs following laparoscopic cholecystectomy. They found that the organisms isolated were resistant to commonly used antibiotics in their hospital[15].

Mycobacterial isolates: Several reports have established the role of rapid growing mycobacteria (RGM), particularly *M. fortuitum* and *M. chelonae* which together have been termed as *M. fortuitum-chelonae complex* that is known to cause disease in humans as well as animals[36]. The endospores of this non-tuberculous mycobacterial (NTM) complex are usually considered saprophytes which colonize in sewage, soil and even tap water. This often cause localized skin infections 3-4 wk post-surgery[37,38]. The NTM complex can cause disseminated disease in immunosuppressive diseases. These atypical mycobacteria have a predilection to involve the skin and subcutaneous tissue. *M. chelonae* and *M. abscessus* have similar characteristics, and hence together were addressed as *M. chelonae/abscessus* group. Vijayaraghavan *et al*[39] reported an outbreak of laparoscopic PSIs due to *M. chelonae* at their center. They had 145 PSIs in 35 patients in a period of 6 wk. The contaminating source was found to be the water being used for washing instruments after chemical disinfection[39]. A series of eight cases of port site tuberculosis after laparoscopy was reported by Ramesh *et al*[40] from India, caused by *M. tuberculosis*.

A case of PSI following laparoscopic cholecystectomy caused by *M. flavescens* has been reported[41]. Duarte *et al*[42] reported an epidemic (74 cases) of postsurgical infections in Brazil, due to *M. massiliense*, after video assisted surgery, which had similar characteristics to *M. abscessus*. Recently, there have been reports of rapid growing mycobacterial infection following laparoscopic gastric banding in obesity[43,44]. Atypical mycobacteria infections following surgery, although rare, are known to occur when a prosthetic material has been used[45].

Clinical presentations of PSIs
Wound discharge and erythema around the port site are the most common presentation of non-mycobacterial infection usually occurring within a week of the surgery. They are usually limited to the skin and subcutaneous tissue[12,14]. There may be surrounding tissue inflammation with pain or tenderness and low grade fever[31].

The delayed type of presentation commonly caused by mycobacteria manifests nearly a month after surgery, in the form of persistent multiple discharging sinuses or lumps/nodules, not responding to antibiotics. There may be pigmentation and induration at the port site starting in a single port and spreading to others.

There are five clinical stages of atypical mycobacterial PSI[46].

First stage: A tender nodule appears in the vicinity of the port site, and its usual timing of appearance is around four weeks following the surgery.

Second stage: Increase in the size of the nodule, and increased tenderness of the site along with other signs of inflammation with eventual formation of a discharging sinus.

Third stage: Reduced pain sensation following discharge of the purulent material and necrosis of the skin surrounding the port site.

Fourth stage: Chronic sinus discharging white or serous fluid.

Fifth stage: Hyper-pigmentation of the skin surrounding the sinus and appearance of multiple nodules at different places.

Diagnosis of the etiological agent with early management

Early PSIs: Gram stains and culture sensitivity of the pus from port site wounds are to be taken. The swabs obtained are processed aerobically and anaerobically by standard methods to find the non-mycobacterial isolates. *Staphylococcus aureus* strains are usually isolated from clean wounds. Their status of β-lactamase production and methicillin resistance needs to be assessed[10]. Daily dressing, cleaning of the wound and a course of empirical antibiotic are started. Specific antibiotics as per the culture and sensitivity report are to be given subsequently. Drainage and debridement may sometimes be required for assisting in wound healing. There are reports of port site abscess presenting as discharging sinus months after surgery due to retained stone at the port site. Wound exploration and removal of the stone is necessary for the healing of such wound[47,48]. Samel *et al*[49] reported a case of gas gangrene of the abdominal wall due to *Clostridial* agents centering around right lateral port following laparoscopic cholecystectomy. There are also reports of life threatening necrotizing fasciitis of the abdominal wall following LS. Significant erythema and wound discharge around the port site along with fever are signs of necrotizing fasciitis[50,51]. A high grade of suspicion and aggressive management are necessary to deal with these life threatening bacterial infections.

Delayed PSIs: Chaudhuri *et al*[46] have shown a raised C-reactive protein level without leukocytosis and a normal differential count in patients with atypical mycobacterial infection[46,52]. Tissue or fluid obtained by biopsy or aspiration needs to be processed for baciloscopy, culture in Lowenstein-Jensen medium and BACTEC technique (Becton-Dickinson Diagnostic Instrument Systems, Sparks, Md). Isolation of the atypical mycobacteria by tissue culture is possible, although it takes time to grow. Moreover, maintaining the stringent environment for its culture is difficult. The most accurate method for rapid presumptive identification of *M. chelonae* is detecting resistance to polymyxin B disc (300 μg)[53]. The routine culture of pus does not grow any bacteria. The diagnosis is often based on the clinical signs and a high index of suspicion[52]. In case of growth of the organism, the isolate is to be confirmed by either biochemical reactions or the more recent nucleic acid amplification tests. Other investigations like tissue culture, real time-PCR, and serology for antitubercular antibody can support the diagnosis[53]. Even these reports are not full proof, as these tests could give a false positive result. The histopathological examination at times may reveal chronic granulomatous inflammation, comprising of epitheloid cells and lympho-plasmacytic infiltration[40].

Treatment of PSIs

Early PSIs, with bacterial isolates, are best managed with local wound care and antibiotics as per antibiogram. The study by Lilani *et al*[10] in clean and clean contaminated cases revealed *Staphylococcal sp.* as the most common isolate, which was resistant to penicillin. The isolates of *Pseudomonas aeruginosa* were totally resistant to gentamicin[10]. Mir *et al*[15] found most of the isolated strains of organisms causing SSI in elective laparoscopic cholecystectomy were resistant to antibiotics used in the hospital. They found the *Pseudomonas sp.* to be sensitive to imipenem in 89.47% of cases, but there was complete resistance to the combination of ampicillin and sulbactam and ceftrixone[15].

Management of PSIs with atypical mycobacteria lacks consensus. They respond poorly to first line anti-tubercular drug treatment. Second line anti-tubercular drugs including macrolides (clarithromycin), quinolones (ciprofloxacin), tetracyclines (doxycycline) and aminiglycosides (amikacin and tobramycin) in various combinations have been used with promising results[37,46,54]. Macrolides including clarithromycin are the only group of antimicrobials active against *M. chelonae* and *M. abscessus*[54]. *Mycobacterium fortium-chelonae* complex has shown resistance to antibiotics because of mutation in the porin channels present in the bacterial wall, which is the site for entry of antibiotic molecules for antimicrobial activity[46,55]. Linezolid was found to be active against *M. chelonae* and has been successfully used for treatment, alone or as combination therapy[56]. The various antibiotics effectively used against the mycobacterial PSIs, as reported in various studies, are described in Table 2.

Prevention of PSIs

The million dollar question is why at all there occur PSIs in clean and clean contaminated wounds after LS. Is it because of the contamination from the endogenous source or through exogenous source? The endogenous source of infection cannot be avoided. But the incidence of PSIs after LS due to endogenous cause can be reduced by using sterile endobag for specimen retrieval.

The exogenous source of infection, however, is avoidable. Non-tuberculous mycobacteria may be present in water from various sources and soil which can contaminate hospital instruments. A breach in sterilization protocol of laparoscopic instruments is the most common cause of PSI with atypical mycobacteria[46]. The infection with atypical mycobacteria is usually limited to the laparoscopic procedure, as most of laparoscopic instruments are not autoclavable because of the heat sensitive outer insulation sheath. Moreover, as most of the laparoscopic instruments have multiple joints and crevices, where blood and tissue can collect. Frequent use of the instrument without optimal cleaning potentially results in contamination with organisms such as atypical mycobacteria. Endospores in the contaminated instrument get deposited in the subcutaneous tissue, which germinate in three to four

Table 2 Different antibiotics effectively used against *Mycobacterial sp.* in port site infections

Ref.	Type of study	Mycobacteria isolated	Treatment given
Ramesh *et al*[40]	Case series in 8 patients	*M. tuberculosis*	Standard first line antitubercular regimen
			Rifampicin, isoniazid, pyrazinamide and ethambutol for 2 mo followed by rifampicin and isoniazid for 9 mo
Chaudhuri *et al*[46]	Case series in 19 patients	Clinically suspected atypical mycobacterial infection. No isolates in culture	Clarithromycin and ciprofloxacin (500 mg each, twice daily) for 28 d to 3 mo
			For persistent local nodules, direct injection of amikacin injections into the nodules daily for 5 d (500 mg twice daily)
Verghese *et al*[37]	Case report	*M. chelonae*	Amikacin 750 mg/d and azithromycin 500 mg BD for 2 wk, followed by linezolid 500 mg BD and azithromycin 500 mg BD for 6 wk
Duarte *et al*[42]	Case series in 74 patients	*M. massiliense*	Sensitive to amikacin and clarithromycin, but resistant to ciprofloxacin, cefoxitine and doxycycline
Sethi *et al*[41]	Case report	*M. flavescens*	Ofloxacin and amikacin for 6 mo
Shah *et al*[61]	Case series in 7 patients	*M. fortuitum* *M. chelonae*	Clarithromycin and ciprofloxacin (500 mg each, twice daily) for 6-9 mo
Rajini *et al*[62]	Case report	*M. chelonae*	Clarithromycin 500 mg BD and doxycycline 100 mg OD for 4 wk

weeks to produce clinical signs and symptoms[42]. A study by Lorena *et al*[57] on *M. massiliense* BRA100 strain showed that it is resistant to even higher concentration of glutaraldehyde (GTA, 7%). Hence, they proved that GTA may not be effective for RGM. Other liquid sterilizing agents like orthophthaldehyde and per acetic acid may substitute GTA for high level disinfection with good efficacy[57].

Ten commandments for preventing PSI[58-61]: (1) Use of disposable trocars and instruments, and adequate availability of properly sterilised reusable trocars to cover all the surgical procedures in a day; (2) Use of autoclavable laparoscopic hand instruments; (3) Use of instruments with good ergonomics, limited joints and facility for proper cleaning of the debris collected in its crevices; (4) A proper cleaning of the instrument is best achieved by ultrasonic technology. Use of autoclaved water for cleaning the instruments after dismantling; (5) Proper guidelines should be followed regarding the concentration, contact time and cycles of use for instrument sterilization with liquid sterilizing agents; (6) Use of plasma sterilizer or ethylene oxide in between the consecutive surgery for instrument sterilization; (7) Avoiding inter-departmental sharing of instruments, such as using instruments used for gynecological or urological procedures; (8) Avoiding spillage of bile or gut content in the operative area or the port site; (9) Use of non-porous specimen retrieval bags for retrieving the specimen; and (10) Thorough irrigation and cleaning of the port site before wound closure.

CONCLUSION

PSI, although infrequent, can be a frustrating complication in MAS, both for the patient as well as the operating surgeon. Leaving aside the bacterial causes, the emerging rapid growing multidrug resistant non-tuberculous mycobacteria are a new threat to the surgical fraternity. Strictly abiding by the commandments of cleaning and sterilization of the laparoscopic instru-

ments, with the appropriate sterilizing agent, the complication can be best avoided.

This review is likely to aid in understanding the relevant studies regarding the appropriate management of PSIs in LS. All the cases of PSI, especially of the atypical mycobacterium should be notified to know the exact incidence, etiology and the sensitivity pattern to various antibiotics. Macrolides, quinolones and aminoglycosides do show promising activity against the atypical mycobacterium. Further research is needed to find out appropriate guidelines for the diagnosis and treatment of this emerging problem.

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