MICROBIOLOGY FOR SURGICAL INFECTIONS

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DIAGNOSIS, PROGNOSIS AND TREATMENT

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Preface

Surgical infections represent a diverse group of diseases, which despite advances in techniques of surgery and anesthesia, the presence of modern equipment and improving perioperative health care in hospitals, still lead to significant morbidity and mortality. The rapid increase in levels of antibiotic resistance and the appearance of new multidrug-resistant pathogens makes it necessary to constantly update recommendations on the management of infections, and the present book reviews the most recent guidelines on the prevention, diagnosis and treatment of surgical infections of different locations, with particular emphasis on intra-abdominal, cardiovascular and skin and soft tissue infections.

The scope of the chapters encompasses reviews of *in vitro* studies of the principles of prevention of surgical infections, such as the evaluation of bacterial adherence to surgical materials, as well as clinical studies on the management of a broad spectrum of surgical infections, including anastomotic leakage after colorectal surgery, infectious complications of dialysis access, infective endocarditis, necrotizing soft tissue infections, diabetic foot infections and others. In addition, alternative methods of antimicrobial treatment of surgical infections are also discussed in several chapters, such as *in vitro* and *in vivo* studies on wound healing and anti-infectious properties of plant extracts, essential oils, and zootherapeutics methods.

Although the most common cause of surgical infections is bacteria, the role of other microorganisms should not be disregarded. In consideration of this fact, one chapter is also devoted to understanding diagnostic approaches for invasive mycoses in surgical patients, as this pathology has attracted much attention in recent years.

Selection of the optimal treatment strategy is impossible without predicting a probable outcome of the infection based on a patient's laboratory and clinical parameters. Nowadays, there are a large number of studies dedicated to the development of scoring systems using modern statistical methods for assessment of the severity of a patient's state and for predicting the course and outcome in different surgical infections. Some such scoring systems have gained great popularity in the medical community, such as APACHE II (Acute Physiology and Chronic Health Evaluation II) system, SAPS (Simplified Acute Physiology Score), MPI (Mannheim Peritonitis Index), etc., and this book also summarizes studies of the efficacy of these and other scoring systems in the prognosis of surgical infections, particularly in secondary peritonitis.

The book explores current trends in the etiology and antibiotic resistance of pathogens causing different types of surgical infections; it discusses recent advances in diagnostic approaches in bacterial and non-bacterial surgical infections; it reviews methods of prognosis of the course and outcome of surgical infections; and it also summarizes recent guidelines for prophylaxis of infectious complications in surgery, and for improvement of diagnosis and treatment of surgical infections.

The book will be very useful to microbiologists, surgeons, infectious diseases specialists, researchers in surgery, clinical microbiologists, pharmacologists, and those who are interested in tackling the problem of antibiotic resistance.

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CHAPTER

1

Infection Control Measures for the Prevention of Surgical Site Infections

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CONSEQUENCES OF SURGICAL SITE INFECTIONS

It is as simple as this: The best you can do about surgical site infections (SSI) is not to let them happen in the first place. Today the occurrence of SSI represents one of the most severe complications in all types of surgical procedures, and it will have an enormous impact on the ongoing course of recovery of the affected patient. It leads to significantly increased morbidity and mortality of patients in various medical disciplines.[1–3] Besides their importance with respect to such clinical consequences, SSI should also concern hospitals and health care systems for economic reasons.[4,5] Depending upon the type of surgery, the prolonged length of stay (LOS) in the hospital may vary from 3 to 21 days.[1] According to a review of the literature on SSI in general[6] and to a recently published large estimation on SSI in orthopedics (412,356 total hip and 784,335 total knee arthroplasties) in particular,[7] SSI will roughly double the magnitude of the cost for a case patient. Based on the 2005 Healthcare Cost and Utilization Project National Inpatient Sample (HCUP NIS), which included 723,490 surgical patients with 6,891 SSI, the average LOS was 9.7 days and costs increased by $20,842 per admission. This leads to nearly 1,000,000 additional inpatient-days and $1,600,000,000 excess costs for the US alone.[8]

Evidence-based infection control guidelines for the prevention of SSI have been published, for example by the Hospital Infection Control Practices Advisory Committee (HICPAC) from the Centers for Disease Control and Prevention (CDC)[9] and by the Society for Healthcare Epidemiology of America (SHEA) in collaboration with the Infectious Diseases Society of America (IDSA) (Table 1.1).[10] This chapter provides an overview of patient-derived (endogenous) risk factors for SSI development, and summarizes the most

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TABLE 1.1 Summary of Evidence-based Recommendations of the Society for Healthcare Epidemiology of America (SHEA) for SSI Prevention

Recommendation	Grade
Use evidence-based standards when implementing prevention measures.	A-II
Control serum blood glucose levels; reduce glycosylated hemoglobin A1c levels to $<7\%$ before surgery, if possible.	A-II
Increase dosing of prophylactic antimicrobial agent for morbidly obese patients.	A-II
Encourage smoking cessation within 30 days before procedure.	A-II
No formal recommendation with respect to immunosuppressive medications; avoid them in the perioperative period, if possible.	C-II
Do not routinely delay surgery to provide parenteral nutrition.	A-I
Do not remove unless hair will interfere with the operation; if removal is necessary, remove by clipping and do not use razors.	A-II
Identify and treat infections remote to the surgical site before elective surgery.	A-II
Wash and clean skin around incision site; use an appropriate antiseptic agent.	A-II
Use appropriate antiseptic agent (e.g., an alcohol-based surgical hand antisepsis product) for a 2−5 minute preoperative surgical scrub.	A-II
Administer antimicrobial prophylaxis only when indicated in accordance with evidence-based standards and guidelines.	A-I
Administer antimicrobial prophylaxis within 1 hour before incision to maximize tissue concentration.	A-I
Select appropriate agents on the basis of surgical procedure, most common pathogens, and published recommendations.	A-I
Do not routinely use vancomycin for antimicrobial prophylaxis.	B-II
Stop prophylaxis within 24 hours after the procedure for all procedures except cardiac surgery (stop within 48 hours here).	A-I
Handle tissue carefully and eradicate dead space.	A-III
Control blood glucose level during the immediate postoperative period for patients undergoing cardiac surgery.	A-I
Adhere to standard principles of operating room asepsis.	A-III
No formal recommendation with respect to operative time; minimize as much as possible.	A-III
Adhere to ventilation, follow American Institute of Architects' recommendations for ventilation.	C-I
Minimize operating room traffic.	B-II
Use an approved hospital disinfectant to clean surfaces and equipment.	B-III
Sterilize all surgical equipment according to published guidelines; minimize the use of flash sterilization.	B-I
Perform surveillance for SSI.	A-II

(*Continued*)

TABLE 1.1 (Continued)

Recommendation	Grade
Provide ongoing feedback on SSI surveillance and process measures to surgical and perioperative personnel and leadership.	A-II
Perform expanded SSI surveillance to determine the source and extent of the problem and to identify possible targets for intervention.	B-II
Measure and provide feedback of SSI rates, antimicrobial prophylaxis, proper hair removal, and glucose control (for cardiac surgery)	A-III
Increase the efficiency of surveillance through the use of automated data.	A-II
Educate surgeons and perioperative personnel about SSI prevention.	A-III
Educate patients and their families about SSI prevention, as appropriate.	A-III

important infection control measures according to the time point of their implementation (before, during or after the operation on the patient).

INFECTION CONTROL MEASURES BEFORE THE START OF THE SURGICAL PROCEDURE

Patient-Derived (Endogenous) Risk Factors for Surgical Site Infections

Diseases. Some patients present with certain characteristics that will increase their risk of subsequent SSI acquisition. Unfortunately, a number of those endogenous risk facts cannot be influenced by proper infection control measures. This includes (but does not exclusively apply to) underlying diseases which increase the overall comorbiditiy burden such as cancer, cirrhosis and other liver diseases, congestive heart failure, coagulopathies, and chronic obstructive lung diseases,[7,11,12] patients with any kind of severe immune-suppression,[13] infants aged less than 1 year,[14,15] older patients aged more than 65 years,[16] a higher score on the American Society of Anaesthesiology (ASA) classification,[16,17] and patients with a need for surgical procedures in microbiologically contaminated areas as expressed by the primary wound contamination class.[18–20] Whenever staff recognizes one or more of the above mentioned risk factors, an increased awareness of potential SSI is necessary. In addition, there are several patient-derived risk factors that can, in fact, be positively influenced in principle. This may often be difficult, but is still worthwhile in terms of the patient's outcome. These modifiable characteristics will be discussed in more detail in the following sections.

Overweight. Overweight patients with an increased body mass index (BMI) show higher SSI rates than do patients with a normal body weight.[13,17,21,22] In a randomized prospective study in a group of 1,032 patients, Beldi et al.[23] showed that a BMI $> 30\,kg/m^2$ doubled the risk of an SSI. Tran et al. checked for SSI risk factors in 969 women after cesarean section: every five-unit increment in the BMI increased the odds ratio (OR) for an SSI by a factor of two.[24] Yeung et al. recruited a consecutive cohort of 210 patients from varicose vein surgery. Nine of 53 patients (17.0%) with a BMI $\geq 30\,kg/m^2$ suffered from an

SSI, compared to 0.7of the remainder.[25] Obese patients should therefore be encouraged to lose weight before elective surgical procedures are performed on them. It is noteworthy that cachexia also worsens the postoperative outcome. Thus, one should aim for a BMI within normal limits.[26]

Diabetes. The risk of an SSI in patients who suffer from diabetes mellitus (DM) may be dramatically increased due to high intra-operative blood glucose levels and poor microcirculation.[27] Bykowski et al. calculated the OR for the risk of SSI in diabetic patients to be as high as 2.8.[28] Similarly Davies found a SSI infection rate after mastectomy in patients with DM of 19.0% vs. 11.2% in patients without DM[17] and, even more striking, 18.75% vs. 1.97% in adult spinal trauma patients.[16] Ensure that blood sugar levels remain within the physiological range.[29]

Smoking. Smokers, too, are more likely to acquire SSI.[22] In a large single-center retrospective review of 8,850 cases, smoking status even tripled the risk of an SSI (OR = 3.0).[28] Sorensen and coworkers performed a systematic review and meta-analysis of 479,150 patients in 140 cohort studies. The pooled adjusted OR for a SSI in smokers was 1.79.[30] Thus the prevention of SSI is just one more good reason among many others to encourage patients to quit smoking.

Infection. Patients who already suffer from a previous SSI infection or an infection at another body site are at higher risk of SSI thereafter. Webster et al. showed in 827 patients undergoing several kinds of elective and emergency surgery that the presence of any previous SSI was associated with an adjusted OR of 2.5.[21] Similar findings are reported by Xing and coworkers in a systematic review of evidence-based independent risk factors for SSI in 226 patients after spinal surgery.[31] Thus, it is strongly recommended that any existing SSI or other infection is cured before performing an elective surgical procedure, if possible.

Colonization. Nasal colonization of the patient by *Staphylococcus aureus*, both methicillin-resistant (MRSA) and methicillin-sensitive (MSSA), increases the risk of subsequent SSI.[32–34] Ramirez et al. found that 6.4% of the 1,137 screened patients were MRSA positive. In 70% of all previously colonized patients, MRSA was also cultured from the wound after major gastrointestinal surgery.[35] Donker et al. calculated a 10-fold increased risk for the development of SSI in patients with *S. aureus* nasal carriage compared to non-carriers in vascular surgery.[36] Thus patients should be screened before elective surgical procedures in order to detect any *S. aureus* colonization – preferably before hospital admission. In colonized patients, appropriate decolonization measures are recommended – such as application of nasal mupirocin ointment, antiseptic mouth wash and whole-body antiseptic scrubs.[37–40] These decolonization measures should be continued after the surgical procedure if necessary.

Hospital-Derived (Exogenous) Risk Factors for Surgical Site Infections

A well-known independent risk factor for SSI occurrence is a prolonged stay by the patient within the hospital prior to surgery; this increases the risk of subsequent SSI occurrence.[21,41] A recently published systematic review on risk-adjusted models for SSI by Gibbons et al.[42] identified the duration of preoperative stay as the most common risk factor in coronary artery bypass graft surgery, large and small bowel surgery, hip and knee prosthesis, and vascular surgery. As a consequence, the time frame between admission of the patient and start of the surgical procedure should be as short as possible.

Expertise. Of course the rate of SSI also depends upon the expertise of staff.[43] A total of 117 hospitals were compared with respect to their trainee-to-bed ratio in the latest American College of Surgeons-National Surgical Quality Improvement (ACS-NSQIP): outlier hospitals with extraordinary high SSI rates also had a significantly increased proportion of trainees among their staff compared to outlier hospitals with extremely low SSI rates.[44] In addition, Meyer et al. recently showed in a comprehensive multivariate analysis of 120,564 procedures in 206 departments that the larger the annual number of specific procedures in a hospital, the lower the resulting SSI rates will be; departments that performed less than 50 knee replacements per year ended up with a SSI rate of 1.81% compared 0.79% in hospitals that performed more than 100 operations of that kind per year. Corresponding data for hip replacement and arthroscopy were 1.11% vs. 0.84% and 2.16% vs. 0.24%, respectively.[45]

Devices. Urinary tract catheters (UTC)[12] and other medical devices[15] may be associated with higher SSI rates. Lonjon et al. report an SSI rate of 2/99 (2.0%) in patients after spine surgery when an UTC was in place for less than five days compared to an infection rate of 4/31 (12.9%) in patients with an UTC for more than five days.[16] Similar results are reported by Bucher et al. in 159 children; usage of an UTC (OR = 3.56) and implanted medical devices (OR = 3.05), respectively, significantly increased the risk for a SSI.[46] Note that the application of total parenteral nutrition may also significantly increase the risk of SSI.[15] It seems reasonable to check for the correct indication of existing medical devices carefully, and to remove them if they are no longer required.

Shaving. Hair should only be removed if it interferes with the site of incision. At present the use of clippers (instead of shaving with razors) seems to be the most appropriate way of hair removal for SSI prevention. If razors are used, keep the time frame short between shaving and incision. Ng et al. used posters and enhanced prenatal education for obstetric patients before cesarean section. The rate of hair self-removal decreased significantly from 41% in 2008 to 27% in 2011. Concurrently, a 51% reduction was seen in the SSI rate following cesarean section.[47] Thus it is strongly recommended that patients are discouraged from shaving themselves on the day before admission.

Antiseptic shower. Preoperative antiseptic showering of the patient e.g., using chlorhexidine gluconate, may be helpful in the prevention of SSI, as it reduces the number of bacteria in the residual skin flora. Studies exist that show a benefit of a total body shower of the patient shortly before the surgical procedure (preferably pre-admission or at the evening before surgery, using an antiseptic lotion).[48] A systematic review of this topic by Kamel et al. suggests that skin antiseptic preparations may be effective in preventing SSI.[49] However, up to now overall data on this measure are sparse, and a meta-analysis by Chlebicki et al.[50] and a recently updated Cochrane review including 7,791 patients failed to show a statistically significant reduction in SSI after bathing with chlorhexidine compared with placebo (risk ratio (RR) = 0.91).[51]

INFECTION CONTROL MEASURES DURING THE SURGICAL PROCEDURE

Antibiotic prophylaxis. Due to conflicting results, the use of antimicrobial prophylaxis (AP) is currently controversial. There are numerous studies that show a drop in the SSI rate when AP is administered properly and multiple Cochrane reviews have been carried out on this topic. The pooled results of a total of nine studies including 2,260 patients who underwent surgery for breast cancer demonstrated that AP significantly reduced the incidence for a SSI with a RR of 0.71.[52] Single dose antibiotic prophylaxis also significantly reduced deep SSI (RR = 0.40) after surgery for closed fracture fixation in 8,447 participants in 23 studies.[53] Recently Ott et al. showed that application of perioperative AP independently reduces the risk for a SSI after arterial vascular surgery by as much as 80%.[13] Darouiche showed that systemic AP significantly reduced the incidence of SSI (RR = 0.14) when performing cardiac implantable electronic device implantation.[54] On the other hand, there are just as many studies that failed to show a benefit of AP, including analysis of patients who have undergone plastic surgery, elective laparoscopic cholecystectomy, neurosurgery, and hernia repair.[55–58] A single-center retrospective review by Bykowski et al. calculated a SSI rate of 0.54% in 2,755 patients who received AP compared to a SSI rate of 0.26% in 6,095 patients who did not.[28] The choice to use AP, and which antimicrobial substance to employ, depends upon the kind of surgical procedure, nasal screening results and existing infections elsewhere,[12,59] but vancomycin is generally not an appropriate substance, and is thus explicitly not recommended for this purpose.[60] No recommendation can be made regarding the use of antimicrobial substances that cover a broad spectrum of Gram-negative and/or anaerobe bacteria as there is still a lack of clinical data. Timely application may also be important.[61–63] It is recommended to aim for highest concentrations of the antimicrobial substance in the tissue at the time point of incision. Brown et al. showed remarkable decline in the SSI rates from 10.8% in 2010 to 2.8% in 2011 after a change of timing of AP application in cesarean section.[64] Once again, contradictory results have also been published. Hawn et al. compared timely application to untimely application of AP in 9,195 elective procedures (orthopedic, colon, and vascular) performed in 95 hospitals. Corresponding SSI rates were 4.6% and 5.8% respectively in a bivariable unadjusted analysis. Use of multiple dosages may be necessary in some cases, especially if the duration of the surgical procedure is prolonged.[53,65,66] AP is discontinued (usually within 24 hours) after the end of surgery, as prolonged AP will not further decrease the risk of an SSI.[67] It might become essential to increase the dosage in order to adapt AP to overweight patients.[68–70] Forse et al. reported a drop in the SSI rate from 16.5% to 5.6% after the dosage of cefazolin PA was changed to 2 g in morbidly obese patients undergoing gastroplasty, compared to 1 g in normal weight patients.[71]

Air flow systems. Laminar air flow (LAF) is often used as a measure for SSI prevention, on the assumption that driving out potentially contaminated room air by directed, filtered air from the ceiling would lower the number of pathogens in the operation area, and thus infections of the patient. However, a recently published study by Breier et al. failed to detect any advantage of LAF use in patients undergoing 20,554 knee, 33,463 elective and 7,749 urgent hip prostheses regardless of the size of the LAF ceiling.[72] Diab-Elschahawi and coworkers showed that a LAF ventilation system does not provide bacteria-free conditions at the surgical site and on the instrument table.[73] A meta-analysis by Gastmeier et al. even questions LAF use in principle, as SSI rates turned out to be higher when LAF systems were used.[74]

Instruments. All medical equipment that comes into contact with primary sterile body sites must previously be sterilized itself.[75] This includes but is not limited to surgical instruments, rinse liquids, suture material, and wound dressings. There are hardly any randomized control trials that address this question for ethical reasons, but several nosocomial outbreaks are reported to have been due to insufficient sterilization processes. For example Dancer et al. experienced such an outbreak involving 15 orthopedic patients following metal insertion, and five ophthalmology patients who developed endophthalmitis. SSIs caused by coagulase-negative staphylococci and *Bacillus* spp. were traced to post-sterilization contamination of sets containing surgical instruments.[76] Rutala et al. published a study of an outbreak of podiatric infections due to *Proteus mirabilis* following outpatient surgery. Bone drills served as the reservoir for the organism, because the gas sterilization procedure that was used to sterilize the drills was found to be deficient.[77]

Clothing. It is more or less common sense that people who participate in a surgical procedure directly at the patient's site need to wear a sterile gown,[78] sterile gloves,[79] and a surgical face mask[80,81] in order to maintain sterile barrier precautions and also to protect themselves from infectious agents that may derive from the patient. It is also recommended to keep the overall number of people in the surgical theater to a minimum, because the quality of the operating room environment is mainly affected by the number of persons in it.[82–84] Talking by the participating staff during the operation should also be minimized, as it is well known that this will promote pathogen spread via the lateral spaces between face mask and the face,[85,86] especially when worn by bearded surgeons.[87] In addition, a thorough surgical hand scrub is highly recommended before each surgical procedure. Parienti et al. could not show a significant difference between the groups using alcoholic hand rub or antiseptic soaps including povidone-iodine or chlorhexidine gluconate. The corresponding SSI rates did not differ at all (2.44% vs. 2.48%), but the alcohol-based hand rub was better tolerated, producing less skin dryness and irritation.[88] A potential influence of nail polish on the number of bacteria on the skin post-scrub – and thus on the SSI rate – cannot be excluded, as the amount of data available is still scarce.[89]

Scrub. Antiseptic is usually administered to the patient's skin at the incision site immediately before the cut is performed. In a prospective observational study in 1,014 patients, Tschudin-Sutter et al. showed that there was no risk of SSI from residual bacteria after disinfection of the preoperative site with povidone-iodine-alcohol.[90] Similar findings are reported by Boston et al.[91]: in their study povidone-iodine for preoperative skin antisepsis was found to be protective against SSI acquisition (OR = 0.16). A systematic review and meta-analysis by Lee et al. on nine randomized controlled trials with a total of 3,614 patients revealed that chlorhexidine/(+/− isopropyl alcohol) antisepsis was associated with significantly fewer SSI incidences (RR = 0.64: CI95%:0.51–0.80) than was iodine/(+/− isopropyl alcohol) antisepsis.[92] Thus proper skin disinfection at the site of incision by an appropriate skin disinfectant is strongly recommended. Skin areas with a higher amount of sebum may require a prolonged time for accurate antisepsis.

Surgical technique. Prolonging the surgical procedure increases the risk for SSI acquisition in most types of surgical procedures, including coronary artery bypass, gastric surgery, total hip replacement, knee prosthesis, large bowel surgery, and vascular surgery.[93] SSI rates after 2,644 procedures of femoral-popliteal bypass with autogenous vein were compared by Tan et al. on the basis of operative duration quartiles. Corresponding SSI rates were 6.3%, 9.0%, 10.1%, and 13.9%.[94] Similar findings have been reported in many studies by other authors.[14,44] Proper surgical technique is itself of great importance.[23,95] Minimize the amount of necrotic tissue,[96–98] avoid excessive bleeding during the surgical procedure,[16,99] and aim for an intra-operative blood glucose level of < 8 mmol/L.[29]

Implants. Foreign material such as implants may be inserted for different reasons during a variety of surgical procedures. Whenever this takes place, the risk of SSI increases dramatically.[83,100,101] Thus, the use of implants should be limited insofar as possible and maximum effort should be employed in terms of infection control measures. In addition, the use of material that has been impregnated with antimicrobial or antiseptic substances may be helpful and should therefore be considered.[102–105]

INFECTION CONTROL MEASURES AFTER THE END OF THE SURGICAL PROCEDURE

Wound dressing. Wounds are often dressed after the end of the surgical procedure. The decision on whether or not to do this, and on what type of wound dressing is used should be made individually. A recently published Cochrane review concludes that:

> "at present, there is no evidence to suggest that covering surgical wounds healing by primary intention with wound dressings reduces the risk of SSI or that any particular wound dressing is more effective than others in reducing the rates of SSI".[106]

A systematic review by Walter et al. of 16 controlled trials with 2,594 participants also found no evidence that dressing wounds reduces rates of SSI compared to uncovered wounds.[107] The frequency at which the dressings are changed should also be determined individually and will depend on the type of surgery, on the kind of wound dressing used, and on host factors of the patient.[108,109]

Drainage. Wound drainage systems are often used when wound secretion is expected. Akinyoola and coworkers observed no benefit in 65 patients from the routine use of wound drains following open reduction and internal fixation of femoral shaft fractures,[110] and a Cochrane review on this topic concluded that there is insufficient evidence from randomized trials to support or refute the routine use of closed suction drainage in orthopedic surgery.[111] So the decision on the use of wound drains should be made individually.[112,113] However, if inserted after surgery the duration of drain usage should be kept short. Arabshahi et al. followed 918 patients for 30 days postoperatively. A total of 77 cases of SSI were observed, and the presence of a wound drain was a significant risk factor for SSI development (OR = 2.2).[114] Rao et al. showed in a retrospective, case-control study on 57 deep SSIs out of 1,587 procedures that the OR increased by 1.6 for every day in which a drain was present.[115] Continuously check whether drainages that are currently in place are still needed or may be removed, and do this as soon as possible.[13,116]

Surveillance. Surveillance of nosocomial infections in general and of SSI in particular may significantly reduce infection rates. Data from the German National Nosocomial Infections Surveillance System (KISS) demonstrates the effect of active surveillance on SSI. Fourteen hospitals participated in KISS continuously for three years and performed 15,457 hip prostheses during this time. A multiple logistic regression analysis confirmed that the