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Improvement of Organization and Tactics of Treatment of Purulent Surgical Patients

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ABSTRACT

The aim of these guidelines is to provide a comprehensive range of evidence-based recommendations for interventions to be applied during the pre-, intra- and postoperative periods for the prevention of SSI, while also considering aspects related to resource availability and values and preferences. Although the guidelines are intended for surgical patients of all ages, some recommendations do not apply to the paediatric population due to lack of evidence or inapplicability and this is clearly stated The primary target audience for these guidelines is the surgical team, that is, surgeons, nurses, technical support staff, anaesthetists and any professionals directly providing surgical care.

Health care-associated infections (HAI) are acquired by patients while receiving care and represent the most frequent adverse event affecting patient safety worldwide. Recent work by the World Health Organization (WHO) shows that surgical site infection (SSI) is the most surveyed and frequent type of HAI in low- and middle-income countries and affects up to one third of patients who have undergone a surgical procedure. Although SSI incidence is lower in high-income countries, it remains the second most frequent type of HAI in Europe and the United States of America (USA).

Many factors in the patient's journey through surgery have been identified as contributing to the risk of SSI. Therefore, the prevention of these infections is complex and requires the integration of a range of preventive measures before, during and after surgery. However, the implementation of these measures is not standardized worldwide. No international guidelines are currently available and inconsistency in the interpretation of evidence and recommendations among national guidelines is frequently identified.

The aim of these guidelines is to provide a comprehensive range of evidence-based recommendations for interventions to be applied during the pre-, intra- and postoperative periods for the prevention of SSI, while also considering aspects related to resource availability and values and preferences. Although the guidelines are intended for surgical patients of all ages, some recommendations do not apply to the paediatric population due to lack of evidence or inapplicability and this is clearly stated The primary target audience for these guidelines is the surgical team, that is, surgeons, nurses, technical support staff, anaesthetists and any professionals directly providing surgical care.Pharmacists and sterilization unit staff will also be concerned by some aspects of these guidelines. The recommendations are also intended to be

used by policy-makers, senior managers and infection prevention and control (IPC) professionals as the basis for developing national and local SSI protocols and policies, and supporting staff education and training.

Guideline development methods

The guidelines were developed according to the processes described in the WHO Handbook for guideline development issued in 2014. In summary, the process included:

1) identification of the primary critical outcomes and priority topics and formulation of a series of questions structured in a PICO (Population, Intervention, Comparison, Outcomes) format;
2) retrieval of the evidence through specific systematic reviews of each topic using a standardized agreed methodology;
3) assessment and synthesis of the evidence;
4) formulation of recommendations; and
5) writing of the guideline content and planning for its dissemination and associated implementation strategy.

The development of the guidelines involved the formation of four main groups to guide the process: the WHO Guideline Steering Group; the Guidelines Development Group (GDG); the Systematic Reviews Expert Group; and the External Review Group.

Using the list of priority topics, questions and critical outcomes identified by the WHO Guideline Steering Group, the GDG and the guideline methodologist in a scoping meeting convened by WHO in September 2013, the Systematic Reviews Expert Group conducted 27 systematic reviews to provide the supporting evidence for the development of the recommendations; summaries of the systematic reviews are available as web appendices of the guidelines. The scientific evidence was synthesized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. WHO convened four GDG technical consultations between June 2014 and November 2015 to formulate and approve the recommendations based on the evidence profiles. In agreement with the methodologist and the WHO Guidelines Review Committee secretariat, five recommendations were re-discussed through GDG on-line consultations after the meetings and slightly modified, based on either comments by the external peer reviewers or emerging new evidence.

The guidelines consist of a core section including a dedicated chapter for each recommendation, which is divided into subsections according to their application in the pre-, intra- and postoperative periods. This is preceded by a section including other important issues in the approach to SSI prevention that were not the subject of recommendations, but of which users should be fully aware. A summary of main existing national guidelines on SSI prevention is also provided as a web appendix of the guidelines The WHO technical consultations led to the adoption of 29 recommendations covering 23 topics for the prevention of SSI in the pre-, intra- and postoperative periods (see Table). For four topics, the GDG considered that the available evidence was not sufficient to develop related recommendations. For each recommendation, the quality of evidence was graded as “very low”, “low”, “moderate” or “high”. The GDG qualified the direction and strength of each recommendation by considering the quality of evidence and other factors, including the balance between benefits and harms, the values and preferences of stakeholders and the resource implications of the intervention. To ensure that each recommendation is correctly understood and applied in practice, the GDG has provided additional remarks where needed. Guideline users should refer to these remarks, as well as to the summary of the evidence provided in each chapter of the recommendations. The summaries of the systematic reviews, including the risk of bias assessments and the GRADE tables, are

available in full as on-line appendices of the guidelines. Each chapter also features a research agenda identified by the GDG for each topic. The recommendations for the prevention of SSI to be applied or considered in the pre-, intra- and postoperative periods are summarized in the Table below, together with the associated PICO questions and their strength and evidence quality. In accordance with WHO guideline development procedures, these recommendations will be reviewed and updated following identification of new evidence at least every five years. WHO welcomes suggestions regarding additional questions for inclusion in future updates of the guidelines. (WHO-2016)

A surgical site infection is defined as infection following an operation at an incision site or adjacent to the surgical incision.1 Infections occur in approximately 0.5% to 3% of patients undergoing surgery2-4 and are among the most prevalent health care–acquired infections.5-7 Surgical site infections are re- sponsible for approximately $3.5 billion to $10 billion in US health care costs annually.8,9 Compared with patients without surgical site infections, those with them remain in the hospital approximately 7 to 11 days longer7,10; 1 study involving 177 706 postsurgical patients reported that 78% were readmitted as a result of the infection.11 This review summarizes current evidence-based interventions for pre- vention of surgical site infection that are applicable to the majority of operations (Box).

We searched PubMed, Google Scholar, and the Cochrane database for English-language studies of pathogenesis, clinical presenta- tion, and prevention of surgical site infections published from Janu- ary 1, 2016, when guidelines were most recently published by the World Health Organization, to September 15, 2022. In addition, we manually searched the references of selected articles for addi- tional relevant publications. We prioritized randomized trials, sys- tematic reviews, meta-analyses, clinical practice guidelines, and ar- ticles pertinent to general medical readership. Of 94 studies identified, 69 were included, consisting of 14 randomized trials, 19 systematic reviews, 12 meta-analyses, 4 clinical practice guide- lines, 17 cohort studies, and 3 cross-sectional studies.

Pathophysiology

Surgical site infection acquisition depends on several factors, namely, exposure to bacteria and the host's ability to control the inevitable bacterial contamination of the incision. They are typically caused by bacteria inoculated into the surgical site at the time of surgery. Approximately 70% to 95% are caused by the patient's endogenous flora.12 The most common organisms are Staphylo- coccus aureus, coagulase-negative Staphylococcus, and Escherichia coli.13 In some patients, introduction of only 100 colony-forming units of bacteria into the surgical site can cause infection.14 How- ever, exogenous sources of contamination during surgery such as bacteria transmitted from surgical personnel or heater-cooler units can also lead to infections.

Pathogens that cause infection vary by surgical location. The most common pathogens are components of skin flora such as S aureus and Streptococcus species. In contrast, infections follow- ing gastrointestinal procedures are typically associated with enteric organisms such as Enterococcus species and E coli.15 Over- all, S aureus is the most common cause of infection; for example, S aureus was associated with 24% of nonsuperficial surgical site infections in a cohort study including 32 community hospitals in the southeastern US.4 Although methicillin-resistant S aureus (MRSA) was previously more likely to cause surgical site infec- tions than methicillin-sensitive S aureus (MSSA), the rate of MSSA-derived infections from 2013 to 2018 was higher (0.07 per 100 procedures) than the rate of MRSA infections during the same period (0.05 per 100 procedures).4 MRSA surgical site infections lead to worse clinical outcomes than those caused by less resistant pathogens.10 Specifically, compared with MSSA sur- gical site infections, those due to MRSA were independently asso- ciated with 5.5 additional hospital days

(95% CI, 1.97-9.11).10 E coli and Enterococcus species respectively cause approximately 9.5% and 5.1% of all surgical site infections.13 Factors Associated With Surgical Site Infection

Factors associated with surgical site infection include older age, presence of immunosuppression, obesity, diabetes, effectiveness of antimicrobial prophylaxis, surgical site tissue condition (such as the presence of foreign material), and degree of wound contami- nation (Table 1 and Table 2). For example, a national study of more than 387 000 patients found that for most surgery types, rates of surgical site infection were increased in patients with obesity.21 The rates of surgical site infection following mastec- tomy among 16 473 patients increased with body mass index (BMI), calculated as weight in kilograms divided by height in meters squared. Those with a BMI of 20 to 25 had a surgical site infection rate of 4.66%; BMI of more than 30 to 40, 7.06%; and

BMI of more than 40, 10.58%. Similarly, after 29 603 laparo- scopic cholecystectomy procedures (urgency not specified), the infection rate increased with BMI: 8.57% with a BMI of 20 to 25; 10.62% with a BMI of 30 to 40; and 17.11% with a BMI of more than 40. Some of these risk factors associated with surgical site infec- tion are modifiable, such as hyperglycemia, obesity, and tobacco use. Other factors are nonmodifiable, such as age, which must be con- sidered when deciding on the surgical intervention for the patient.26,49

Clinical Presentation

The median time to diagnosis of surgical site infection varies by procedure.50 For example, S aureus infection is typically diag- nosed a median of 14 days after plastic surgery, 24 days after gen- eral orthopedic surgery, and 28 days after orthopedic surgery where a prosthetic device was inserted. A surgical site infection is suspected when purulent drainage is present at the incision site or when there is evidence of an abscess involving the surgical bed. Physical examination findings such as systemic signs of infection (eg, fevers, rigors), local erythema, wound dehiscence, pain, nonpurulent drainage, or induration are the most common. However, the presence or absence of these symptoms varies depending on factors such as surgical site, host, and time from surgery to presentation. For example, fevers can be present in 14% of patients with a chronic prosthetic joint infection but up to 75.5% of patients if the etiology of the prosthetic joint infection is hematogenous.51 Articular effusion and swelling may be present in 29% to 75% of prosthetic joint infections of the knee,52 and delayed wound healing, wound dehiscence, or wound drainage may accompany up to 44% of prosthetic joint infections. Joint stiffness has a reported sensitivity of 20.5% and specificity of 99% in patients with a hematogenous source of prosthetic joint infection.56 Many of the aforementioned presentations may overlap with noninfectious conditions, such as a hematoma, seroma, or stitch abscess at points of suture pen- etration.

Classification of Surgical Site Infection

Despite variable presentations of surgical site infections, the US Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) and the National Surgical Quality Improvement Program (NSQIP) provide specific surgical site infection definitions for surveillance and epidemiological purposes.57,58 Surveillance consists of systematic monitoring of patients following surgery to detect variance in surgical site infec- tion rates and to develop quality improvement initiatives to lower infection rates. The goal of these definitions is to be simple and objective but flexible enough to encompass clinically relevant infections. Both NHSN and NSQIP categorize surgical site infec- tions into 3 groups: superficial-incisional (involving the skin or subcutaneous tissue layers of the incision), deep-incisional (in- volving muscle or connective tissue layers of the incision), and organs/spaces deep to the incision. Surveillance for surgical site infections continues for 30 days for most procedures and 90 days for specific procedures involving implanted materials. The NHSN collects data on all NHSN-eligible procedures, and NSQIP analyzes a subsample of 20% of cases for analysis via an 8-day

systematic sampling cycle.

Prevention

Preoperative Period

A recent meta-analysis including 19 randomized and 6 quasi- randomized trials involving 8919 patients evaluated various approaches to preoperative hair removal for reducing surgical site in- fection (Table 3).59 Across 7 randomized clinical trials (RCTs), hair removal with a razor was associated with a higher rate of surgical site infection: 4.4% (84 of 1889) patients whose hair was removed with a razor experienced an infection vs 2.5% (46 of 1834) whose hair was removed with clippers experienced an infection (relative risk [RR], 1.64 [95% CI, 1.16-2.33], P = .005). Across 9 RCTs, hair re-moval with a razor was associated with a higher rate of surgical site infection: 7.8% (68 of 868) patients vs 3.6% (26 of 725) patients whose hair was removed with a depilatory cream (RR, 2.28 [95% CI, 1.12-4.65]; P = .02). Seven RCTs demonstrated that removing hair with a razor was associated with an increased risk of surgical site in- fection: 4.2% (34 of 819) patients vs 2.1% (19 of 887) patients whose hair was not removed at all (RR, 1.82 [95% CI, 1.05-3.14]; P = .03).59 Three RCTs reported that hair removal with clippers did not in- crease the risk of surgical site infection: 5.7% (49 of 863) patients vs 6.0% (52 of 870) patients whose hair was not removed (RR, 0.95 [95% CI, 0.65-1.39]; P = .80). If hair removal is necessary, it should be removed in the preoperative holding area and not in the operat- ing room.

One method used to reduce surgical site infections is decolo- nization, in which patients are treated with an intranasal antimicro- bial, skin antiseptic agent, or both to eliminate or temporarily re- duce S aureus colonization prior to surgery. Evidence to support this recommendation is strongest for high-risk surgical procedures such as cardiothoracic surgeries and prosthetic joint replacement. This process typically includes an intranasal treatment with an antistaphy- lococcal agent (eg, mupirocin ointment or povidone iodine) and/or application of an antistaphylococcal skin antiseptic agent (eg, chlorhexidine gluconate solution or wipes) for 5 days. However, the precise timing, agent, and frequency of application are unclear be- cause trials addressing this issue have used different strategies. The decolonization strategy should be completed as close to the surgi- cal procedure as possible. A meta-analysis that included 5 RCTs and 12 observational studies showed that nasal decolonization was as- sociated with lower rates of surgical site infections caused by gram- positive bacteria than no decolonization: 0.8% (152 of 19 940) vs 2.0% (253 of 12 790; RR, 0.41 [95% CI, 0.30-0.55]; P < .001).60

This association persisted among the 11 studies in which pa- tients were decolonized regardless of S aureus colonization status (RR, 0.40; 95% CI, 0.29-0.55) and among the 6 studies in which na- sal decolonization was combined with skin antisepsis (RR, 0.29; 95% CI, 0.19-0.44, primary data not provided).60 In contrast, other trials that included a more heterogeneous group of surgeries did not find a difference in surgical site infection incidence with decolonization.71 For example, a prospective cohort study that included 8 surgical cat- egories (abdominal, orthopedic, urological, neurological, cardiovas- cular, thoracic, and plastic surgery and solid organ transplant) found that decolonization strategies did not reduce MRSA surgical site infections.72 The authors identified 60 MRSA infections (0.55%) among 10 910 procedures in the control group compared with 70 MRSA infections (0.65%) among 10 844 procedures during the in- tervention period (P = .29). As a result, decolonization is typically focused on orthopedic, cardiothoracic, or high-risk procedures such as spine and brain surgeries. The intervention requires a significant amount of coordination to perform the appropriate test prior to surgery, have the result reviewed, and ensure the appropriate decolonization approach was applied. Given the number of steps required, some hospitals perform decolonization on all patients undergoing high- risk surgical procedures, an approach that may ultimately be cost- effective (estimated $153 per person) based on modeling studies.73 In contrast, widespread use of antistaphylococcal

anti- biotics such as mupirocin may ultimately increase rates of resis- tant S aureus infections.

Conducting RCTs for surgical site infection prevention is challenging given the relatively low incidence of the outcome of interest. Thus, additional prevention strategies in the preop- erative setting exist, but lack high-quality evidence. As a result, these interventions are predicated on expert opinion and results from retrospective cohort studies. For example, in contrast to postoperative glucose control, no RCTs have found a clear asso- ciation between a specific hemoglobin A1c cutoff and surgical site infections.

The administration of antibiotic prophylaxis is recommended in all surgical site infection prevention guidelines, despite the ab- sence of RCTs.14,17,76,77 One multicenter cohort study involving 4186 patients found that risk of infection increased as the time from an- tibiotic infusion to incision increased, although the trend was not sta- tistically significant: administration within 30 minutes prior to inci- sion was associated with a risk of 1.6% (22 of 1339) vs 2.4% (38 of 1558) with administration of antibiotic between 31 and 60 minutes before surgery (P = .13).61 In the absence of trial data, guideline con- sensus is that antibiotics should be given within 60 minutes of the incision to maximize tissue concentration of the antibiotic. Addi- tional recommendations include dosing antibiotics according to the patient's weight to ensure that adequate tissue concentrations are achieved and administering subsequent doses of antibiotics for lengthy procedures if excessive bleeding occurs. For example, ce- fazolin, the most commonly used agent for antimicrobial prophy- laxis, should be redosed every 4 hours until completion of the pro- cedure. These recommendations are mainly based on older cohort studies and evaluation of secondary outcomes (eg, tissue concen- trations of antibiotics).62 Although the optimal duration of prophy- lactic antibiotics is not known, prolonged antimicrobial prophy- laxis is increasingly associated with patient harm, such as acute kidney injury.78 Authors of a systematic review of 28 randomized trials involving 9478 patients receiving either a single dose for pro- phylaxis or multiple doses concluded that additional doses did not reduce the risk of infection 6.2% (278 of 4499) vs 5.9%(261 of 4440;

OR, 1.06 [95% CI, 0.89-1.25]).79 Thus, guidelines recommend stop- ping antibiotic prophylactic antibiotics when the surgical wound is closed.

The WHO's surgical safety checklist is a 19-item list to improve adherence with best practice and decrease surgical site infection incidence. WHO developed this safety checklist to promote more consistent implementation of best practices. This 19-item checklist included surgical site infection (eg, antimicrobial prophylaxis) and non–surgical site infection components (eg, surgical time-out). A mul- ticenter, quasi-experimental study of 8 sites and 3733 patients showed that the infection rate prior to the implementation of the checklist was 6.2% compared with 3.4% after implementation of the checklist (P value <.001 for the risk difference).65 These results have been supported by subsequent multi- and single-center pro- spective studies.63,64 However, the exact mechanism of improve- ment is unclear and most likely multifactorial.

Intraoperative

Topical alcohol is highly bactericidal but does not have persistent ac- tivity when used as monotherapy for skin antisepsis (Table 3). Mul- tiple guidelines recommend that surgical site antisepsis should be performed with a product that contains alcohol and another anti- septic agent (eg, chlorhexidine gluconate or povidone iodine).17,76,80 Products that combine alcohol and antiseptic agents are available in the US. Chlorhexidine gluconate plus alcohol appears to be supe- rior to povidone iodine plus alcohol for the prevention of surgical site infections.81 In a meta-analysis of data from 4 RCTs involving 6916 women who had cesarean deliveries, the authors concluded that sur- gical site preparation with chlorhexidine gluconate plus alcohol was associated with lower rates of infection than preparation with po- vidone iodine plus alcohol: 4.0% (54 of 1337) vs 6.5% (86 of 1326;

RR, 0.62 [95% CI, 0.45-0.87]; P = .005).66 Similarly, a meta- analysis of 20 RCTs and 5 prospective, 4 retrospective, and 1 ambi- spective studies, including more than 29 000 participants found that skin preparation with chlorhexidine gluconate was associated with fewer surgical site infections than povidone iodine: 4.8% (725 of 15 263) vs 6.7% (925 of 13 743; RR, 0.65 [95% CI, 0.55-0.77]; P < .001).82

Normothermia to keep core body temperatures from drop- ping during surgery is maintained by combinations of forced warm air, skin warming, and warmed intravenous fluids (Table 2). Targets for core temperatures vary: more than 35.5 °C and more than 36 °C. Asystematic review of 3 RCTs examining active body surfacing warm systems for preventing complications of inadvertent perioperative hypothermia in adults found that using a forced air warming device was associated with lower rates of the risk of surgical site infection than no forced air warming: 4.7% (14 of 299) vs 13% (37 of 290; RR,

0.36 [95% CI, 0.20-0.66]; P = .008; Table 3).67

Postoperative

Although there are no RCTs that have evaluated intensive glucose control to lower the preoperative average glucose (hemoglobin A1c) vs usual care before surgery, postoperative hyperglycemia was as- sociated with an increased risk of surgical site infections in patients with and without diabetes (Table 3).48,83,84 As a result, strategies to prevent hyperglycemia to prevent surgical site infection are rec- ommended in all major guidelines. Most data to support this strat- egy are from RCTs involving patients with diabetes. In a meta- analysis of 15 RCTs comparing the use of tight glycemic control (<150 mg/dL; 8.32 mmol/L) with conventional control (>150 mg/dL), tight control was associated with lower rates of surgical site infection: 9.4% (231 of 2464) vs 16% (392 of 2488; RR, 0.59 [95% CI, 0.50-0.68];

P < .001).68

Incisional negative pressure wound therapy, defined as wound dressing systems that continuously or intermittently apply subat- mospheric pressure to the system, can reduce the risk of surgical site infection by promoting reducing fluid accumulation in the wounds, thereby accelerating primary wound healing. Authors of a meta- analysis of 23 RCTs involving 2547 patients undergoing various sur- gical procedures (eg, abdominal, cesarean delivery, orthopedic, vas- cular) concluded that use of incisional negative pressure wound therapy for primary wound closure was associated with lower rates of surgical site infection than use of standard dressings: 9.7% (124 of 1279) vs 15% (191 of 1268; RR, 0.67 [95% CI, 0.53-0.85]; P < .001);

however, the effect varied by procedure type.69 The authors indicated that they did not find evidence for substantial differences be- tween the different types of surgery. Similarly, authors of a recent meta-analysis of 28 RCTs concluded that incisional negative pres- sure wound therapy was associated with lower rates of surgical site infection than standard dressing: 8.8% (194 of 2193) vs 14% (315 of 2205; RR, 0.61 [95% CI, 0.49-0.76]; P < .001).85 The authors speci-fied that when stratified by surgical discipline, the greatest ben- efits for surgical site infection reduction occurred in vascular sur- gery (RR, 0.45; 95% CI, 0.32-0.65; P < .001) and cardiac surgery (RR, 0.17; 95% CI, 0.03-0.96; P = .05), whereas the intervention was not associated with statistically significant benefit for abdominal sur- gery (RR, 0.56; 95% CI, 0.30-1.03), obstetric surgery (RR, 0.73; 95% CI, 0.44-1.20), orthopedic or trauma-derived surgery (RR, 0.68; 95% CI, 0.43-1.08), and plastic surgery (RR, 0.82; 95% CI, 0.26-2.63). The broader CIs for these later 4 subgroups suggest the possibility that they were underpowered to find a significant difference.

Hospital-Wide Surveillance

As one of the original surgical site infection prevention investiga- tions, data from the Study on

the Efficacy of Nosocomial Infection Control (SENIC)86 supported the use of routine surveillance and feed- back to reduce infections. The multicenter, 1985 SENIC study, evalu- ated infection prevention practices and found that the use of stan- dardized surgical site infection surveillance by trained infection prevention personnel and routine feedback to surgeons was asso- ciated with an estimated reduction in infections in US hospitals from 586 000 to 510 000 compared with when no surveillance and feed- back were given. Current recommendations advise health care in- stitutions to identify high-volume, high-risk procedures and imple- ment asystem for collecting and storing data. Periodic reports should be prepared and given to key stakeholders to provide feedback on infection rates. Surveillance and feedback, along with several other quality improvement strategies (eg, education of surgeons, surgi- cal staff, and patients) are endorsed by all surgical site infection pre- vention guidelines.14,17,77,80

Limitations

This review has several limitations. First, this review focused on pre- vention of surgical site infection following general, commonly per- formed surgical procedures. Second, not all recommendations in pre- viously published guidelines were summarized herein given the lack of available RCT data. Third, some interventions had been studied in only a small number of RCTs. Fourth, in some cases, the only avail- able studies were older. Fifth, quality of included literature was not assessed. Sixth, some relevant studies may have been missed.

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