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Effect of Surgical Skin Antisepsis on Surgical Site Infections in Patients Undergoing Gynecological Laparoscopic Surgery
A Double-Blind Randomized Clinical Trial

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IMPORTANCE Gynecological laparoscopies are one of the most common surgical procedures worldwide. Limited evidence exists on rates of surgical site infections in patients undergoing gynecological laparoscopies and strategies to prevent these infections.

OBJECTIVE To compare rates of port-site infections, organ or space infections, and any type of surgical site infections among patients who underwent gynecological laparoscopies and received 1 of 3 types of skin preparation solutions.

DESIGN, SETTING, AND PARTICIPANTS A double-blind randomized clinical trial was conducted between February 28, 2017, and November 26, 2018, at a tertiary university-affiliated referral center. A total of 661 patients 18 years or older who underwent an elective operative laparoscopy for treatment of nonmalignant gynecological disorders were randomly assigned in a 1:1:1 ratio to have their skin cleaned before surgery with alcohol-based chlorhexidine, alcohol-based povidone-iodine, or water-based povidone-iodine. Statistical analysis was performed from February 28, 2017, to November 26, 2018. Analyses were performed on a modified intention-to-treat basis.

INTERVENTIONS A total of 221 patients were randomized to have their skin prepared preoperatively with water-based povidone-iodine, 220 were randomized to alcohol-based povidone-iodine, and 220 were randomized to alcohol-based chlorhexidine. The patients were blinded to the solution used to clean their skin. Patients were followed up 1 and 4 weeks after surgery by a physician who was blinded to the skin preparation solution used at surgery. Evidence of infection according to Centers for Disease Control and Prevention criteria were documented.

MAIN OUTCOMES AND MEASURES The primary outcome of this study was port-site infection 30 days after surgery. Secondary outcomes were organ or space infections and any type of surgical site infections; the study also aimed to prospectively describe rates of surgical site infections in gynecological laparoscopies.

RESULTS Of the 661 patients, 640 (96.8%; mean [SD] age, 36.2 [10.6] years) were examined after surgery by a physician at the study site and were included in the modified intention-to-treat analysis. The overall rate of port-site infection was 10.2% (65 of 640), rate of organ or space infection was 6.6% (42 of 640), and rate of any surgical site infection was 16.3% (104 of 640). The odds ratio for port-site infection for alcohol-based chlorhexidine vs water-based povidone-iodine was 1.13 (95% CI, 0.61-2.08), for alcohol-based chlorhexidine vs alcohol-based povidone-iodine was 1.34 (95% CI, 0.71-2.52), and for water-based povidone-iodine vs alcohol-based povidone-iodine was 1.19 (95% 0.62-2.27).

CONCLUSIONS AND RELEVANCE Surgical site infections were more common than expected among patients who underwent gynecological laparoscopies. No skin preparation solution provided an advantage compared with the other solutions in reducing infection rates.

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Supplemental content

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Surgical site infections (SSIs) are one of the most common complications of surgery.[1] They are a leading cause of repeat medical visits and substantially increase the cost of care.[2] The Centers for Disease Control and Prevention (CDC) provide standardized criteria for defining SSIs and classify them as incisional or organ or space.[3]

Preventive measures have been implemented in surgical practice to prevent SSIs, including perioperative antibiotic prophylaxis and skin decontamination with antiseptic solutions. Nongynecological studies have consistently shown body mass index to be associated with SSI risk.[4,5]

National Institute for Health and Care Excellence guidelines state that alcohol-chlorhexidine is the preferred type of skin preparation to prevent SSIs. These guidelines were based mostly on studies assessing open and nongynecological surgical procedures.[6,7] Two previous randomized clinical trials (RCTs) that compared alcohol-chlorhexidine with iodine skin preparation solutions for surgical site antisepsis in open surgical procedures of various types[8] and in cesarean deliveries[9] have shown alcohol-chlorhexidine to be superior.

Laparoscopic surgery, offering smaller scars, faster recovery, and decreased cost, is a rapidly developing field and is currently used for many procedures that were traditionally performed via laparotomy.[10] Gynecological laparoscopies are unique, as a large proportion of them include vaginal instrumentation, leading to 2 possible sources of microbial pathogens.[11] To date, to our knowledge, no prospective or fully powered RCTs have evaluated SSI rates in patients undergoing gynecological laparoscopies or the effect of various skin preparations on SSI rates. The aim of this study was to prospectively assess and compare the effect of 3 types of skin preoperative preparations on SSI rates in patients undergoing gynecological laparoscopies.

Key Points

Question Does the type of skin preparation solution affect the rate of skin infections and any type of surgical site infections in patients undergoing gynecological laparoscopies?

Findings In this double-blind randomized clinical trial of 640 patients, the rate of skin infections was 10%, and the overall rate of surgical site infections was 16%. No skin preparation solution provided an advantage compared with the other solutions in reducing infection rates.

Meaning Rates of surgical site infections in patients undergoing gynecological laparoscopies, one of the most common surgical procedures worldwide, are higher than expected; because the type of skin preparation does not affect rates of surgical site infections, exploring other methods to reduce surgical site infections in patients undergoing gynecological laparoscopies is warranted.

Methods

Study Design

We conducted a double-blind RCT between February 28, 2017, and November 26, 2018, at a tertiary university-affiliated hospital (trial protocol in Supplement 1). To be able to perform a sample size calculation, the study was planned to have an internal pilot design, where an initial pilot study was performed to allow calculation of sample size, and to then continue as a full study, incorporating the data from the pilot study. The Royal Women's Hospital Research and Human Research Ethics Committees approved the pilot study phase, as well as the continuation as a full study. All study methods of both phases, the pilot and the continuation to a full study, were identical. All participants provided written informed consent. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Patient Selection

Patients included were 18 years or older who underwent an elective operative laparoscopy for the treatment of nonmalignant gynecological disorders. Patients were excluded if they were allergic to 1 of the skin preparation solutions, had evidence of active infection, or were unable to attend follow-up. At enrollment, patients' demographics and medical history were documented.

Randomization and Interventions

Randomization was performed within the statistics package R (R Foundation for Statistical Computing), using blocks of 6 to allocate patients into 3 groups. Patients were randomly assigned in a 1:1:1 ratio to 1 of the following groups: (1) abdominal preparation with alcohol-chlorhexidine solution (tinted-red chlorhexidine gluconate, 2% weight/volume [w/v], and ethanol, 70% volume/volume; PharmAust, $2.30 AUD) and vaginal and vulvar preparation with aqueous-chlorhexidine solution (chlorhexidine, 0.015% w/v, and cetrimide, 0.15%; Baxter) (Alc-CHX); (2) abdominal and vaginal and vulvar preparation with aqueous povidone-iodine solution (povidone-iodine, 10% w/v equivalent to 1% w/v available iodine, aqueous-based; HERRO, $1.14 AUD) (Aqu-PVP-I); and (3) abdominal preparation with alcohol-povidone-iodine solution (alcoholic povidone-iodine, 10% w/v [70% ethanol]; Pfizer, $5.00 AUD) (Alc-PVP-I) and vaginal and vulvar preparation with Aqu-PVP-I. Randomization was stratified by antibiotic regimen into 2 groups based on whether a body cavity (vagina, uterus, or bowel) might be breached (eg, total laparoscopic hysterectomy).

After initiation of anesthesia, the sealed envelope was opened and the chosen solution was brought to the operating theater. Two staff confirmed that the solution matched the randomization slip. Patients were blinded to the solution used. Per our hospital policy, patients did not receive any preoperative surgical site skin optimization (such as hair shaving). The patient's abdomen was painted with the chosen solution from the rib margin to top of the mons and laterally to the midpoint of the iliac crest. The vaginal and vulvar solution was used to cover the mons, vulva, top 4 cm of the inner thighs, vagina, and the visible aspects of the buttocks. The solutions were allowed to evaporate. With poor evidence on antibiotic prophylaxis in gynecological laparoscopies and to prevent confounding, a standardized antibiotic protocol was applied. All patients received 2 g of cefazolin sodium before skin incision.

If cavities were or might be breached, patients also received 500 mg of metronidazole hydrochloride. Patients allergic to cephalosporins were instead treated with clindamycin phosphate, 600 mg. An additional antibiotic dose was administered when surgery was longer than 3 hours. There were no diagnostic laparoscopies in this study.

Laparoscopies were performed by 2 gynecology units. Both units have a wide range of laparoscopic surgeons. One unit has a special interest in endometriosis and pelvic pain and the other in fibroids and menorrhagia. All surgical procedures were performed while the patient was under general anesthesia. At the end of surgery, standardized information was recorded, including all surgical times, the number and location of laparoscopic ports, main surgical findings, and surgical complications.

Skin incisions were uniformly closed with interrupted 3-0 Prolene sutures (Ethicon). On completion of surgery, residual skin preparation on the skin was cleaned with water or normal saline.

Outcomes and Follow-up

The primary outcome was to compare the rate of skin port-site infection among the 3 types of skin preparation. Per the CDC criteria available at the start of the study,[3] a superficial skin infection was defined as an infection occurring within 30 days after surgery and involving only skin or subcutaneous tissue of the incision and at least 1 of 4 criteria defined in the guideline. Secondary outcomes were organ or space infections and total SSI rates among the 3 types of skin preparation. Patients were followed up by a physician (U.P.D., S.K., or C.R) in our hospital 1 week and 4 weeks after surgery. Evidence of infection according to CDC criteria[3] was documented in a standardized fashion, including (1) findings of each port site (redness, swelling, purulent discharge, pain, heat, and other findings), (2) findings related to organ or space infections, (3) CDC SSI criteria, and (4) presence or absence of SSI and type of SSI, if diagnosed. If an infection was diagnosed, relevant microbiologic samples were collected where possible and oral antibiotics were administered. At the first follow-up visit, the patients were handed a similar form to give to their primary care physician in case the patients presented to their primary care physician between the 2 follow-up visits. The physician performing the follow-up examination was blinded to skin preparation solution(s). Patients who did not attend the follow-up visit were contacted via telephone and information regarding follow-up with their primary care physician was obtained. Patients who did not attend any of the study follow-up visits were excluded from the analysis. Findings from the 2 follow-up visits were combined and SSI was considered positive if an infection was diagnosed at either of the postoperation visits. An independent data and safety monitor reviewed the conduct of the study every 6 months or in the case of any adverse event. The study team met every 3 months to review the study conduct.

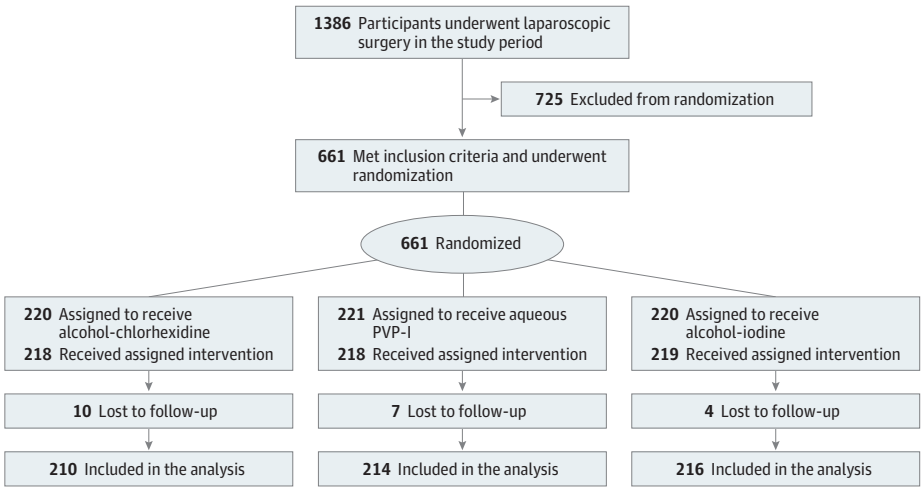
Statistical Analysis

Statistical analysis was performed from February 28, 2017, to November 26, 2018. As there were no previous studies reporting SSI rates in gynecological laparoscopies, to our knowledge, this study started as a pilot study. After recruiting 160 patients, the skin infection rate was 15% (24 of 160). Blinding was not breached at this point. Based on a power level of 80%, a 2-tailed $P < .05$ was considered significant, and on the assumption that a 10% absolute difference between at least 2 of the treatments (ie, 10% vs 20% of skin infection) would be clinically significant (ie, promote change of practice), the required sample size of each group to perform a fully powered study considering superiority was calculated to be 198. This calculation was not modified for the internal pilot design. Recruitment continued until 600 eligible patients completed their follow-up. We then allowed patients who had already provided consent for the trial to complete their follow-up, and they were also included in the analysis.

As we excluded patients who were lost to follow-up, this is a modified intention-to-treat study and the main data analyses were carried out accordingly. Baseline characteristics between the 3 study groups were assessed with the analysis of variance test for continuous variables and 2-tailed Fisher exact test for categorical variables. Using multivariable logistic regressions, the odds of skin infections, any organ or space infection, urinary tract infection, endometritis or vaginal vault infection, and any SSI were compared among the 3 study groups. The active controls were Aqu-PVP-I and Alc-PVP-I.

Separate logistic regression modeling was performed for each SSI grouping. The model's independent variables were skin antisepsis group and antibiotic group (stratification variable), while total and specific types of SSIs were the dependent variables. Although there was no difference in baseline characteristics among the 3 study groups, we performed an additional logistic regression including potential explanatory variables that are clinically relevant to the association between skin preoperative prophylaxis and SSIs, including previous SSI history, age, duration of operation, body mass index, smoking status, history of any medical illness, gynecological unit, and category of surgery. The Akaike information criterion was calculated. Interactions between the antisepsis group and the explanatory variables were modeled and retained if their inclusion produced a reduction in the model's Akaike information criterion of more than 2. To achieve parsimony, explanatory variables with $P > .20$ were removed from the logistic regression model in a stepwise descending order based on P value. At each step, if the new model's Akaike information criterion increased by more than 2, the variable was reentered. Variables used to calculate an interaction variable were not removed unless the interaction variable itself had already been deleted. The 3 continuous variables (age, duration of operation, and body mass index) were centered on zero prior to entry into the model. Odds ratios (ORs), 95% CIs, and 2-sided P values were calculated to allow comparison between the 3 skin preparations. We performed further regressions in a similar manner, comparing ORs for SSIs between chlorhexidine and both iodine solutions, and aqueous and both alcoholic solutions. We also performed multiple imputation (number of imputations = 100) to adjust for missing data including patients who were lost to follow-up. In this analysis, we used single variable models with the specific SSI outcome as the dependent

Figure 1. Randomization and Follow-up of Study Participants



PVP-I indicates povidone-iodine solution.

variable and the study group as the single independent variable. We then performed the logistic regressions again as a sensitivity check and pooled results were quoted.

Results

Trial Participants

A total of 1386 laparoscopies were performed during this study. **Figure 1** depicts the participant flow. Lost to follow-up rates were 4.5% (10 of 218) for the Alc-CHX group, 3.2% (7 of 218) for the Aqu-PVP-I group, and 1.8% (4 of 219) for the Alc-PVP-I group (P = .26). A total of 640 patients (mean [SD] age, 36.2 [10.6] years) attended at least 1 follow-up visit and were included in the final analysis. Of them, 553 (86.4%) attended both follow-up visits at the study site. In detail, 608 patients (95.0%) attended the first follow-up visit and 586 patients (91.6%) attended the second follow-up visit. Twenty-five of the patients who did not attend the first follow-up visit and 37 of the patients who did not attend the second follow-up visits were successfully contacted via telephone. Patients who did not attend the first follow-up visit were questioned at the second follow-up regarding the findings at 7 days after surgery; 23 of 25 patients who were contacted via telephone reported examination by their primary care physician 1 week after surgery at the time of suture removal. Seventeen patients (2.7%) did not attend the second follow-up and, despite repeated attempts, were unable to be contacted by telephone.

Baseline characteristics for the 3 study groups are found in **Table 1**. Of the 640 study participants included in the analysis, 187 (29.2%) underwent surgical procedures in which cavities might be breached. Distribution of groups in the 2 stratification layers was similar (layer 1: 151 of 453 [33.3%] for the Aqu-PVP-I group, 152 of 453 [33.6%] for the Alc-PVP-I group, and 150 of 453 [33.1%] for the Alc-CHX group; and layer 2: 63 of 187 [33.7%] for the Aqu-PVP-I group, 64 of 187 [34.2%] for the Alc-PVP-I group, and 60 of 187 [32.1%] for the Alc-CHX group; P = .97).

All but 9 patients received surgical antibiotic prophylaxis (time of antibiotic administration was missing for 13 patients); 589 of 627 patients (93.9%) received the antibiotics before the skin incision. In 70 surgical procedures (10.9%), 2 laparoscopic ports were used; in 480 procedures (75.0%), 3 or 4 ports were used; and in 89 procedures (13.9%), 5 or 6 ports were used. Most surgical procedures were for endometriosis (n = 370 [57.8%]), followed by adnexal surgery (n = 122 [19.1%]), total laparoscopic hysterectomy (n = 97 [15.2%]), and other surgical procedures (n = 51 [8.0%]). The mean (SD) duration of surgery from skin preparation to the end of surgery was 99.2 (66.7) minutes and from skin incision to the end of surgery was 89.1 (66.4) minutes.

Infection Rates According to Skin Preparation Solution

Skin was prepared with Aqu-PVP-I in 214 patients, Alc-PVP-I in 216, and Alc-CHX in 210. The OR for port-site infection for alcohol-based chlorhexidine vs water-based povidone-iodine was 1.13 (95% CI, 0.61-2.08), for alcohol-based chlorhexidine vs alcohol-based povidone-iodine was 1.34 (95% CI, 0.71-2.52), and for water-based povidone-iodine vs alcohol-based povidone-iodine was 1.19 (95% 0.62-2.27) (**Table 2**). No statistically significant differences in the odds of total and specific types of SSIs were observed when comparing solutions containing iodine with chlorhexidine (OR, 1.21; 95% CI, 0.79-1.89) and alcohol-based solutions with Aqu-PVP-I (OR, 0.96; 95% CI, 0.61-1.50). These results among the 3 groups of the study remained with the multivariable logistic regression (eTable 1 in Supplement 2) and with the multiple imputation analysis (eTable 2 in Supplement 2). A total of 61.5% of the infections (64 of 104) were diagnosed at the first follow-up, 22.1% (23 of 104) between the 2 follow-up visits, and 16.3% (17 of 104) at the second follow-up visit.

The overall rate of any SSI was 16.3% (104 of 640). Skin SSI rates were not statistically different between the 2 units who participated in this trial (unit A, 25 of 196 [12.8%]; unit B, 40 of 444 [9.0%]; P = .16) and across the study treatment groups (unit A, 9 of 70 [12.9%] for the Aqu-PVP-I group, 7 of 67 [10.4%]

Table 1. Baseline Characteristics of Study Participants[a]

Characteristic	Chlorhexidine-alcohol (n = 210)	Alcohol iodine (n = 216)	Aqueous PVP-I (n = 214)
Age, mean (SD), y	35.5 (10.3)	37.1(10.8)	36.1 (10.8)
BMI, mean (SD)	26.3 (6.1)	26.6 (6.7)	26.5 (6.3)
Prophylactic antibiotics, No. (%)			
None	5 (2.4)	3 (1.4)	1 (0.5)
Cefazolin sodium	138 (65.7)	142 (65.7)	142 (66.4)
Cefazolin sodium and metronidazole hydrochloride	62 (29.5)	70 (32.4)	68 (31.8)
Clindamycin phosphate	5 (2.4)	1 (0.5)	3 (1.4)
Type of surgery, No. (%)			
Endometriosis treatment	127 (60.5)	125 (57.9)	118 (55.1)
Total laparoscopic hysterectomy	28 (13.3)	34 (15.7)	35 (16.4)
Adnexal surgery	37 (17.6)	37 (17.1)	48 (22.4)
Other surgery	18 (8.6)	20 (9.3)	13 (6.1)
Duration of surgery, mean (SD), min[b]	93.4 (67.3)	86.2 (62.9)	87.7 (68.9)
No. of laparoscopic ports, mean (SD)	3.6 (0.8)	3.6 (0.9)	3.6 (0.9)
Presence of at least preexisting medical condition, No. (%)	35 (16.7)	49 (22.7)	52 (24.3)
Current smoking No./total No. (%)[b]	42/209 (20.1)	41/215 (19.1)	37 (17.3)
SSI in previous surgical procedures, No. (%)	13 (6.2)	15 (6.9)	11 (5.1)
Gynecology unit, No./total No. (%)			
Unit A	59/196 (30.1)	67/196 (34.2)	70/196 (35.7)
Unit B	151/444 (34.0)	149/444 (33.6)	144/444 (32.4)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); PVP-I, povidone-iodine; SSI, surgical site infection.

[a] There were no significant differences between groups for all variables.

[b] Missing data: duration of surgery was missing for 1 patient and smoking status was missing for 2 patients.

Table 2. Odds Ratios for Surgical Site Infection According to Type of Infection (Modified Intention-to-Treat Population)[a]

	Patients, No. (%)			Alcohol-chlorhexidine and aqueous PVP-I		Alcohol-chlorhexidine and alcohol iodine		Aqueous PVP-I and alcohol iodine		
Type of infection	Alcohol-chlorhexidine (n = 210)	Aqueous PVP-I (n = 214)	Alcohol iodine (n = 216)	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	*P* value[b]
Incisional	24 (11.4)	22 (10.3)	19 (8.8)	1.13 (0.61-2.08)	.70	1.34 (0.71-2.52)	.37	1.19 (0.62-2.27)	.60	.67
Any organ or space	15 (7.1)	13 (6.1)	14 (6.5)	1.21 (0.56-2.65)	.63	1.13 (0.53-2.44)	.75	0.93 (0.42-2.06)	.93	.89
Urinary tract	10 (4.8)	7 (3.3)	10 (4.6)	1.52 (0.56-4.11)	.41	1.05 (0.42-2.61)	.92	0.69 (0.26-1.88)	.47	.68
Endometritis or vaginal vault	5 (2.4)	7 (3.3)	4 (1.9)	0.73 (0.23-2.34)	.59	1.31 (0.35-4.99)	.69	1.81 (0.52-6.30)	.35	.64
Any surgical site	38 (18.1)	34 (15.9)	32 (14.8)	1.18 (0.71-1.97)	.53	1.27 (0.77-2.16)	.34	1.09 (0.64-1.85)	.75	.62

Abbreviations: OR, odds ratio; PVP-I, povidone-iodine.

[a] A logistic regression including the study group and the randomization stratification variable.

[b] For the overall randomized group effect (with 2 *df*).

for the Alc-PVP-I group, and 9 of 59 [15.3%] for the Alc-CHX group; *P* = .72, and unit B, 13 of 144 [9.0%] for the Aqu-PVP-I group, 12 of 149 [8.1%] for the Alc-PVP-I group, and 15 of 151 [9.9%] for the Alc-CHX group; *P* = .85).

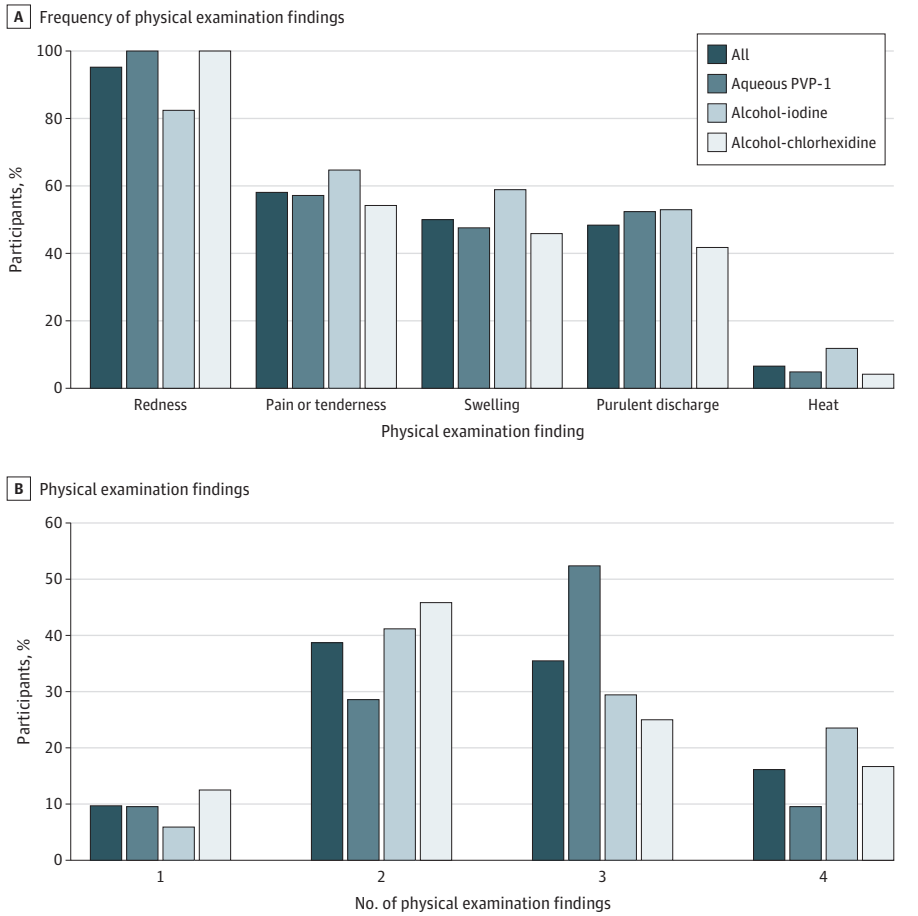
Incisional Infection Diagnosis

The overall port-site infection rate was 10.2% (65 of 640) and the organ or space infection rate was 6.6% (42 of 640). The location and symptoms of the port-site infection was documented in 95.4% of cases (62 of 65). In 45 of 62 port-site infections (72.6%), the infection involved the umbilicus, while in 20 of 62 port-site infections (32.3%) an accessory-port incision was involved. **Figure 2** presents the signs displayed by patients with an incisional infection. Redness was present in almost all patients with an incisional infection. Pain (36 of 62 [58.1%]), swelling 31 of 62 [50.0%]), and purulent discharge (30 of 62 [48.4%]) were also common. Most patients (40 of 62 [71.0%]) displayed 2 or 3 signs.

Risk Factors for Infection and Interaction Analysis

Table 3 presents the association of potential risk factors for SSIs, while taking into account the skin preparation solution, and the diagnosis of all SSIs and specific types of SSIs. History of SSI was associated with any organ or space infection (OR, 3.99; 95% CI, 1.53-10.41), urinary tract infection (OR, 4.82; 95% CI, 1.68-13.88), and any type of SSI (OR, 4.75; 95% CI, 2.23-10.12). Age was associated with urinary tract infection (OR, 1.05; 95% CI, 1.01-1.09) but not with endometritis and vault infections. Body mass index was associated with skin infections (OR, 1.07; 95% CI, 1.03-1.11) and with any type of SSI (OR, 1.07; 95% CI, 1.03-1.11). Total laparoscopic hysterectomy was associated with any organ or space infection (OR, 4.17; 95% CI, 1.47-11.84) and

Figure 2. Frequency of Findings in Cases of Incisional Infections and Number of Reported Findings at Time of Incisional Infection Diagnosis



A, Frequency of physical examination findings reported by physicians at the study follow-up visit of the whole cohort and according to the study group. B, Frequency of the number of physical examination findings reported by physicians at the study follow-up visit of the whole cohort and according to the study group. Numbers presented are percentage of the following numbers: all groups = 62, aqueous PVP-I (povidone-iodine) = 21, alcohol iodine = 17, and alcohol-chlorhexidine = 24. Information is missing for 3 patients who were diagnosed by their primary care physician.

with endometriosis and vault infections (OR, 25.47; 95% CI, 2.11-308.17).

Rates of cardiometabolic disorders (including type 1 or 2 diabetes, hyperlipidemia, and hypertension) and of diseases associated with immunosuppression were similar between the 3 groups of the study. Presence of cardiometabolic disorders was associated with risk of organ or space infection (7 of 37 [18.9%] vs 35 of 603 [5.8%]; $P = .007$), urinary tract infection (5 of 37 [13.5%] vs 22 of 603 [3.6%]; $P = .02$), and any SSI (14 of 37 [37.8%] vs 90 of 603 [14.9%]; $P = .001$). Rates of all SSIs and specific types of SSIs did not differ between patients with and without diseases associated with immunosuppression. Of the interactions tested, the only interaction we found to be significant was the interaction of type of skin preparation and history of SSIs with the risk of incisional infection.

Adverse Events and Operative Complications

The study had 1 serious adverse event. A patient allocated to the Aqu-PVP-I group had her skin mistakenly prepared with Lugol solution, labeled as "aqueous iodide." This mistake was noted shortly after applying the solution and it was washed off the visible areas of skin. The patient presented with blisters on the back, presumably owing to solution pooling under her. The blisters healed with no scars. The ethics committee was notified and the study was halted for 10 weeks until adequate measures were instituted to prevent the use of incorrect solutions.

There were 15 intraoperative complications (2.3%), including 6 uterine perforations and 4 conversions to laparotomy (1 due to failure to access the peritoneal cavity via laparoscopy, 1 due to continuous ooze and difficult views, and 2 due to bowel injuries). There were 4 additional cases of bowel injuries that were not full thickness and were repaired laparoscopically, as was 1 superficial bladder injury. Operative complications were not differentially distributed with rates of 2.4% (5 of 210) in the Alc-CHX group, 1.4% (3 of 216) in the Alc-PVP-I group, and 2.3% (5 of 214) in the Aqu-PVP-I group ($P = .42$).

A further 3 conversions were not due to complications but to intraoperative assessment of better surgical outcome. All patients who had complications, including conversions to open surgery, were included in the final analysis.

Discussion

This double-blind RCT found that the odds of incisional, organ or space, and total SSIs in patients undergoing gyneco-

Table 3. Parsimonious Logistic Regression Models for Each SSI Group[a,b]

	Incisional infection		Any organ/space infection		Urinary tract infection		Endometritis/vaginal vault infection		Any SSI	
Study variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Alcohol-chlorhexidine and aqueous PVP-I	0.90 (0.46-1.74)	.75	1.32 (0.59-2.97)	.50	1.47 (0.53-4.05	.46	0.79 (0.24-2.65)	.70	1.16 (0.68-1.98)	.58
Alcohol-chlorhexidine and alcohol iodine	1.20 (0.60-2.37)	.61	1.31 (0.59-2.89)	.51	1.30 (0.50-3.36)	.59	1.12 (0.28-4.41)	.87	1.39 (0.81-2.40)	.23
Aqueous PVP-I and alcohol iodine	1.34 (0.69-2.60)	.39	0.99 (0.43-2.20)	.97	0.89 (0.32-2.49	.82	1.42 (0.39-5.18)	.60	1.12 (0.69-2.09)	.51
Randomization stratification variable (antibiotic group)	0.53 (0.24-1.16)	.11	1.50 (0.56-4.05)	.42	3.52 (1.54-8.03)	.003	0.35 (0.03-3.50)	.37	1.60 (1.01-2.55)	.046
History of SSI	0.61 (0.08-4.92)	.65	3.99 (1.53-10.41)	.005	4.82 (1.68-13.88)	.004	NA	NA	4.75 (2.23-10.12)	<.001
Age	NA	NA	NA	NA	1.05 (1.01-1.09)	.006	0.93 (0.86-1.00)	.06	NA	NA
Body mass index	1.07 (1.03-1.11)	.001	NA	NA	NA	NA	1.06 (0.99-1.14)	.09	1.07 (1.03-1.10)	<.001
Presence of medical comorbidities	NA	NA	1.87 (0.92-3.81)	.08	NA	NA	NA	NA	NA	NA
Type of surgery										
Total laparoscopic hysterectomy	NA	NA	4.17 (1.47-11.84)	.007	NA	NA	25.47 (2.11-308.17)	.01	NA	NA
Adnexal surgery	NA	NA	0.78 (0.25-2.43)	.67	NA	NA	0.70 (0.08-6.07)	.74	NA	NA
Other	NA	NA	1.14 (0.31-4.28)	.84	NA	NA	NA	NA	NA	NA
Hospital unit B	0.57 (0.32-1.00)	.048	NA	NA	NA	NA	NA	NA	0.63 (0.40-1.00)	.05
Interaction of history of SSI with skin preparation type	3.58 (0.94-13.64)	.06	NA	NA	NA	NA	NA	NA	NA	NA

Abbreviations: NA, not applicable; PVP-1, povidone-iodine; OR, odds ratio; SSI, surgical site infection.

[a] Age, duration of surgery, and body mass index (centered around zero).

[b] The starting logistic regression prior to stepwise variable removal included the variables listed in the table, in addition to smoking and duration of surgery.

logical laparoscopies did not differ among 3 different types of preoperative skin preparations. The overall rate of clinically diagnosed SSIs was higher than expected and involved mainly incisional infections at the umbilical port site.

Two previous nonblinded RCTs evaluated SSI rates according to skin preparation solution in abdominal surgical procedures. Darouiche et al[8] performed a multicenter RCT comparing infection rates between patients who had skin preparation with Alc-CHX or Aqu-PVP-I. Their study included multiple disciplines: general surgery, urology, chest surgery, and gynecological surgery. Total SSI rates in this study were similar to those in our present study; however, they found lower rates of SSIs with Alc-CHX, presumably due to its more rapid action and persistent activity.[12] Another study compared Alc-CHX and Alc-PVP-I in patients undergoing cesarean delivery.[9] That study found lower rates of SSIs with Alc-CHX; however, the absolute difference between skin preparation groups was minor. Although those studies examined different types of open surgical procedures, no previous prospective trial has assessed or compared SSI rates in patients undergoing gynecological laparoscopies, to our knowledge.

Our study, focusing on gynecological laparoscopies, aimed to also assess the effect of chlorhexidine vs iodine and water-based solutions vs alcohol-based solutions separately. Our finding of similar rates of SSIs across all groups of skin preparations is at odds with the findings of the previous 2 studies and suggests that any difference in efficacy is less than previously claimed. Laparoscopy is becoming the surgical method of choice in many disciplines.[13,14] A particularly steep rise in endoscopic abdominal surgical procedures was observed during the last 2 decades in gynecology.[15]

Although some studies, mainly from the field of general surgery, suggested lower rates of SSIs in patient undergoing laparoscopic surgical procedures,[16,17] other prospective trials assessing SSIs after laparoscopic surgical procedures found similar rates to those in patients who underwent open surgical procedures.[18] Although the overall rates of SSIs in our study were higher than those reported in retrospective studies assessing patients who underwent gynecological laparoscopies,[19] they are lower than those reported in nongynecological trials that investigated SSIs and also used CDC criteria to diagnose infections.[20,21] In most laparoscopies, the main port-site entry is the umbilicus, which is a potential site of microbiological growth.[22] In addition, our study consisted of 2 postsurgical hospital visits with careful physical examination. Most infections were diagnosed at the 1-week postsurgical visit. In other studies without an early postoperative review, such infections would often remain undetected, as these patients would be unlikely to present to the hospital again with a superficial skin or uncomplicated organ or space infection.

Our findings have shown that history of SSI, older age, higher body mass index, and type of surgery were associated with a higher risk of specific types of infections. Those find-

ings are in agreement with previous retrospective studies assessing SSIs after hysterectomies.[23,24]

Strengths and Limitations

This study has some strengths. To our knowledge, our study is the first RCT to assess and compare SSIs in patients undergoing gynecological laparoscopies. This study started as a pilot study and then continued as a full, adequately powered study. Skin infection rate of the full study was close to the rate measured at the interim analysis; therefore, the assumption underlying the statistical power calculation was met. We used a very robust protocol, the study was double-blinded, and our protocol included standardized measures to prevent bias (a standardized antibiotic prophylaxis protocol, uniform skin closure sutures, uniform skin wash at the end of surgery, and blinding of the patient and the examining physician).

This study also has some limitations. We have not formally documented reasons for nonrecruitment. However, selection bias is unlikely, as in most of the nonrecruited cases the reasons were nonavailability of study staff to recruit and patients residing far from the hospital, and therefore unable to attend follow-up visits.

Compared with other RCTs, our dropout rate (21 of 661 [3.2%]) was very low,[25] and patients who were lost to follow-up were similarly distributed between the study groups. Therefore, and as confirmed by our sensitivity analysis, it is unlikely that this introduced a bias to our findings.

With regard to the generalizability of the study, although this study was undertaken in a single center, it involved 2 units and more than 20 gynecological surgeons, operating on patients with all benign gynecological diseases, excluding urogynecology. However, repeating our study at other sites may be of benefit, as there may be local site variations.

This study was powered to detect a pairwise difference between the 3 groups of preoperative skin antisepsis on the assumption that a 10% absolute difference in skin infection rates would promote change in practice. Detection of smaller differences will require more and larger studies that are also likely to narrow the 95% CIs and the error range of our findings as well as introduce benefits of multicentered recruitment. With our internal pilot design, the sample size calculation may elevate risk of type 1 error. However, as our main findings were negative, there is less concern for false-positive results.

Conclusions

Although the clinical effect of SSIs after laparoscopic surgery might be lower than that of open surgical procedures, infection still causes major discomfort to the patient and poses a significant economic burden.[26,27] Although antibiotic prophylaxis when appropriate and proper sterile environment may reduce SSIs, no skin preparation solution provides an advantage by reducing infection during gynecological laparoscopy. Exploring other methods such as routine bathing or cleaning, specific preparation of the umbilicus, and antibiotic prophylaxis protocols to reduce SSIs in patients undergoing gynecological laparoscopies is warranted.

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Statistical analysis: Dior.
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