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# Chlorhexidine 0.5%/70% Alcohol and Iodine 1%/70% Alcohol Both Reduce Bacterial Load in Clean Foot Surgery: A Randomized, Controlled Trial

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ABSTRACT

No consensus exists regarding which cleansing technique, solution, and concentration should be used in orthopedic surgery. The aim of this randomized, controlled trial was to compare the effect of chlorhexidine 0.5%/70% alcohol with iodine 1%/70% alcohol on lowering positive cultures before elective foot surgery and to study any wound complications, infections and allergic reactions. Consecutive patients ≥18 years of age scheduled for a hallux valgus correction or arthrodesis of the first metatarsophalangeal joint were included. Swabs were taken from 2 sites before and twice after preparing the skin and were quantitatively and qualitatively analyzed. The study group consisted of 49 patients with a mean age of 52.3 ± 14.4 (range 22 to 75) years of whom 42 (86%) were female. No significant differences were observed for positive cultures between the chlorhexidine (73%, 2%, and 12%) and iodine (68%, 7%, and 9%) group at any time point. Coagulase-negative staphylococci were the most commonly isolated micro-organisms found after skin preparation. Occasionally, *Bacillus* spp and *Corynebacterium* spp were cultured. The complication rate 2 weeks postoperatively was 0% in the chlorhexidine group versus 8.7% (n = 2) in the iodine group (delayed wound healing; $p = .215$). The complication rate at 6 weeks postoperatively was, respectively, 3.8% (n = 1) versus 4.3% (n = 1; both showed swelling and redness; $p > .999$). There was no significant difference in postoperative wound problems or infection rates between the 2 skin preparation solutions. Chlorhexidine 0.5%/70% alcohol and iodine 1%/70% alcohol both decreased the amount of positive cultures in elective foot surgery.



Surgical site infections after orthopedic surgery result in a major increase in morbidity, duration of hospital stay, and extra costs (1–4). Although surgical site infection is multifactorial, it is known that effective preoperative skin preparation has a great influence on diminishing postoperative wound infections (3). During the past years, many different solutions have been used for preoperative skin preparation, including alcohol, chloroxylenol, chlorhexidine, and iodophors such as iodine and povidone-iodine, whether or not dissolved in alcohol. Several studies compared different kinds of solutions as well as different applying techniques (2,3,5–13) and a few systematic review including meta-analyses were performed to pool the results (14–16).

In a previously performed meta-analysis, it was concluded that chlorhexidine should be used instead of povidone-iodine (15). However, the 6 included studies differed in concentrations and none of the povidone-iodine solutions were alcohol based, whereas 4 of the 6 chlorhexidine solutions were. Another meta-analysis based on only 2 studies concluded that alcohol-based chlorhexidine had a significantly better efficacy than alcohol-based povidone-iodine (16). One of these studies compared povidone-iodine 1%/23% alcohol with chlorhexidine 0.5%/70% alcohol in forefoot surgery and showed a large reduction in bacterial load for both solutions without any significant difference (11). The other included study found a significant difference between povidone-iodine 0.7%/74% isopropyl alcohol and chlorhexidine gluconate 2%/70% isopropyl alcohol in favor of chlorhexidine (8). A third meta-analysis suggested that products containing alcohol had the highest probability of being effective. However, they also said that the quality of the evidence was very low (14).

Despite all previous research, still no consensus exists on which cleansing technique, solution, and concentration should be used in orthopedic surgery (3,11). To our knowledge, no prospective randomized trial has been performed in the field of orthopedic surgery comparing the efficacy of iodine 1%/70% alcohol with chlorhexidine 0.5%/70% alcohol in these specific concentrations. Because the literature shows higher infection percentages in foot and ankle surgery compared with other sites, foot surgery was chosen as most suitable research area

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(3,4,7,16–19). The aim of this randomized prospective trial was to compare the effect of chlorhexidine 0.5%/70% alcohol with iodine 1%/70% alcohol on decreasing the amount of positive cultures before elective foot surgery and to study any wound complications, infections, and allergic reactions.

## Patients and Methods

From March 2013 to April 2014, this prospective randomized trial was undertaken in the St. Antonius Hospital, the Netherlands, to evaluate all consecutive patients ≥18 years of age scheduled for a hallux valgus correction or arthrodesis of the first metatarsophalangeal (MTP1) joint. Exclusion criteria were any current infection, hematologic disorders, the use of antibiotics within 30 days of surgery, any skin defects or abrasion on the operative limb, dementia, and known allergy to iodine or chlorhexidine. Eligible patients were verbally and by letter informed about the study and asked for participation, thereby signing informed consent (M.B.S.). The study protocol was registered at ClinicalTrial.gov (NCT01583192) and approval to conduct the study was obtained by the Medical Ethics Committee and institutional review board of the St. Antonius Hospital.

Each patient was randomly assigned to 1 of the 2 preparation treatments—chlorhexidine 0.5%/70% alcohol paint or iodine 1%/ 70% alcohol paint. The research coordinator (N.W.) generated the random allocation sequence using www.randomization.com. Randomization was performed in a 1:1 fashion with random permuted blocks (size 6). An independent secretary kept the randomization list in a secure location and informed the surgical team on the day of surgery about the allocation of that specific patient. Because of the different colors of chlorhexidine and iodine on the skin, surgeons and patients could not be blinded for treatment arm. However, patients were not informed about which color belonged to which treatment.

### *Surgical Procedure*

Patients undergoing a hallux valgus correction or arthrodesis of the MTP1 joint were included. Patients were operated by 1 of 4 surgeons. Hallux valgus correction was performed by a chevron osteotomy of the first metatarsal bone with a distal soft tissue procedure. Arthrodesis of the MTP1 joint was performed with 1 screw (QWIX, Integra Life Sciences, Plainsboro, NJ) and 1 crossed Kirschner wire. On the day of surgery, patients followed their normal personal hygiene routine; no specific instructions were given. As is standard in our institution, preoperative prophylactic intravenous antibiotics (cefazoline 2000 mg) were administered to all patients 15 to 60 minutes before incision and ≥10 minutes before a tourniquet was applied. No plastic adhesive drapes were used during the procedure. All patients received similar postoperative care.

### *Skin Preparation and Culture Swabs*

In total, 6 skin swabs were taken during the procedure. The first 2 skin swabs were obtained before skin preparation from the proposed surgical incision site at the medial site of the MTP1 joint and from the interdigital web space between the first and second toe. These swabs were obtained to determine possible interindividual variations in pretreatment bacterial load. After the first 2 swabs, an orthopedic registered nurse used a sterile gauze to apply either iodine 1%/ 70% alcohol (Orphi Farm B.V., Dordrecht, the Netherlands) or chlorhexidine 0.5%/ 70% alcohol (Orphi Farm B.V.) on and around the skin of the surgical incision site. The skin was allowed to dry for approximately 2 minutes (20), after which the 2 skin swabs were repeated.

Subsequently, the surgical procedure was performed. Immediately after skin closure, the last 2 culture swabs were obtained from the same 2 sites. Thus, we were able to differentiate between the direct effect of the skin preparation and the bactericidal effect after the procedure. All culture swabs were taken by the surgeon wearing sterile hand gloves using a cotton-tipped sterile swab, which was wiped over a length of 2 cm at the incision sites or interdigital web space. All swabs were instantly streaked on a blood agar plate and quantitative and qualitative analysis was performed by independent technicians who were blinded for treatment allocation. After 24 hours of incubation at 35°C, cultures were scored as no, <10, and ≥10 colonies grown. Any growth detected resulted in a positive finding (3).

### *Outcome Measures*

Patient demographic data such as gender, age, diabetes, smoking history, and body mass index (BMI) were recorded. The primary outcome of this study was the difference in positive cultures between chlorhexidine 0.5%/70% alcohol and iodine 1%/70% alcohol skin preparation at any of the 3 time points. Secondary outcomes were wound complications (delayed healing, leakage, redness, swelling), infection, allergic reaction to the used solution, and general complications scored as present or not present at day 1, and 2 and 6 weeks after surgery. To prevent bias, wounds were assessed by independent physicians who were not involved in this study. The evaluation and classification of wound infection was performed using the Centers for Disease Control and Prevention (20) criteria and classification, and evaluation of an allergic reaction was performed using the criteria and classification of the World Allergy Organization (21).

### *Sample Size*

Based on the existing literature, the number of patients needed for this study was set on a minimum of 50. Similar studies indicated that this number would provide 80% power to determine a statistically significant difference ($p \leq .05$) in positive cultures (3,11). To take into account possible dropouts, the goal was to include 30 patients in each group.

### *Statistical Analysis*

Data were analyzed using SPSS (version 24, IBM Corp., Armonk, NY) and according to the intention-to-treat principle (N.W.). Categorical data such as patient demographics and culture results were presented as frequencies and percentages and analyzed using a 2-sided Fisher's Exact test. Independent *t* tests were performed on the continues variables such as age at surgery, BMI, and mean duration of the procedure. Statistical significance was defined at the 5% ($p \leq .05$) level.

## Results

### *Participants*

Fifty-nine patients were prospectively randomized in this study. However, from 10 of these patients, 5 in each group, the procedure was postponed long term for personal reasons or preoperative infection. Hence, these patients were excluded (Fig. 1). Therefore, the study group

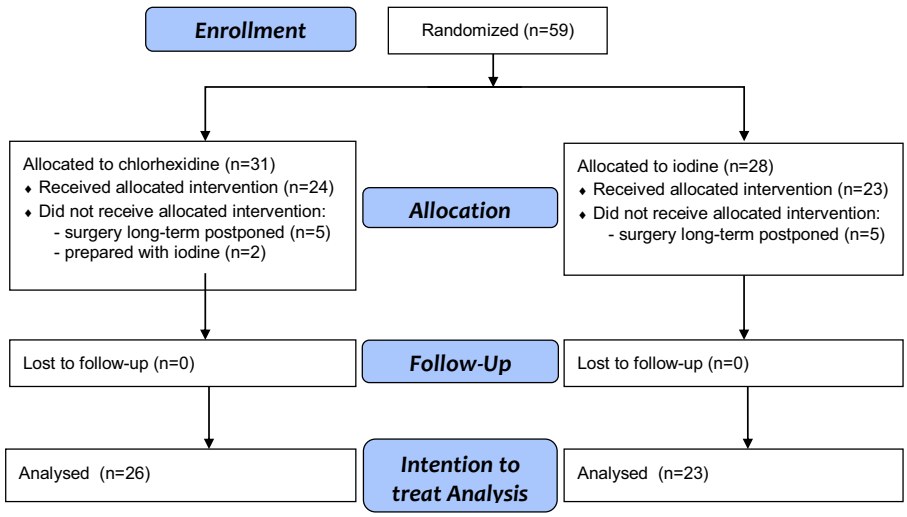


**Fig. 1.** Flow chart including patient enrollment, allocation, and analysis.

consisted of 49 patients with a mean age of 52.3 ± 14.4 (range 22 to 75) years of which 42 (86%) were female. Of the 49 surgeries, 33 (67.3%) were a chevron osteotomy of the first metatarsal bone and 16 (32.7%) were an arthrodesis of the MTP1 joint. Twenty-six patients were randomized for skin preparation with chlorhexidine/alcohol, and 23 were randomized for iodine/alcohol (Table 1). Unfortunately, during preparation, 2 patients randomized for chlorhexidine were unintentionally prepared with iodine, because that was standard for our surgeries. All data presented are according to the intention-to-treat principle. Per protocol analysis showed that results did not change when these 2 patients changed groups.

None of the included patients were diagnosed with diabetes mellitus or had known problems with their immune system. Despite randomization, BMI ($p = .034$) and mean duration of the procedure ($p = .038$) were significantly different between the groups. No significant differences between other patient characteristics were found (Table 1). All patients were discharged 1 day after surgery.

### *Cultures*

The overall rate of positive cultures before skin preparation was 69.4%—40.8% of the MTP1 and 98.0% of the first interdigital web space ($p < .001$; Table 2 and 3). Coagulase-negative staphylococci and especially *Staphylococcus epidermidis* were the most commonly isolated micro-organisms found before skin preparation. For 1 patient in the iodine group, the skin swabs before skin preparation were forgotten and are therefore missing. The overall rate of positive cultures direct post-preparation was 4%; 1 (1.9%) in the chlorhexidine group (MTP1) versus 3 (6.5%) in the iodine group. Two of the positive swabs in the iodine group were obtained from the same patient. After skin closure, there was an increase in overall positive cultures to 10.2%—11.5% in the chlorhexidine and 8.7% in the iodine group. Fourteen positive cultures were found divided over 10 patients—6 patients in the chlorhexidine group and 4 in the iodine group. In 2 patients (1 in each group) both the MTP1 and web space culture was positive. Coagulase-negative staphylococci were the most commonly isolated micro-organisms found after skin preparation. Occasionally, *Bacillus* spp and *Corynebacterium* spp were cultured.

**Table 1**
Baseline characteristics of the study population (N = 49)

| | Chlorhexidine (n = 26) | Iodine (n = 23) | *p* Value |
|---|---|---|---|
| Gender | | | |
| Female | 22 (85) | 20 (87) | >.999 |
| Male | 4 (15) | 3 (13) | |
| Surgery side | | | |
| Right | 15 (58) | 16 (70) | .554 |
| Left | 11 (42) | 7 (30) | |
| Type of surgery | | | |
| Chevron | 18 (69) | 15 (65) | >.999 |
| Arthrodesis | 8 (31) | 8 (35) | |
| Age at surgery (y) | 51.5 ± 15.1 | 53.2 ± 13.8 | .683 |
| Mean duration procedure (min) | 32.0 ± 9.9 | 38.0 ± 9.7 | .038 |
| Smokers | 5 (19) | 5 (22) | >.999 |
| Body mass index | 24.6 ± 4.1 | 27.6 ± 5.3 | .034 |

Binary variables are presented as frequencies (%). Continues variables are presented with the mean ± standard deviation.

**Table 2**
Colonies grown (no, <10, and ≥10) before and after skin preparation for the first interdigital web space (N = 49)

| | | Colonies, no (%) | | | |
|---|---|---|---|---|---|
| Web Space | Group | No | <10 | ≥10 | *p* Value |
| Before skin preparation* | Chlorhexidine | 0 (0) | 8 (30.8) | 18 (69.2) | .746 |
| | Iodine | 0 (0) | 5 (22.7) | 17 (77.3) | |
| After skin preparation | Chlorhexidine | 26 (100) | 0 (0) | 0 (0) | .215 |
| | Iodine | 21 (91.3) | 2 (8.7) | 0 (0) | |
| After skin closure | Chlorhexidine | 23 (88.5) | 2 (7.7) | 1 (3.8) | >.999 |
| | Iodine | 21 (91.3) | 1 (4.3) | 1 (4.3) | |

* One missing value in the iodine group.

**Table 3**
Colonies grown (no, <10, and ≥10) before and after skin preparation for the medial site of the first metatarsal phalangeal joint (N = 49)

| | | Colonies, no. (%) | | | |
|---|---|---|---|---|---|
| First Metatarsal Phalangeal Joint | Group | No | <10 | ≥10 | *p* Value |
| Before skin preparation* | Chlorhexidine | 14 (53.8) | 9 (34.6) | 3 (11.5) | .912 |
| | Iodine | 14 (63.6) | 6 (27.3) | 2 (9.1) | |
| After skin preparation | Chlorhexidine | 25 (96.2) | 1 (3.8) | 0 (0) | >.999 |
| | Iodine | 22 (95.7) | 1 (4.3) | 0 (0) | |
| After skin closure | Chlorhexidine | 23 (88.5) | 3 (11.5) | 0 (0) | >.999 |
| | Iodine | 21 (91.3) | 2 (8.7) | 0 (0) | |

* One value is missing in the iodine group.

### *Complications*

Wound complications (delayed healing, leakage, redness, swelling), infection, allergic reaction, and general complications were scored as present or not present at day 1, and 2 and 6 weeks after surgery. Throughout the study, no allergic reactions to the solution used or general complications were observed in either group. At 1 day postoperatively, there were no signs of wound complications or infections. At 2 weeks after surgery, there were 2 patients in the iodine group with delayed wound healing. In both patients, a positive culture (coagulase-negative staphylococci) was found. One was found directly after preparation (web space) and the other after skin closure at MTP1. At 6 weeks postoperatively, the wound problems were resolved in both patients. However, at 6 weeks postoperatively, in each group a new patient was scored as having minor wound problems (swelling and redness) without signs of an infection. In both patients, 1 of 4 the postpreparation cultures was found to be positive (coagulase-negative staphylococci). This resulted in a wound complication rate 2 weeks postoperatively of 0% in the chlorhexidine group versus 8.7% in the iodine group. The wound complication rates at 6 weeks were 3.8% and 4.3%, respectively. At both time points, the complication rates were not significantly different between groups ($p = .215$ and $p > .999$, respectively).

## Discussion

The present study was the first to evaluate the effect of chlorhexidine 0.5%/70% alcohol and iodine 1%/70% alcohol in these specific concentration on decreasing bacterial load, wound complications, infections, and allergic reactions in elective foot surgery. The main finding is that there was no significant difference in positive cultures rates, postoperative wound problems, or infection rates between the 2 preparation agents. No allergic reactions or unexpected events occurred in either group.

### *Cultures*

Before skin preparation, the overall rate of positive cultures was 69.4%. Directly after preparation, this rate decreased to 4.1%, and after skin closure it was 10.2%. Coagulase-negative staphylococci were the most commonly isolated micro-organisms found after skin preparation. Three of the 4 patients developing wound complications had a positive postpreparation culture. In contrast, 7 of the 10 patients with a positive postpreparation culture did not develop any wound complication. Therefore, bacteria found directly after preparation and after skin

closure did not necessary result in wound complication or infection. This finding may be due to the fact that the most commonly found micro-organisms were coagulase-negative staphylococci, which are part of the normal skin flora and have a relatively low virulence (22). This finding may not apply to other orthopedic surgical interventions, because the risk for developing an infection with coagulase-negative staphylococci is greater for patients with foreign devices such as orthopedic implants (22).

Although 4 patients demonstrated wound complications, none of the patients showed a clearly detectable infection and no difference was found between preparation agents. This finding is in accordance with the literature and could be explained by the administration of preoperative antibiotic prophylaxis (2,3,11,13). Furthermore, the overall percentage of infections after elective surgery is so small that infections may only be observed in much larger patient groups (2).

*Preparation Solutions*

Iodine and chlorhexidine have their own advantages and disadvantages. Iodine in alcohol works by slowly releasing iodine and is effective against bacteria, fungi, protozoa, and viruses without intoxicating human cells. The main disadvantage of iodine-based solutions is skin irritation (11). Skin irritation is not an issue when using chlorhexidine. Chlorhexidine disrupts the cell membrane, which kills the bacteria (23). It is mainly effective against gram-positive and gram-negative bacteria and is thought to be effective longer compared with iodine (11).

A recurring assumption in literature is that it does not really matter which type of solution is used, that the concentration of alcohol is the most important consideration in determining the effectiveness of reducing bacterial load. Alcohol is on itself effective against gram-positive and gram-negative organisms, the tubercle, bacillus and numerous viruses and fungi (14).

Based on the previous literature and on the present study, there is no eminent evidence to choose 1 solution above the other. However, orthopedic surgeons may have a strong preference for using iodine in all foot, knee, and shoulder surgeries because of the color. Iodine is yellowish whereas chlorhexidine is pink. The pink color of chlorhexidine makes it much more difficult to check for postoperative refill, vascularization, and signs of infections.

*Limitations and Strengths*

This study had several limitations. Because iodine solution was the standard for preoperative skin preparation, this agent was used twice in patients randomized for chlorhexidine. Per protocol analyses showed that this step did not influence the results. Also, despite randomization, BMI ($p = .034$) and the mean duration of the procedure ($p = .038$) were significantly different between the groups. This phenomenon was due to change. We are aware that this study has a small sample size. Unfortunately, in 10 randomized patients the procedure was postponed for personal reasons or preoperative infection and they could not undergo surgery in this study's time frame. This factor further decreased the sample size. Because of the small sample size and because infections are rare, correlations between positive cultures and wound infections could not be determined. Last, a quantitative analysis with absolute numbers of colonies might be a more accurate way to determine decreases in bacterial load. Unfortunately, it was not possible to have this information from the independent laboratory. It was therefore decided to score the colonies grown as no, $<10$, and $\geq 10$. Because of our primary goal, this factor did not have any effect on the results or the conclusion. The subdivision into these 3 categories provides sufficient information to compare the 2 skin preparation agents (13).

This study had several strengths, including the prospective randomized setup with strong methodology, prepreparation cultures to take into account interindividual variations in bacterial load, real patients instead of healthy volunteers, swabs taken at multiple locations and time points, and an analysis and interpretation performed by independent and blinded technicians.

In conclusion, there was no significant difference in postoperative wound problems or infection rates between the 2 skin preparation solutions. Chlorhexidine 0.5%/70% alcohol and iodine 1%/70% alcohol both decrease the amount of positive cultures in elective foot surgery.

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