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# Effect of 4% Chlorhexidine Gluconate Predisinfection Skin Scrub Prior to Hepatectomy: A Double-Blinded, Randomized Control Study

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**This trial was designed to compare the efficacy of 4% chlorhexidine gluconate (CHG) with normal saline (NS) as a predisinfection skin-scrub solution prior to standard presurgical skin preparation. Data was collected at a single transplantation center where patients electing resection of hepatic tumors were recruited between October 2011 and September 2012. In total, 100 patients were consecutively enrolled for random assignment to either 4% CHG or NS as a predisinfection skin-scrub solution prior to surgery. Our aim was to assess the comparative antiseptic efficacy of CHG in this setting, focusing on cutaneous microbial colonization (at baseline, preoperatively, and postoperatively) and postsurgical site infections as primary outcome measures. Positivity rates of baseline, preoperative, and postoperative cultures were similar for both groups, showing significant declines (relative to baseline) after skin preparation and no significant postsurgical rebound. Rates of surgical site infection were also similar in both groups (CHG, 6.0%; NS, 4.1%; $P = 1.0$). For patients with hepatic tumors undergoing hepatectomy, the effect of 4% CHG as a predisinfection scrub solution was similar to that of NS in terms of skin decontamination and surgical site infections.**

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Surgical site infections (SSIs) are the most common type of hospital-acquired infection in surgical departments.[1] They delay wound healing, prolong postoperative hospitalization, increase costs, promote antibiotic use, inflict unwanted pain, and in extreme cases cause fatalities.[2] Due to recent advances in surgical technique and perioperative management, hepatic resection has evolved from a risky endeavor to a safe and effective therapy for many liver diseases.[3,4] However, SSI rates after hepatic resection remain high, ranging from 4.6% to 25.2%.[4–6]

Following elective procedures, SSI usually results from colonization by the patient's native skin flora.[7] The most common pathogens, thus, are *Staphylococcus aureus* and coagulase-negative *Staphylococci*.[1,8,9] As such, preoperative disinfection of the surgical site to decrease skin microbial counts prior to incision is standard practice before any surgical intervention[1] as an important step in limiting surgical wound contamination and preventing infection.

A variety of skin-preparation agents and methods are available for SSI prevention, and techniques for preoperative skin cleansing vary among hospitals and surgeons. In Taiwan, the standard preoperative skin preparation used by many hospitals includes a scrub with chlorhexidine gluconate (CHG), followed by painting with alcoholic povidone-iodine (P-IO). There is currently a pressing need to determine the actual contribution of CHG toward preventing SSI when used in this way. Studies comparing CHG with P-IO for cutaneous disinfection have shown that CHG cleansing before intravascular insertions substantially reduces the incidence of related infection and that CHG aids in postinfection site care.[10–12] Hence, this study was conceived to test whether a CHG scrub prior to routine disinfection would reduce microbial growth in surgical site cultures and lower infection rates after resection.

## Patients and Methods

### *Patients and study design*

A series of 100 patients undergoing elective hepatectomy at our hospital from October 2011 to September 2012 was prospectively randomized to receive 1 of 2 skin-preparation techniques. Prior to patient enrollment, a qualified institutional review board approved the trial protocol, which is illustrated in a flow-chart schematic (Fig. 1) and was enabled by access to the infection-tracking database at a single center. Informed consent was obtained from all study participants.

Patients electing hepatectomy for treatment of hepatic tumors were consecutively enrolled for prospective study, with the following criteria as grounds for exclusion: (1) age <18 years, (2) history of radiation therapy to operative site, (3) repeat hepatectomy, (4) history of allergy to any agents used during surgical preparation (*i.e.*, CHG, ethyl alcohol, P-IO), and (5) metastatic cancers. Given no suspicion of active remote infection preoperatively, enrollees were randomly assigned to either 4% CHG (Antigerm, Panion & BF Biotech Inc, Taipei, Taiwan) or normal saline (NS) as a cutaneous, predisinfection scrubbing solution. All were included in the intention-to-treat analysis, but those who were lost to follow-up or who had only open-close surgery or liver biopsy were excluded from the per-protocol analysis.

For routine antimicrobial prophylaxis, each subject received cefazolin (Winston Co, Tainan, Taiwan) 30 minutes before surgery and an intraoperative antimicrobial every 3 hours.

### *Preoperative skin preparation protocol and aerobic cultures*

**Baseline culture**

Protocol sequence at this point was as follows: (1) with the patient on the operative table (prior to skin preparation), a baseline culture was obtained by pressing a swab onto the skin at the presumptive incision site then vigorously rolling clockwise and counterclockwise for 10 seconds; (2) after sealing and labeling the culture swab, it was transported to the microbiology laboratory for aerobic culture; and (3) the patient was randomly assigned to a skin-scrub solution, either CHG (4%) or NS. Random treatment assignments were placed in a set of sealed envelopes. When a participant was randomized, the envelope was opened.

**Preoperative culture**

Surgical skin preparation was performed thereafter as follows: (1) a sterile washcloth was saturated with a solution of either CHG (4%) or NS; (2) the

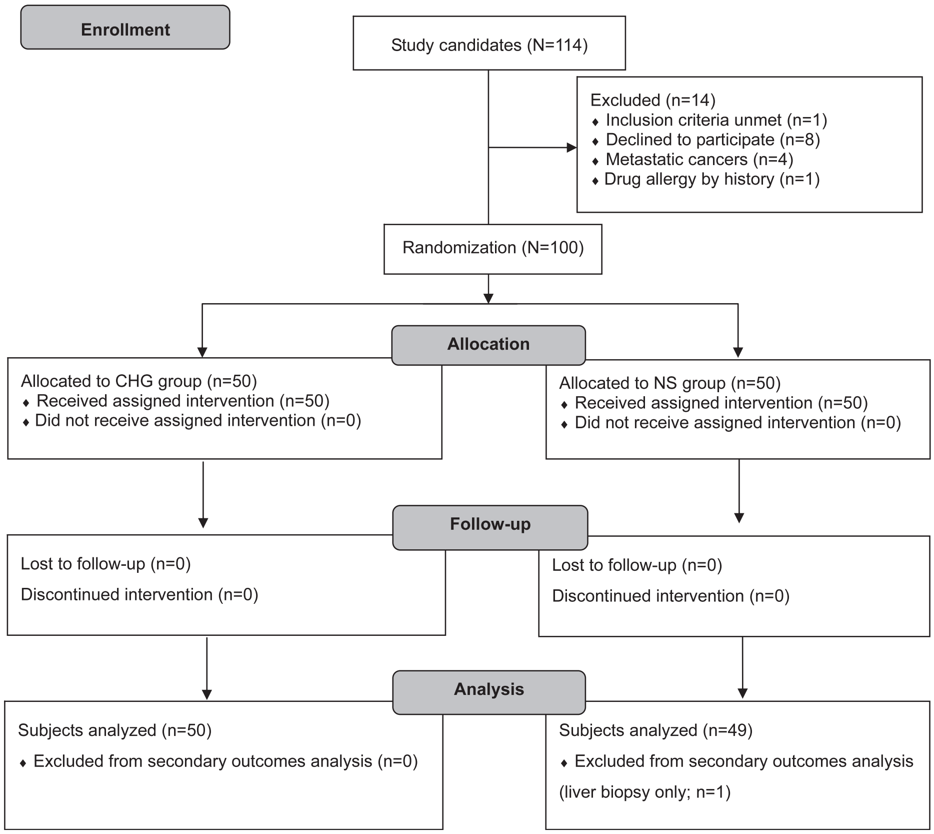


**Fig. 1** Flow chart of trial protocol.

saturated cloth was applied to the presumptive surgical site for 3 minutes of vigorous scrubbing, verified by electronic timer; and (3) a standard 3-step disinfection was done (after patting dry with sterile towel) using iodine-alcohol solution (95% ethyl alcohol, 70 mL, and P-IO, 10 g/100 mL; Sindine, Sinphar Co, Taipei, Taiwan).

Upon completing the surgical skin preparation, each patient was draped in a sterile fashion with the abdomen exposed, allowing full air drying of skin before incision. Using the above technique, a same-site preoperative culture was similarly obtained.

**Postoperative culture**

Next, an adhesive drape was applied to the operative field. Standard surgical technique and intraoperative care were exercised by the same surgical team for each patient: a J-shaped or upper-midline incision for abdominal access, gentle hepatic dissection via Cavitron Ultrasonic Surgical Aspirator (Integra LifeSciences Corp, Plainsboro Township, New Jersey), and systematic ligation of all sizable vessels and bile ducts. During hepatic resection, silk ligatures and vessel clips were used to ligate vessels/ducts. Intraoperative control of bleeding was achieved by way of the Pringle maneuver. One or two closed drains were inserted near any surface-cut liver parenchyma, and fascia was closed with continuous Biosyn 0 absorbable sutures (Covidien Inc, Marsfield, MA, USA). All surgical incisions were irrigated with saline solution prior to skin closure with interrupted transdermal sutures (3-0 monofilament nylon).

After closure of the wound, a same-site postoperative culture was obtained according to protocol. The microbiological evaluation was performed by an independent microbiological core laboratory that had no knowledge of the randomized study group.

*Outcome measures*

The sequential cultures taken (baseline, preoperative, and postoperative) served as measures of primary outcome and were interpreted as positive if any yielded growth of microorganisms. The

*Table 1 Baseline patient characteristics by group*

| Parameters[a] | CHG (4%) (n = 50) | NS (n = 50) | *P* value[b] |
|---|---|---|---|
| Females | 15 (30.0) | 16 (32.0) | 0.83 |
| Mean age, y | 62.7 ± 11.4 | 62.4 ± 10.0 | 0.88 |
| Body mass index, kg/m$^2$ | 24.7 ± 3.3 | 24.4 ± 3.8 | 0.63 |
| Diabetes mellitus | 8 (16.0) | 8 (16.0) | 1.0 |
| Hemoglobin, g/dL | 13.0 ± 1.9 | 13.4 ± 1.6 | 0.25 |
| PT prolongation ≥4 s, % | 1 (2.0) | 0 (0.0) | 1.0 |
| APTT prolongation ≥1.5-fold, % | 1 (2.0) | 0 (0.0) | 1.0 |
| Serum albumin level preoperative, g/dL | 3.9 ± 0.4 | 3.9 ± 0.6 | 0.54 |
| Serum albumin level postoperative, g/dL | 3.1 ± 0.3 | 3.0 ± 0.5 | 0.53 |
| Extent of hepatic resection, segments | 2.0 (1.75–3.0) | 2.0 (1.0–3.25) | 0.76 |
| Pringle maneuver frequency | 1.0 (0–1.25) | 1.0 (0.0–1.25) | 1.0 |
| Duration of surgery, min | 132.2 ± 42.6 | 132.3 ± 45.4 | 0.92 |
| Intraoperative estimated blood loss, mL | 250.0 (100.0–462.5) | 250.0 (137.5–425.0) | 0.87 |
| Tissue glue used | 29 (58.0) | 32 (64.0) | 0.38 |
| Ascites score | 0.0 (0.0–0.0) | 0.0 (0.0–0.25) | 0.23 |
| Ishak score | 4.0 (2.75–5.0) | 4.0 (3.0~6.0) | 0.75 |
| Metavir score | 3.0 (1.75–4.0) | 3.0 (2.0–4.0) | 0.90 |

APTT, activated partial thromboplastin time; CHG, chlorhexidine gluconate; IQR, interquartile range; NS, normal saline; PT, prothrombin time.

[a]Data expressed as n (%); mean ± SD; or median (25%–75% IQR). Hemoglobin: normal range 13.5 to 17 g/dL. Albumin: normal range 3 to 5 g/dL. Ascites score: 0, no ascites; 1, mild ascites; 2, bloody ascites.

[b]The Pearson $\chi^2$ test or Fisher exact test, independent Student *t* test, and Mann-Whitney *U* test were used as appropriate.

following constituted secondary outcome measures: (1) postoperative SSI, (2) length of hospitalization on first admission and on re-admission for complications, and (3) mortality during the follow-up period.

SSI was diagnosed using modified United States Centers for Disease Control and Prevention definitions of nosocomial infection and was documented by author C.S.H., who visited the surgical wards every day during the 30 days after surgery. Patients discharged before this were reviewed weekly in author Y.L.C.'s outpatient clinic to assess the surgical sites for signs of infection, such as erythema, swelling, warmth, pain, and drainage. Each SSI was classified as either a wound infection (superficial or deep) or as an organ/space infection. Both physicians who evaluated SSIs and all patients were blinded to the method of surgical site skin preparation.

Mortality included SSI-related deaths and all-cause mortality. Any fatality due to uncontrolled infection or infection-related multiple-organ failure was considered SSI-related. All-cause mortality equated with any cause of death after surgery, including in-hospital deaths or those occurring after discharge.

### *Statistical analysis*

All data were captured in a computerized database. Pearson $\chi^2$ test or Fisher exact test, independent Student *t* test, and Mann-Whitney *U* test were applied to examine differences between the 2 study groups in terms of demographics and clinical characteristics. Paired proportions were compared using the McNemar test. Values for continuous variables were expressed as mean ± SD or median (interquartile range, 25%–75%) All statistical analyses used standard software (SPSS, v13.0, SPSS Inc, Chicago, Illinois), with statistical significance set at $P \leq 0.05$.

The estimated SSI rate after hepatic resection ranged from 4.6% to 25.2%[4–6]; thus, we proposed that the incidence rates of SSI were 5% in the CHG group and 25% in the NS group, respectively. With a 2-side alpha value of 0.05 and a power of 80% ($\beta = 0.20$), it was estimated that the number required in total was at least 98.

## Results

### *Patient demographics*

From October 2011 to September 2012, 114 patients were admitted with hepatic tumors and scheduled for elective hepatectomy. Of these, 14 patients were not included in the trial: 1 failed to meet the inclusion criteria, 8 declined to participate, 4 had metastatic cancers, and 1 had a history of allergy to alcohol. In total, 100 patients (hepatocellular carcinoma, 84; cholangiocarcinoma, 6; benign/other tumors, 10) were consecutively enrolled for the prospective study and randomly assigned to either

*Table 2* *Analysis of primary outcomes*

| Parameters | CHG (4%) (n = 50), n (%) | NS (n = 50), n (%) | P value[a] |
|---|---|---|---|
| Primary outcomes | | | |
| Baseline culture | 50 (100.0) | 49 (98.0) | 1.0 |
| Preoperative culture | 0 (0) | 2 (4.0) | 0.50 |
| Postoperative culture | 4 (8.0) | 2 (4.0) | 0.68 |
| P value[a] | <0.001[b,c], 0.13[d] | <0.001[b,c], 1.0[d] | |

CHG, chlorhexidine gluconate; NS, normal saline.

[a]$P$ value assessed by Pearson $\chi^2$ test or McNemar test as appropriate.

[b]Preoperative culture versus baseline culture.

[c]Preoperative culture versus baseline culture (CHG and NS).

[d]Preoperative culture versus postoperative culture (CHG and NS, respectively).

the CHG (n = 50) or NS (n = 50) scrub-solution group for primary outcome evaluation (Fig. 1). Three hundred skin cultures taken from these patients were analyzed. One patient in the NS group who had liver biopsy only was excluded from secondary outcome analysis, leaving 99 patients for this purpose (Fig. 1).

Patient characteristics, including gender, mean age, body mass index, diabetes mellitus, hemoglobin, prothrombin time prolongation ≥4 seconds, activated partial thromboplastin time prolongation ≥1.5-fold, preoperative or postoperative serum albumin level, extent of hepatic resection, frequency of Pringle maneuver, duration of surgery, estimated intraoperative blood loss, use of tissue glue, and clinical scoring (ascites, Ishak, and Metavir) were similar for the 2 study groups ($P >$ 0.2; Table 1 ).

*Results of baseline, preoperative, and postoperative cultures*

Nearly all baseline cultures (99.0%) yielded growth of microorganisms (Table 2). There were no significant differences between groups (CHG, 100%; NS, 98%; $P$ = 1.0). In preoperative cultures, none (0%) were positive for CHG, and few (2/50, 4.0%) showed growth with NS ($P$ = 0.50). Culture positivity remained low in the postoperative period (CHG, 4/50, 8.0%; NS, 2/50, 4.0%; $P$ = 0.68).

After the skin preparation protocol, culture positivity declined significantly (relative to baseline) for both CHG and NS in the preoperative (both $P <$ 0.001) and postoperative (both $P <$ 0.001) periods (Table 2). Preoperative and postoperative culture positivity rates of each solution did not differ significantly (CHG, $P$ = 0.13; NS, $P$ = 1.0; Table 2).

*Skin disinfection status after skin preparation and postoperative rebound growth*

The 5 most common microorganisms isolated from baseline cultures in both groups (by order of frequency) were as follows: Gram-positive bacilli (71.0%), coagulase-negative *Staphylococcus* (59.0%), Gram-positive cocci (31.0%), micrococcus (13.0%), and Gram-negative bacilli (8.0%). Only 2 microorganisms were cultured after the skin-preparation protocol, both in the NS group; 6 microorganisms were cultured postoperatively (CHG, 4; NS, 2). Growth of the 3 most common microorganisms—Gram-positive bacilli, coagulase-negative *Staphylococcus*, and Gram-positive cocci (Fig. 2)—declined significantly (relative to baseline) for both the CHG and NS solutions after executing the skin-preparation protocol (preoperative cultures: both $P <$ 0.001) and after surgery (postoperative cultures: CHG, $P <$ 0.001; NS, $P \leq$ 0.001). Rates of preoperative and postoperative culture positivity did not differ significantly for either solution (both $P \geq$ 0.5).

Using either solution, microbial isolates of lesser frequency (micrococcus, fourth; Gram-negative bacilli, fifth) were eradicated after the skin-preparation protocol and did not rebound postoperatively.

*Secondary outcomes*

SSI developed in 5 patients, including 3 of 50 patients (6.0%) subjected to CHG (all superficial infections) and 2 of 49 patients (4.1%) subjected to NS (both deep infections), constituting similar rates of SSI ($P$ = 1.0; Table 3). No organ/space infections developed. All affected patients were diagnosed after hospital discharge and were managed successfully as outpatients. Two patients underwent early removal of skin sutures, and 3 were treated with antibiotics alone. Preoperative and postoperative skin cultures uniformly yielded no growth, so residual bacteria could not be directly implicated.

Mean duration of hospitalization was similar for both solutions (CHG, 8.0 days; NS, 8.0 days; $P$ = 0.69). A single mortality due to hepatic failure was recorded in the NS group, unrelated to SSI (preoperative and postoperative cultures yielding no growth; no SSI evident). Mortality rates were, thus, similar (CHG, 0%; NS, 2.0%; $P$ = 0.5; Table 3).

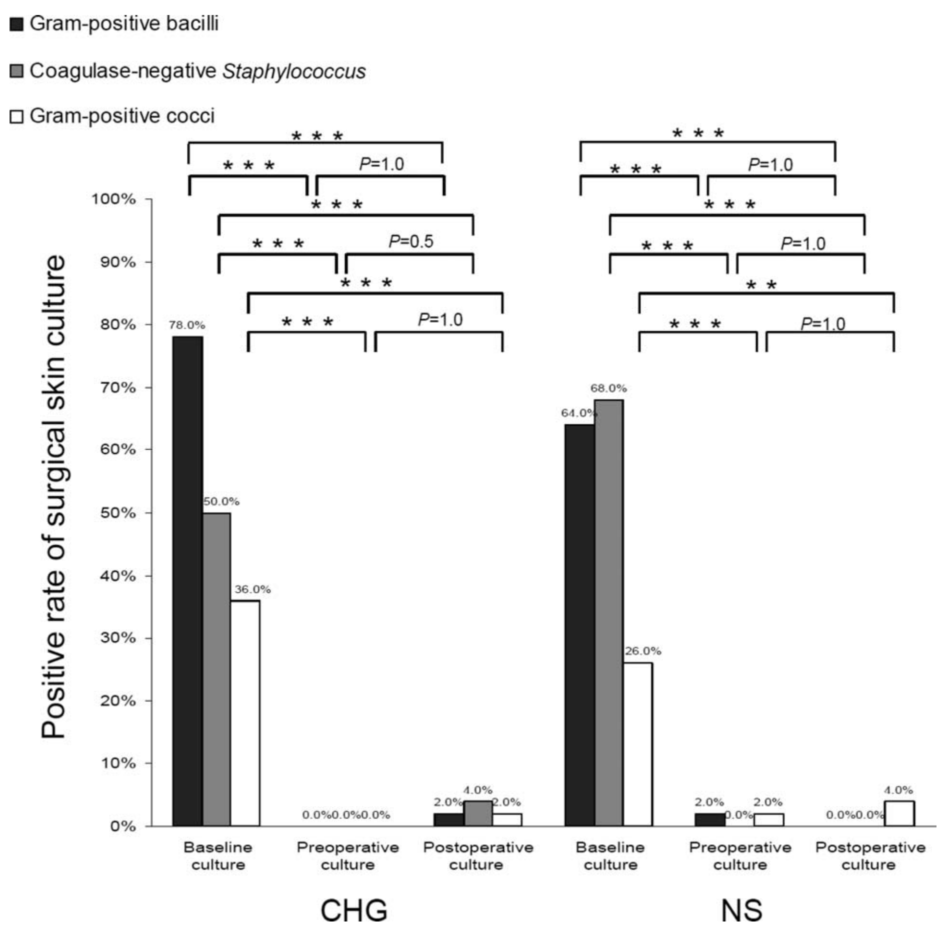


**Fig. 2** Efficacies of CHG and NS scrubs: most common bacterial isolates significantly disinfected after skin preparation; no postsurgical rebound growth using either solution. $^{**}P < 0.01$, $^{***}P < 0.001$.

No adverse events (such as pruritus, erythema, or chemical burn) were manifested relative to the agents/solutions used for skin antisepsis.

## Discussion

This study demonstrated that solutions of CHG (4%) and NS displayed similar efficacy in reducing skin bacterial loads and constituted similar rates of SSI when used for predisinfection scrubbing, prior to standard 3-step disinfection. Our data clearly indicated that a 3-minute predisinfection scrub with either CHG (4%) or NS solution, followed by painting with P-IO-alcohol, was efficacious as a surgical preparation technique for aerobic bacterial decontamination of abdominal skin.

SSI accounts for 38% of nosocomial infections among surgical patients.[1,13] As a consequence, medical costs rise, hospitalization is prolonged, and quality of life in the postoperative course is reduced.[14] A patient's own skin flora is the major source of pathogens responsible for SSI.[15] Thus, by decreasing the burden of skin microbials, the risk of SSI is reduced.[16] For efficient removal of resident organisms, use of both mechanical and chemical methods is required. The mechanical process involves the application of skin antisepsis solution with adequate friction of the applicator to ensure that all the cracks and fissures in the skin are sufficiently coated with the solution. The chemical process involves both the destruction of microorganisms and the prevention of rebound colonization after cleansing.[17] Skin antisepsis is, thus, aimed at transient removal of microorganisms to minimize the opportunity for infection.[18]

A variety of skin preparations and methods are available, and the 2 active agents most commonly used in preoperative antiseptics are CHG and P-IO, either as aqueous solution or alcoholic.[19–22] CHG is a biguanide effective against a wide range of Gram-

*Table 3 Analysis of secondary outcomes*

| Parameters[a] | CHG (4%) (n = 50) | NS (n = 49) | *P* value[b] |
|---|---|---|---|
| Secondary outcomes | | | |
| Surgical site infection | 3 (6.0) | 2 (4.1) | 1.0 |
| Hospital stay, days | 8.0 (7.0–10.0) | 8.0 (7.0–10.0) | 0.69 |
| Mortality rate, all-cause | 0 (0.0) | 1 (2.0) | 0.50 |

CHG, chlorhexidine gluconate; NS, normal saline; IQR, interquartile range.

[a]Data expressed as n (%), median (25%–75% IQR).

[b]*P* value assessed by Pearson $\chi^2$ test or Mann-Whitney *U* test as appropriate.

positive and Gram-negative bacteria, lipophilic viruses, and yeasts.[2] Several studies have maintained that CHG is preferable, rather than P-IO, for preoperative antisepsis in clean-contaminated surgery because of immediate and persistent bactericidal activity.[23–26] In this study, we applied the mechanical process as a 3-minute predisinfection scrub with either a CHG (4%) or NS solution and then followed that with a chemical process with P-IO-alcohol. Our results showed that the decontamination effects were similar both in preoperative (CHG, 0%; NS, 4.0%; $P = 0.50$) and postoperative cultures (CHG, 8.0%; NS, 4.0%; $P = 0.68$). This means both the mechanical process with scrub and the chemical process with P-IO-alcohol eradicated most common skin microorganisms, and the microorganisms did not rebound postoperatively. The results met the criteria of the Food and Drug Administration for adequate skin site treatment.[27]

The reasons why scrubbing with either CHG (4%) or NS does not have a significant difference were proposed. Magera *et al*[15] reported that topical scrubbing with 4% chlorhexidine has a lower preoperative perineal colonization rate than with soap and water only, but the benefit was not seen in the preoperative abdomen. The abdomen is generally believed to be easier to sanitize than the perineum. Moreover, Tschudin-Sutter *et al*[1] reported that P-IO-alcohol is effective in decreasing the residual bacterial colonization and SSI of the preoperative site. Furthermore, chlorhexidine is highly cationic and may be inactivated by iodine.[17] Accordingly, scrubbing with CHG did not take greater advantage of its antiseptic properties than scrubbing with NS prior to a chemical process with P-IO-alcohol in our trial.

It is well known that the incidence of SSI is greatly influenced by many perioperative factors.[3,5,19,28,29] As a transplantation center, our hospital is one of the top 5 hospitals in Taiwan, with the highest overall 3-year survival rate after liver transplantation. Our facility has developed strict infection-control measures, incorporating standard perioperative protocols. We believe that these policies are also responsible for lowering the rates of culture positivity after surgery and SSI. In this study, SSI developed in 6.0% of cases with CHG use and 4.1% with NS use ($P = 0.1$). None of these patients expired. Moreover, the mean duration of hospitalization (CHG, 8 days; NS, 8 days; $P = 0.69$) and mortality (CHG, 0%; NS, 2.0%; $P = 0.5$) were similar in these two groups. Given adequate infection-control measures, a predisinfection scrub in clean-contaminated surgery, such as hepatectomy, could be superfluous.

There are several limitations to our study, including the fact that the data accrued is qualitative rather than quantitative. Quantitative assessment of the cultures obtained might have added information on the antiseptic efficacies of these solutions.[30] However, in clinical practice, qualitative culture data generally suffice for decision making, and the lowering of bacterial loads after skin preparation was significant.[16,30] To our knowledge, this is the first use of qualitative cultures to evaluate preoperative surgical scrubs in this particular arena. The sample size was also limited as a consequence of the chosen setting. We ultimately terminated this study when each of the study groups reached at least 50 patients, because all outcome data were equivalent. Perhaps an alternate approach could be taken, identifying a scenario where CHG predisinfection might confer greater benefit.

In conclusion, before a standard 3-step disinfection process with iodine-alcohol solution prior to hepatectomy, using 4% chlorhexidine gluconate as a predisinfection scrub solution did not take more advantage of its antiseptic properties than using normal saline scrub.

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## References

1. Tschudin-Sutter S, Frei R, Egli-Gany D, Eckstein F, Valderrabano V, Dangel M *et al*. No risk of surgical site infections from

residual bacteria after disinfection with povidone-iodine-alcohol in 1014 cases: a prospective observational study. *Ann Surg* 2012;**255**(3):565–569
2. Tanner J, Swarbrook S, Stuart J. Surgical hand antisepsis to reduce surgical site infection. *Cochrane Database Syst Rev* 2008; **23**(1):CD004288
3. Okabayashi T, Nishimori I, Yamashita K, Sugimoto T, Yatabe T, Maeda H *et al*. Risk factors and predictors for surgical site infection after hepatic resection. *J Hosp Infect* 2009;**73**(1):47–53
4. Liu CL, Fan ST, Lo CM, Wong Y, Ng IO, Lam CM *et al*. Abdominal drainage after hepatic resection is contraindicated in patients with chronic liver diseases. *Ann Surg* 2004;**239**(2): 194–201
5. Harimoto N, Shirabe K, Abe T, Yukaya T, Tsujita E, Gion T *et al*. Prospective randomized controlled trial investigating the type of sutures used during hepatectomy. *World J Gastroenterol* 2011; **17**(18):2338–2342
6. Togo S, Matsuo K, Tanaka K, Matsumoto C, Shimizu T, Ueda M *et al*. Perioperative infection control and its effectiveness in hepatectomy patients. *J Gastroenterol Hepatol* 2007;**22**(11):1942–1948
7. Zywiel MG, Daley JA, Delanois RE, Naziri Q, Johnson AJ, Mont MA. Advance pre-operative chlorhexidine reduces the incidence of surgical site infections in knee arthroplasty. *Int Orthop* 2011;**35**(7):1001–1006
8. Noble W. Skin as a source for hospital infection. *Infect Control* 1986;**7**(suppl 2):111–112
9. Van Ek B, Bakker FP, van Dulken H, Dijkmans BA. Infections after craniotomy: a retrospective study. *J Infect* 1986;**12**(2):105–109
10. Hibbard JS, Mulberry GK, Brady AR. A clinical study comparing the skin antisepsis and safety of ChloraPrep, 70% isopropyl alcohol, and 2% aqueous chlorhexidine. *J Infus Nurs* 2002;**25**(4):244–249
11. Hibbard JS. Analyses comparing the antimicrobial activity and safety of current antiseptic agents: a review. *J Infus Nurs* 2005; **28**(3):194–207
12. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002;**136**(11):792–801
13. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol* 1999;**20**(4):250–278
14. Sheng WH, Wang JT, Lu DC, Chie WC, Chen YC, Chang SC. Comparative impact of hospital-acquired infections on medical costs, length of hospital stay and outcome between community hospitals and medical centres. *J Hosp Infect* 2005; **59**(3):205–214
15. Magera JS Jr, Inman BA, Elliott DS. Does preoperative topical antimicrobial scrub reduce positive surgical site culture rates in men undergoing artificial urinary sphincter placement? *J Urol* 2007;**178**(4 - pt 1):1328–1332
16. Roukis TS. Bacterial skin contamination before and after surgical preparation of the foot, ankle, and lower leg in patients with diabetes and intact skin versus patients with diabetes and ulceration: a prospective controlled therapeutic study. *J Foot Ankle Surg* 2010;**49**(4):348–356
17. Scowcroft T. A critical review of the literature regarding the use of povidone iodine and chlorhexidine gluconate for preoperative surgical skin preparation. *J Perioper Pract* 2012; **22**(3):95–99
18. Tanner J. Surgical hand antisepsis: the evidence. *J Perioper Pract* 2008;**18**(8):330–334
19. Ellenhorn JD, Smith DD, Schwarz RE, Kawachi MH, Wilson TG, McGonigle KF *et al*. Paint-only is equivalent to scrub-and-paint in preoperative preparation of abdominal surgery sites. *J Am Coll Surg* 2005;**201**(5):737–741
20. Towfigh S, Cheadle WG, Lowry SF, Malangoni MA, Wilson SE. Significant reduction in incidence of wound contamination by skin flora through use of microbial sealant. *Arch Surg* 2008; **143**(9):885–891
21. Beldi G, Bisch-Knaden S, Banz V, Mühlemann K, Candinas D. Impact of intraoperative behavior on surgical site infections. *Am J Surg* 2009;**198**(2):157–162
22. Fletcher N, Sofianos D, Berkes MB, Obremskey WT. Prevention of perioperative infection . *J Bone Joint Surg Am* 2007;**89**(2): 1605–1618
23. Noorani A, Rabey N, Walsh SR, Davies RJ. Systematic review and meta-analysis of preoperative antisepsis with chlorhexidine versus povidone-iodine in clean-contaminated surgery. *Br J Surg* 2010;**97**(11):1614–1620
24. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, Carrick MM *et al*. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;**362**(1):18–26
25. Denton G. Chlorhexidine. In: Block SS, ed. *Disinfection, Sterilization, and Preservation*. 4th ed. Philadelphia, PA: Lea and Febiger, 1991:274–289
26. Atiyeh BS, Dibo SA, Hayek SN. Wound cleansing, topical antiseptics and wound healing. *Int Wound J* 2009;**6**(6):420–430
27. O'Malley P. Chlorhexidine wipes: the new weapon against surgical site infections? *Clin Nurse Spec* 2008;**22**(2):61–62
28. Togo S, Kubota T, Takahashi T, Matsuo K, Morioka D, Tanaka K *et al*. Usefulness of absorbable sutures in preventing surgical site infection in hepatectomy. *J Gastrointest Surg* 2008;**12**(6): 1041–1046
29. Moreno Elola-Olaso A, Davenport DL, Hundley JC, Daily MF, Gedaly R. Predictors of surgical site infection after liver resection: a multicentre analysis using National Surgical Quality Improvement Program data. *HPB (Oxford)* 2012; **14**(2):136–141
30. Ostrander RV, Brage ME, Botte MJ. Bacterial skin contamination after surgical preparation in foot and ankle surgery. *Clin Orthop Relat Res* 2003;(406):246–252