Iodine-impregnated incision drape and bacterial recolonization in simulated total knee arthroplasty

A controlled, randomized experimental trial

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Background and purpose — Iodine-impregnated incision drapes (IIIDs) are used to prevent surgical site infection (SSI). However, there is some evidence to suggest a potential increase in SSI risk as a result of IIID use, possibly from promotion of skin recolonization. A greater number of viable bacteria in the surgical field of an arthroplasty, and surgery in general, may increase the infection risk. We investigated whether IIID use increases bacterial recolonization compared to no drape use under conditions of simulated total knee arthroplasty (TKA).

Methods — 20 patients scheduled for TKA were recruited. Each patient had 1 knee randomized for draping with IIID, while the contralateral knee was left bare. The patients thus served as their own control. The operating room conditions and perioperative procedures of a TKA were simulated. Cylinder samples were collected from the skin of each knee prior to disinfection, and again on 2 occasions after skin preparation—75 min apart. Quantities of bacteria were estimated using a spread plate technique under aerobic conditions.

Results — We found similar quantities of bacteria on the intervention and control knees immediately after skin disinfection and after 75 min of simulated surgery. These quantities had not increased at the end of surgery when compared to baseline, so no recolonization was detected on the draped knees or on the bare knees.

Interpretation — The use of IIIDs did not increase bacterial recolonization in simulated TKA. This study does not support the hypothesis that IIIDs promote bacterial recolonization and postoperative infection risk.

Surgical site infections (SSIs) remain a serious complication in orthopedic surgery. In total knee arthroplasty (TKA), deep infection leading to revision surgery has an incidence of around 1% in Scandinavia, with an increased risk in obese and diabetic patients (Jamsen et al. 2012). Surgical infections can be superficial or deep, and they are thought to come from various bacterial sources and through different pathways. These may include contamination of the incision with endogenous organisms from the patient's skin or with air-borne organisms from the operating room and surgical staff. Their relative contribution to surgical wound contamination is, however, still uncertain (Gosden et al. 1998, Gallo et al. 2003).

SSIs are predominately caused by coagulase-negative staphylococci (CoNS) and *Staphylococcus aureus* (Stefansdottir et al. 2009, Zimmerli and Moser 2012), which are highly prevalent skin flora in the TKA patient and frequent wound contaminants during arthroplasty surgery (Tanzer et al. 1994, Davis et al. 1999, Stefansdottir et al. 2013, Jonsson et al. 2014). Thus, the occurrence of CoNS implicates the endogenous route as a pathway for SSI. Prophylactic strategies to prevent wound contamination, such as preoperative skin disinfection, are effective in reducing bacterial colonization prior to surgical incision and result in lower postoperative infection rates (Dumville et al. 2013). It is impossible to create a completely aseptic environment for the duration of surgery, however, as preoperative skin disinfection cannot reach residual organisms, and the surface of the skin can be recolonized by the patient's endogenous flora from hair follicles, sebaceous glands, and sweat glands (Selwyn 1985, Fleischmann et al. 1996). CoNS have been shown to constitute the majority of the recolonizing organisms (Fleischmann et al. 1996, Falk-Brynhildsen et al. 2013b)

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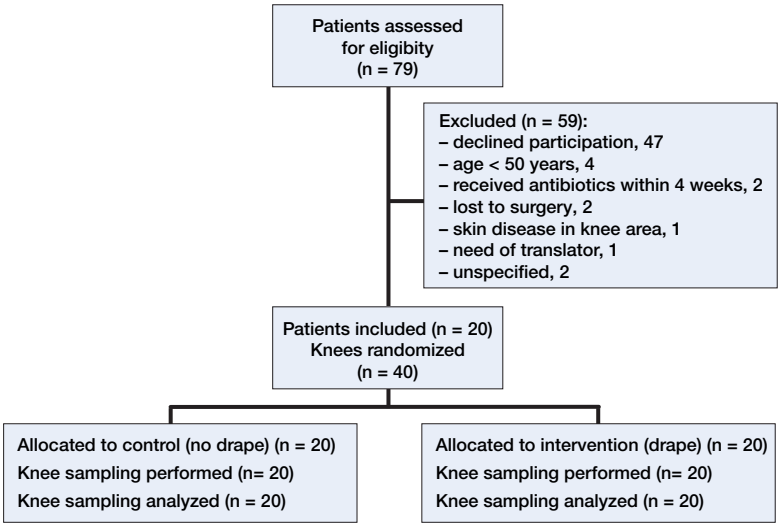

Figure 1. CONSORT flow diagram. 79 patients were screened and 20 patients were finally included.

Plastic incision drapes were introduced several decades ago to act as a physical barrier to block the translocation of recolonizing bacteria from the skin adjacent to the surgical site into the surgical wound. These types of drapes have subsequently been suggested to increase recolonization rates, possibly due to relative occlusion of the skin leading to greater skin hydration (Marples and Kligman 1969, Falk-Brynhildsen et al. 2013a).

Newer types of drapes that incorporate an antiseptic iodine complex in the adhesive of the drape facing the skin have since been introduced. Although the use of these iodine-impregnated incision drapes (IIIDs) has not altered SSI rates in a broad range of surgical specialties (Webster and Alghamdi 2013), with early-generation antimicrobial drapes intraoperative drape-lift has been associated with increased SSI risk (Alexander et al. 1985). The use of IIIDs in arthroplasty surgery has seldom been investigated, and there is little evidence to support their use in reducing SSI rates.

The aim of this self-controlled, randomized experimental study was to investigate whether intraoperative draping with an IIID would increase recolonization with skin microbes compared to no use of a drape, during simulated TKA surgery. The outcomes were microbial quantity and identification of viable organisms on the skin. Our hypothesis was that recolonization of skin microbes would be greater with an IIID than with no drape.

Methods

Participants

We recruited patients who were scheduled for TKA at Odense University Hospital, Denmark. 20 patients were prospectively included from January 2015 to May 2015, and we excluded 59 (Figure 1).

We assigned the intervention and the control treatment at an equal allocation ratio, with the patients serving as their own controls—resulting in a split-person design. Assuming a standard deviation of 1.0 $\log_{10}$ with a 2-tailed $\alpha = 0.05$ and 80% power, 16 patients would be needed in order to detect a 1.0 $\log_{10}$ difference, which we judged to be clinically relevant.

Allocation of the patients' knees to the intervention (drape) and control (no-drape) group was carried out through envelope randomization using serially numbered envelopes with a group allocation number enclosed, which had been prepared by a third party. The envelope was opened in the operating room prior to the first sampling round and the allocation was revealed to both the patient and the researcher(s). Thus, there was no blinding during the intervention or during data analysis.

Intervention

The patient was positioned supine in a standard operating theater with active laminar flow and surgical lamps. Both knees were disinfected using curcumin-colored 0.5% chlorhexidine gluconate in 96% ethanol, by skin painting in 2 sessions separated by a drying period. The disinfected area was then left to dry completely. Skin disinfection was followed by standard covering of the patient with surgical drapes (BARRIER; Mölnlycke Health Care, Göteborg, Sweden). 1 knee was subsequently draped with an iodine-impregnated incision drape (Ioban 2™; 3M Health Care), while the other knee was left uncovered. Application of the incision drape was done in accordance with 3M guidelines. Patients were instructed not to use any skin products on their legs on the day of the intervention. The researcher and surgical nurse responsible for the intervention wore surgical caps, facemasks, sterile operation garments, and sterile surgical gloves during disinfection and application of draping.

The patient remained supine on the operating table for 75 min, simulating the surgical duration of uncomplicated TKA surgery. Patients were allowed to move their legs, but avoided cross-contamination between the knees. The patient's torso was covered with a Bair Hugger (Associated Health Systems Inc., Edmonton, AB, Canada), which was turned on at the beginning of surgery to prevent hypothermia. The patient was observed by at least 1 staff member at all times, and 2 to 3 staff members were present for most of the duration of the intervention. Opening of doors was minimized.

Skin sampling (Figure 2)

The surface of the skin was sampled with a modified version of the cylinder-sampling method/cup-scrub technique (Williamson and Kligman 1965, Bashir et al. 2012). We restricted the sampling area using a steel cylinder with an inner diameter of 23 mm, adding 1 mL of sampling solution to the cylinder.

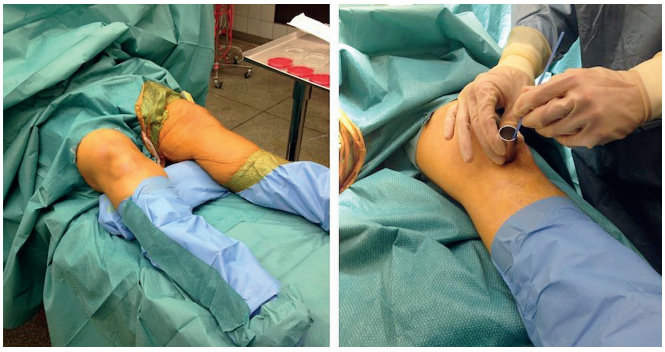

Figure 2. The experimental setup after application of the IIID (left panel) and during skin sampling using the cylinder-sampling method (right panel). The intervention knee was covered for 75 min. Samples were collected before skin disinfection and on 2 occasions after skin preparation.

The sampling site was then rubbed with moderate pressure in an even grid formation for 1 min with a sterile, plastic inoculation loop. The sampling solution was collected in a sterile test tube using a sterile pipette. The sampling process was then repeated, giving another sample that was pooled with the first sample. This method was developed based on pilot studies done in our laboratory. The sampling solution consisted of deionized water containing 0.1% Triton-X 100. To neutralize carry-over contaminants, we added 10% polysorbate 80 (Tween 80), 1.2 w/v% lecithin, 0.5 w/v% sodium thiosulfate pentahydrate, 1.0 w/v% Na_2HPO_4, and 0.04 w/v% KH_2PO_2. The pH was adjusted to 7.8–7.9 using 0.1 M NaOH.

Samples were taken on 3 occasions from each knee: before and immediately after disinfection, and after simulated surgery. Pre-disinfection samples measured the patient's habitual skin flora, while samples collected immediately after disinfection served as a baseline for the intervention. At the end of the simulated surgery, post-intervention samples were collected from the no-drape knee, followed by opening of the IIID using scissors and surgical tweezers to expose the skin for sampling. Pre-disinfection samples were taken bilaterally from the distal, anterior thigh. The samples after both disinfection and drape-opening were taken from the suprapatellar skin area, corresponding to the borders of the quadriceps femoris muscle tendon, and from the infrapatellar area of skin covering the borders of the patellar ligament. A new area of skin was chosen for each sample. The same researcher performed all the sampling, assisted by a surgical nurse, and both adhered to local antiseptic protocol.

The samples were serially diluted in 10-fold dilutions to 10^{-3} for pre-disinfection samples and 10^{-1} for post-disinfection and post-intervention samples using a phosphate buffer solution (PBS) at pH 7.4. Aliquots of each diluted and undiluted sample were then spread in duplicate on 5% blood agar plates. The inoculation volume was 100 µL in the pre-disinfection samples and 200 µL in all other samples. Plating was performed immediately in the operating room, following the end of each sampling round. A randomly chosen, unused sample of the sampling fluid was also plated in duplicate and served as a negative control for that particular patient.

3 plates containing 5% blood agar were placed on a table within the laminar flow field. These plates were uncovered for air inoculation after drape application and were closed at the end of the simulation to enable us to measure the degree of contamination from air-borne organisms during the intervention. All plates were then incubated aerobically for 48 h at 35°C.

Evaluation of neutralization efficacy

To validate the efficacy of the neutralization formulation, we disinfected the skin of the anterior thigh of a healthy volunteer using curcumin-colored 0.5% chlorhexidine gluconate in 96% ethanol. Following complete evaporation of alcohol from the prepared skin, we sampled the skin using the cylinder-sampling method with PBS as the sampling fluid. This procedure was repeated on the contralateral thigh of the volunteer, differing in the application of an Ioban 2™ incision drape for 75 min prior to sample collection. The collected samples served as the antiseptic challenger in an in-vitro validation assay, performed in accordance with ASTM standard E-1054-08. An ATCC 14990 strain of *Staphylococcus epidermidis* was employed as the challenge organism. Exposure durations of < 1 min and 30 min were used, and the test organism was recovered on a semi-solid medium. The neutralization solution provided complete recovery of the test organism, preventing loss of viability following exposure to the carry-over antiseptics that would otherwise be present in samples from disinfected skin.

Outcome analysis

Serving as the primary outcome, the colony forming units (CFU) of all plates were manually counted following incubation. We made between-group and within-group comparisons at the end of the surgical simulation, comparing the bacterial density on the skin at the start and end of the draping period.

The first dilution step with growth of ≤ 300 CFU in both duplicates was chosen for analysis. During the study, we recognized that the sampling fluid had some microbial contamination with bacillus organisms and could not be sterilized using available techniques. The mean of the samples from each knee was therefore adjusted for growth in the negative control samples and then converted to $\log_{10}$ CFU/cm^2 of skin, with a floor set to zero. Because of a flooring effect from log-transformation, the analysis within and between knees was performed using the Wilcoxon signed-rank test on unadjusted data. The analysis was performed using STATA 13.

As a secondary outcome, we isolated unique colonies from the undiluted growth plates of the post-intervention samples of each patient. The organisms were identified using matrix-assisted laser desorption/ionization - time of flight mass spectrometry (MALDI-TOF MS) (Harris et al. 2010) and grouped into the following categories: coagulase-negative staphylo-

Table 1. Bacterial growth in skin samples collected before and after disinfection, median $\log_{10}$ CFU/cm^2 with interquartile range (IQR)

	Microbial growth ($\log_{10}$ CFU/cm^2) [a]				
	Before disinfection	After disinfection		End of surgery	
Knee allocation	Median (IQR)	Median (IQR)	p-value [b]	Median (IQR)	p-value [b]
Ioban 2 incision drape	2.99 (0.92)	0.26 (0.63)	< 0.001	0.00 (0.94)	0.9
Control (no drape)	2.91 (0.45)	0.32 (0.93)	< 0.001	0.26 (0.73)	0.3
p-value [c]	1.0	0.8		0.6	

[a] Plate growth from the skin samples was adjusted for negative control growth. Comparisons were made using Wilcoxon signed-rank tests on unadjusted data.
[b] p-value for analysis of the same knee; comparison was made with the previous sample.
[c] p-value for analysis between knees.

cocci, *Staphylococcus aureus, Corynebacterium,* enterococci, and *E. coli*.

Ethics and registration

The study was approved by the Regional Ethical Committee for Southern Denmark (project ID S-20140060), and was carried out in accordance with the Danish Code of Conduct for Research Integrity and the Helsinki Declaration (II). Written informed consent was obtained from all participants. The study was also registered at ClinicalTrials.gov (identifier: NCT02342561).

Results

Baseline data

13 women and 7 men, mean age 68 (SD 10) years, were included in the study.

Before disinfection, the median bacterial density of the knee samples, adjusted for growth levels in the negative control plates was 2.99 $\log_{10}$ CFU/cm^2 in the drape group and 2.91 $\log_{10}$ CFU/cm^2 in the no-drape group (Table 1). No statistically significant difference were detected between the knees (p = 1.0).

Microbial density

All the participants received the allocated treatment and were included in the analysis (Figure 1). Disinfection of the skin resulted in a statistically significantly reduced microbial density in both groups, with no difference between the knees (p = 0.8), suggesting that there were comparable microbial conditions prior to IIID application.

Samples taken at the end of surgical simulation showed a similar number of viable bacteria on the skin of the draped knee, compared to the control knee (p = 0.6). The median difference in bacterial recolonization between the knees during the draping period was calculated to be 0.00 $\log_{10}$ CFU, with a lower and upper quartile of −0.30 and 0.59 $\log_{10}$ CFU.

When samples taken at the beginning and end of the draping period were compared, we could not detect any recolonization—either on the knees that had been draped with IIID or on the knees that had not been draped.

10 of the 60 plates that had been left open and exposed to the air of the operating room showed bacterial growth. The contaminants were predominately CoNS, with a maximum of 1 colony per plate.

Species of organisms

We identified the species of viable organisms from the samples taken at the end of the surgical simulation, corresponding to the time of wound closure. Coagulase-negative staphylococci were identified in the samples from 7 of the 20 draped knees and 5 of 20 control knees (p = 0.7). Corynebacteria were grown from the samples collected from the draped knee in 2 patients, with no cases in the control group. We did not identify any growth of *S. aureus, Enterococcus,* or *E. coli* in either group.

Discussion

An increase in bacterial recolonization rates resulting from the intraoperative use of IIIDs could compromise the antiseptic environment during surgery. The findings from this randomized, controlled trial did not support our hypothesis that an IIID increases recolonization with skin microbes compared to no use of a drape during TKA surgery. Covering of the skin with an IIID after chlorhexidine gluconate-based skin disinfection did not increase microbial quantities on the skin when compared to the skin preparation alone; nor did the use of an IIID have any effect on the prevalence of common pathogenic bacteria on the skin. This suggests that IIIDs can be used in TKA surgery for an uncomplicated procedure lasting 75 min, without any increased risk of potentially pathogenic endogenous organisms being present in the surgical field. We did not detect any recolonization on the control knee during the simulation. One might therefore question the necessity of using IIIDs to prevent substantial recolonization in TKA surgery; however, the use of incision drapes may be preferred for other reasons, such as improved fixation of the surgical drapes throughout surgery.

Only a few studies have been published on the microbial skin density associated with incision drapes. Our findings contrast with a study performed on the abdominal skin using an earlier IIID product, where samples were taken by contact plating (Johnston et al. 1987). The authors found a statistically significant reduction in recolonization after 60 min in favor of IIID. Another study focusing on microbes in the surgical wound found reduced wound contamination rates by swab sampling when using IIIDs during abdominal surgery (Dewan

et al. 1987). Other studies have demonstrated skin recolonization, i.e. regrowth of bacteria, after only 60 min on skin disinfected with chlorhexidine gluconate for open heart surgery (Falk-Brynhildsen et al. 2013a).

It is possible that recolonizing organisms adhere to the adhesive of the drape when the drape is taken off, thereby removing organisms from the skin prior to sampling. We consider it unlikely that such microbes adhering to the antimicrobial surface of the drape in this way would be a potential source of wound contamination. Exposure to recolonizing organisms in deeper layers of the skin by drape removal or intraoperative drape-lift could, however, be a possible cause of microbial wound contagion (Alexander et al. 1985). Organisms exposed on the skin by drape removal would be revealed by our sampling method. Settle plates left in the laminar flow revealed only sporadic, low air contamination. Thus, we do not believe that the settling of microbes on the undraped knee was of any importance to our results.

Our study had several strengths. We used a chlorhexidine gluconate-based skin preparation protocol in combination with IIID draping, which is common practice for IIID use in TKA surgery in Scandinavia. Most of the earlier studies have used iodine-based skin preparation, which has less residual antimicrobial properties than chlorhexidine gluconate-based products (Faoagali et al. 1995, Fletcher et al. 2007). Alcohol-based chlorhexidine products have become standard for skin disinfection in Scandinavian surgical wards. We could not find any earlier studies comparing IIID draping on chlorhexidine-prepared skin to chlorhexidine-based skin disinfection alone.

The female-to-male ratio in our study was 1.9, with a mean age of 68 years, and the patients included were scheduled for TKA surgery. This makes our cohort representative of the typical TKA patient. The study was further strengthened by its paired split-person design whereby both knees of each patient were used, either as an intervention knee or as a control knee. This minimizes bias from the large inter-patient variations in numbers of skin flora organisms. Our sampling protocol also gave multiple samples from each knee at all sampling times; even so, we do recognize that with our sampling method we may only have sampled a fraction of the total residual skin flora (Selwyn 1985, Chevalier et al. 1987). However, the use of a validated neutralization system ensured the viability of the organisms collected—in spite of carry-over contamination from topical antiseptics, which is known to result in overestimation of antiseptic efficacy (Kampf et al. 2005).

The cylinder-sampling method that we used is a standard method for testing topical antiseptics, and had a validated neutralization system incorporated in the sampling fluid. This method has been shown to provide a more complete sampling of the skin flora, compared to contact plates and swabbing methods, and is truly quantitative when compared to these semi-quantitative sampling methods (Selwyn 1985, Hambraeus et al. 1990). The growth levels were compatible with earlier studies using this method of sampling (Bashir et al. 2012, Carty et al. 2014).

The study also had limitations. Because we performed our sampling under simulated conditions, our study failed to reproduce the effects of blood and other fluids in the surgical field that may have influenced the residual effect of chlorhexidine gluconate on the disinfected skin and the quality of drape adherence. The same study design could be used during actual surgery. This would limit the split-person design, however, which we consider to have been one of the main strengths of our study. The sampling procedure would also be potentially disruptive to the surgical procedure, possibly necessitating a reduced number of samples collected. Incubation was limited to aerobic conditions, as most pathogenic organisms in orthopedic SSI are either aerobes or facultative anaerobes (Stefansdottir et al. 2009). The incubation period was 48 h, which was also chosen by other authors (Williamson and Kligman 1965, Falk-Brynhildsen et al. 2013b). We cannot be sure that a longer culture period would not have grown more bacteria, but probably not staphylococci.

The primary outcome of our study was chosen as a surrogate outcome for SSI risk. Surgical wound contamination has been established as a risk factor in the development of postoperative wound infection (Raahave 1991, Knobben et al. 2006). The effect on SSI rates of minor increases in the number of viable organisms in the surgical field is, however, still unclear.

Conclusion

The results of this controlled, randomized experimental trial do not support the hypothesis that the use of iodine-impregnated incision drapes increases bacterial recolonization during surgery. Moreover, there was no difference between draped and non-draped knees with regard to type of bacteria present. We recommend further clinical research on IIIDs to assess whether their use in preventing surgical site infection in clean orthopedic surgery is justified.

NM was principal investigator in charge of conducting the study, who also performed data analysis and wrote the manuscript. TN, HJK, CE, and SO contributed to the design of the study and manuscript revision.

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