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Systemic iodine levels increase with povidone-iodine irrigation, but does this affect thyroid functions? A case-control study

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Abstract

Background Intraoperative irrigation with diluted povidone iodine (PI) can be used to reduce the incidence of infection-related complications in arthroplasty surgeries. Since PI is associated with many interventions, especially skin antisepsis, its systemic effects are being studied. The aim of our study is to evaluate the systemic effects of PI, which we use as an irrigation solution, by means of urine iodine and thyroid function tests.

Methods In this case-control study, 96 patients who underwent knee or hip arthroplasty were included and divided into two groups according to the irrigation solution. In the first group, PI was added to the standard irrigation. The second group was considered as the control group and only standard irrigation was applied. Urine iodine, thyroid stimulating hormone, free T3 and free T4 values were compared in the preoperative and postoperative periods of these two groups. In this way, the effect of absorbed iodine on thyroid functions was investigated.

Results In the diluted PI group, urinary iodine levels were measured at maximum levels (450 µg/L) in the early postoperative period in most of the patients. The statistically significant difference in urinary iodine levels between the PI group and the control group, which started in the early postoperative period, continued until the last follow-up on the 14th postoperative day. In terms of thyroid functions, the observed differences were not statistically significant.

Conclusion Studies to reduce periprosthetic infection show that PI can be preferred for irrigation before the closure of the joint area in total joint arthroplasty. Although the success of this treatment in periprosthetic infection has been investigated, its systemic examination has not been demonstrated. It was determined that PI treatment, which was seen to decrease in the systemic circulation within 14 days, did not show a statistically significant change in terms of thyroid functions when used at the determined concentration and duration. These results should be evaluated with larger and longer-term studies.

Trial registration Clinical trials ID no. NCT05599841.

Keywords Povidone iodine, Periprosthetic joint infection, Thyroid functions, Urine iodine

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Introduction

Periprosthetic joint infections (PJI) are the most common cause of readmission following total joint arthroplasty (TJA) [1, 2]. Revision surgeries for PJI are challenging [3, 4] and put a significant social and financial burden on the healthcare system, despite advances in infection prophylaxis and reduction of risk factors [5, 6]. Due to the increasing bacterial antibiotic resistance and complexity of revision TJA, the importance of additional applications to prevent infection during surgery is increasing [7].

Among various bactericidal solutions that can be applied intraoperatively for PJI prevention, povidone iodine (PI) is relatively inexpensive, widely available, and has effective antimicrobial properties at low concentrations with less cytotoxicity to normal host cells [8, 9]. Dilute PI lavage with broad efficacy against microorganisms can safely reduce infection rates in spine and arthroplasty surgeries [10–13]. Furthermore, two main guidelines published by the World Health Organization and the Centers for Disease Control and Prevention recommended intraoperative irrigation with dilute PI during surgery prior to wound closure [14, 15].

Even if PI has no association with microorganism resistance [16, 17], it can be chondrotoxic in long-term administration and may cause cytotoxicity if not diluted and wound complications that put patients at risk of different microorganisms [18–21]. Some studies have examined the systemic effects of povidone-iodine use. These include oropharyngeal disinfection during COVID-19, evaluation of the impact on the newborn and the mother after use in caesarean section surgeries, intrarectal applications in tumor or ocular applications in cataract surgeries [9, 22–24]. Although studies on the systemic effect of PI have been examined in many surgical departments, the systemic consequences of its use for intraoperative irrigation during TJA have not been presented in detail. Therefore, this study aimed to investigate our hypothesis that PI, which is a reliable and cost-effective antiseptic used prior to the surgical area closure, can affect iodine levels in the body by getting absorbed; however, that the levels will not impair thyroid function values.

Material & methods

Patients

This research has been approved by the institutional review board of the authors' affiliated institutions (approval no. 19-1291-18). The study was performed in accordance with the Declaration of Helsinki. This is a non-randomized, consecutively enrolled, two-group (case control), comparative prospective trial to evaluate the systemic effects of PI irrigation solution in 96 patients who underwent primary total knee or hip arthroplasty between January 2019 and December 2020. In 2019, PI was used for skin cleansing and irrigation. In 2020, PI was

applied only for skin cleansing in arthroplasty patients. The cases with surgeries performed with intra-articular PI irrigation were matched with subsequent cases with surgeries performed with standard irrigation. The cases of two groups were matched exactly according to surgical site (hip/knee), sex and age (in terms of decades). Thus, errors that may be associated with standardization of surgical site absorption and iodine metabolism in the body were reduced. Patients with abnormal thyroid function tests in the preoperative period, a history of the previous thyroid-related disease, a history of iodine allergy, a lack of laboratory data, and unmatched patients were excluded from the study. This study was prepared in line with the strengthening the reporting of cohort studies in surgery (STROCSS) 2021 guideline [25].

Surgical technique

All surgeries were performed under spinal anaesthesia. The incision site was scrubbed with a PI-containing agent before surgery. Antisepsis of the whole extremity was then performed by painting with 10% concentrated PI content. The incision site was wiped again with a mixture of 70% ethyl-15% isopropyl alcohol, and a drape was placed (Ioban 2, 3 M, St. Paul., MN). The surgical procedure was the same in both groups until the original implants were placed. Groups differ according to the contents of the irrigation solutions applied before the closure and after the original implant placement. In both groups, pulse irrigation was performed with a total of 6,000 cc of fluid. 6,000 cc of 0.9% isotonic sodium chloride was used in the standard irrigation group. In the second group, irrigation was performed with 3,000 cc of 0.9% isotonic sodium chloride and 3,000 cc of <2% concentrated PI content. The PI solution was left in the joint for 3 min. The concentration and application time of this PI solution have been shown to be effective and safe [26, 27]. While the surgical area was closed, no suction drainage was placed in any patient. Current studies also show that the choice of the suction drainage placement does not have superior outcomes. [28, 29]

The cases' body mass index (BMI), American Society of Anaesthesiologists score (ASA) and Charlson comorbidity index (CCI) data were collected. In addition, thyroid-stimulating hormone (TSH), free T3 (fT3), and free T4 (fT4) tests were taken preoperatively and on the 14th day after surgery. Considering the half-lives of the evaluated thyroid function tests, the last follow-up date was determined as 14 days. A urinary catheter was placed as a standard in the operating room in all patients. During this application, 10% concentrated PI content was not used for periurethral disinfection due to the possibility of affecting the test results. Instead of PI-containing solution, sterile isotonic liquid, which was previously shown to be used for disinfection, was preferred [30]. Urine

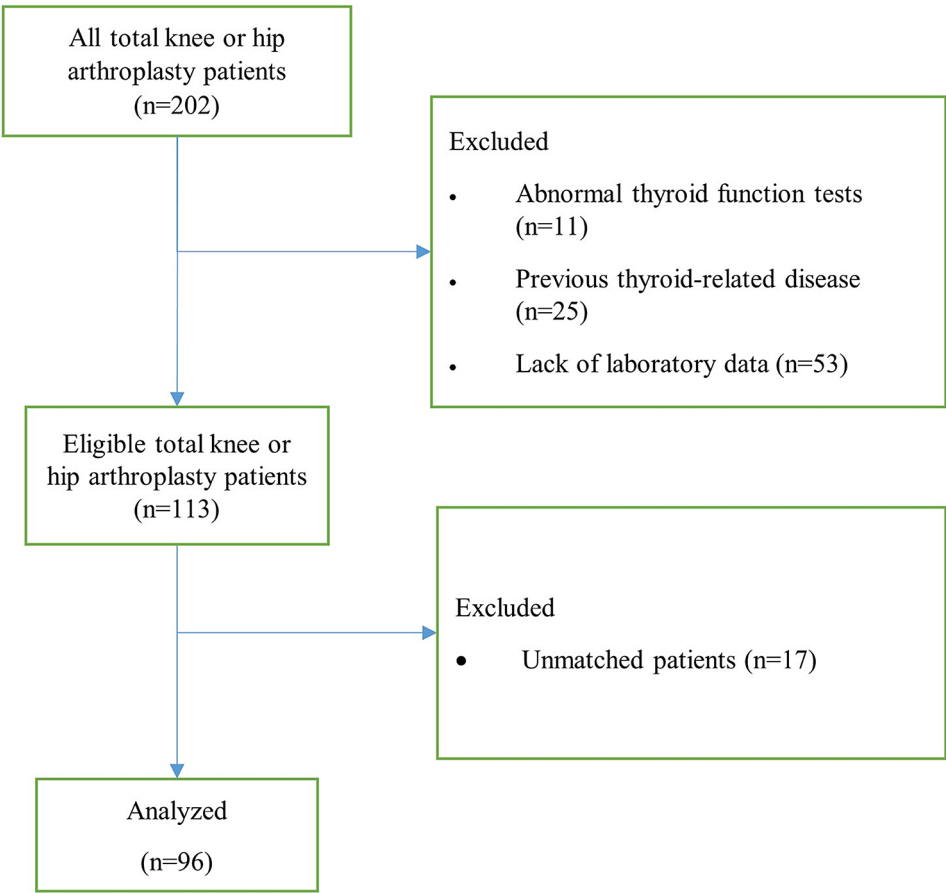


Fig. 1 Flow chart of excluded and matched patients

iodine tests of the sample were first taken following the insertion of a urinary catheter in the operating room. Other urine iodine samples were taken on the 1st and 4th postoperative days before discharge. A urine iodine sample was taken again on the 14th postoperative day, which was the first control after discharge. Urine iodine results could be measured at a maximum level of 450 µg/L. Statistical analyses were also performed with these data.

Statistical analysis

IBM SPSS Statistics 20 program (SPSS Inc., Chicago, IL, USA) was used for evaluations. In descriptive statistics, continuous data are expressed as mean, standard deviation, median, minimum, and maximum values, and percentage values indicate discrete data. Kolmogorov–Smirnov test was used to examine the conformity of the data to normal distribution. According to the normal distribution results of the groups, The Mann-Whitney U test was used for comparisons between groups, and the Wilcoxon test was used for time-based variables within the group. Statistical significance was set at $p<0.05$. Power analysis performed with postoperative urine iodine

Table 1 Comparison of patients by BMI, ASA, CCI, age, sex and surgical site data

	Group 1 (Standard)	Group 2 (PI)	P value
BMI (kg/m2)	29.47 ± 5.33	28.16 ± 3.93	0.303
ASA	2,15 ± 0.80	2.04 ± 0.94	0.372
CCI	2.40 ± 1.48	2.33 ± 1.60	0.869
Age (years)	62.08 ± 11.19	61.52 ± 11.21	0.730
Sex (female: male)	38:10	38:10	1.000
Surgical site (hip: knee)	11:37	11:37	1.000

Data are shown as mean ± standard deviation; Body Mass Index (BMI), American Society of Anaesthesiologists Score (ASA), Charlson Comorbidity Index (CCI)

results revealed that at least 46 patients from both groups were required for 90% power.

Results

As a result of inclusion and exclusion in line with the determined criteria, the study was conducted with 96 patients (Fig. 1). Patients were matched according to surgical site (hip/knee), sex and age (in terms of decades). In addition, these matched patients were compared in terms of exact age, ASA, CCI, and BMI data (Table 1). A comparison of all data revealed no statistically significant difference in any of the parameter between the two groups.

The urine iodine and thyroid function values, according to time, in the groups that were irrigated with diluted PI and standard are shown in Table 2 and Fig. 2. There was no statistically significant difference in preoperative laboratory results. Urinary iodine results of most patients in the PI group were measured at the maximum level (450 µg/L) on the first postoperative day. Although the average urine iodine values decreased on the 4th postoperative day, it was observed that the maximum urine iodine values continued in some patients. The iodine difference in the urine, which increased significantly in the postoperative period in the irrigation group with diluted PI, continued on the 14th postoperative day ($p=0.019$). In the group treated with standard irrigation, only the iodine level in the urine on the first postoperative day showed a significant difference compared to the preoperative period. This difference disappeared on the fourth day ($p=0.105$). There was a significant difference in the urine iodine results between the two groups at all time periods except the preoperative period (Table 2).

This difference observed among the iodine results in the urine was not observed between preoperative and postoperative thyroid function values. There was no statistically significant difference between the two groups in terms of thyroid function (Table 2).

Table 2 Comparison of patients with urinary iodine and thyroid functional hormones in the preoperative and postoperative periods

		Group 1 (Standard)	Group 2 (PI)	P value
Urine Iodine Levels (µg/L)	Preoperative	115.2 ± 32.8	126.1 ± 56.6	0.505
	Postoperative 1st day	176.8 ± 52.6	421.6 ± 65.4	<0.001*
	Postoperative 4th day	120.5 ± 38.0	281.8 ± 141.9	<0.001*
	Postoperative 14th day	112.2 ± 41.1	154.8 ± 76.9	0.004*
Thyroid Stimulating Hormone (mIU/L)	Preoperative	2.1 ± 1.2	1.9 ± 1.1	0.273
	Postoperative	2.4 ± 1.4	2.0 ± 1.0	0.286
Free T3 (pmol/L)	Preoperative	4.9 ± 0.6	5.0 ± 0.7	0.122
	Postoperative	4.8 ± 0.6	5.1 ± 1.5	0.214
Free T4 (pmol/L)	Preoperative	12.1 ± 1.9	12.5 ± 2.1	0.381
	Postoperative	12.0 ± 1.9	12.0 ± 2.4	0.429

Discussion

Dilute PI lavage can also be used in orthopaedic surgeries to reduce infection-related complications. However, systemic evaluation of the use of diluted PI for intraoperative irrigation during TJA has not been shown in detail.

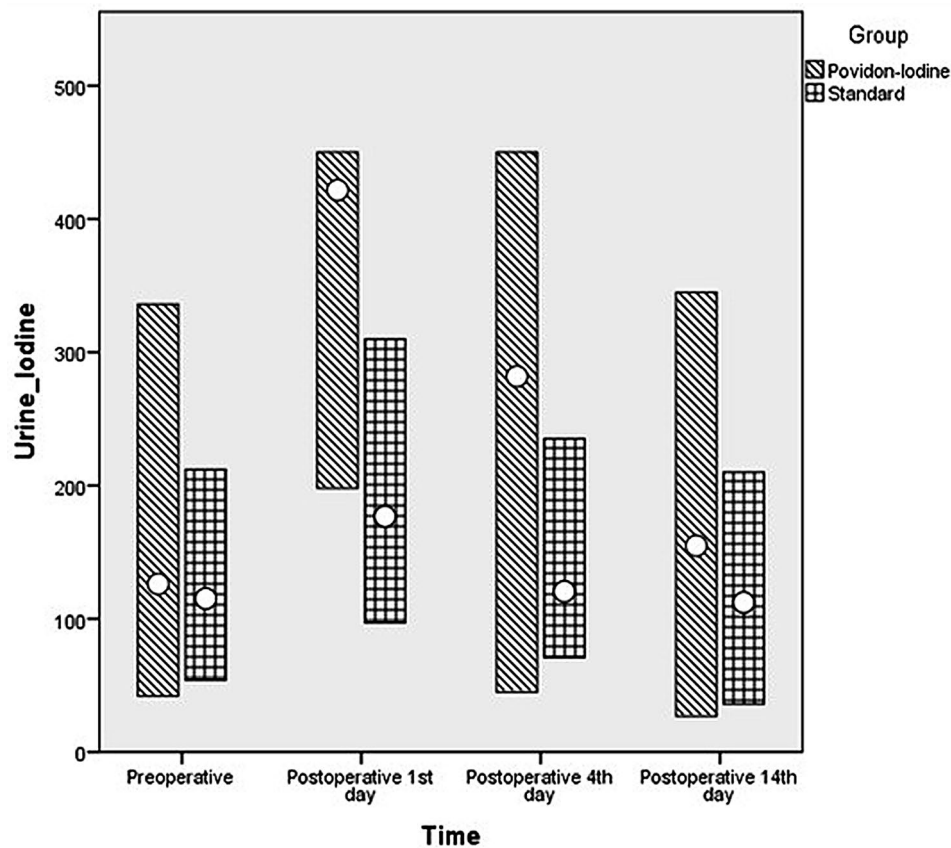


Fig. 2 Clustered range bar chart of urine iodine results of the groups in the preoperative and 3 different postoperative periods

Irrigation with diluted PI, performed to reduce the risk of periprosthetic infection did not affect thyroid function results in the selected patient group. Urinary iodine levels in the PI irrigation group were higher in the early postoperative period than in the standard irrigation group, and the statistically significant difference continued the postoperative 14th day. In fact, urinary iodine levels were measured at maximum levels (450 µg/L) in the early postoperative period in most of the patients in the PI group. On the other hand, if diluted PI treatment, which is used to prevent infection-related complications, especially surgical site infections and PJI, is applied at recommended concentrations, no obvious risk was found in terms of thyroid functions.

Diluted PI is a solution used in pre-closure irrigations to reduce the risk for infections in joint arthroplasty surgeries [31, 32]. In a controlled randomized study of aseptic revision joint arthroplasty consisting of 478 patients, Calkins et al. reported that there was significantly less acute infection in the patient group using PI [12]. In this study, 0.35% PI solution was used for 3 min, primary arthroplasty patients were not included, and patients were followed up for 3 months for periprosthetic infection. In another study, 2,550 primary arthroplasty patients were retrospectively analysed by Brown et al. in terms of acute periprosthetic infection rates for 90 days, and the patients were compared as groups with and without PI irrigation [19]. In this study, the concentration of the PI solution and the irrigation duration were the same as in study by Calkins et al. acute infection was observed at the rate of 0.15% in the group using PI, and 0.97% in the group not using PI, with statistically significant difference ($p=0.04$). However, reviewing seven studies and 31,213 patients in a recent meta-analysis, Kim et al. reported that irrigation with PI before closure had no significant effect on infection [33].

To the best of our knowledge, the systemic effects of PI, which is recommended as an irrigation solution and is an applicable standard technique in orthopaedic surgeries, have not been examined. There were several studies related to other specialties examining the systemic effects of both skin cleansing and application on the wound. Quek et al. examined the effect of PI application to the oropharyngeal area on thyroid function as a case-control study [9]. When comparing this treatment method applied during the Covid period with 177 patients, no statistically significant difference was detected between the two groups in terms of thyroid functions at the 6th week. In a prospective randomized study with 86 patients, Tahirovic et al. investigated the effect of PI applied for skin cleansing in caesarean section operations on postpartum TSH values in newborns and postpartum urine iodine values in both the mother and newborn [24]. While elevated urine iodine values

were found in both the mother and newborn in the PI group, there was no statistically significant difference in TSH values between the groups. As in this study, the elevation in urine iodine values was not reflected in thyroid function values in our study. In another study, Tsunoda et al. investigated the systemic absorption of PI after intrarectal administration and its effect on thyroid function [22]. Patients with sigmoid colon and rectum carcinoma were compared with the control group by taking multiple blood samples before surgery and until the second week after surgery. As a result of the evaluations made in terms of electrolytes, total iodine and thyroid function tests, it was observed that the total iodine value in patients receiving PI continued to be high until the second week after surgery, especially in the sigmoid colon group. There was no statistically significant difference between the groups in terms of thyroid functions. In the study by Findik et al., the effect of intraoperative lavage with PI on thyroid function values in patients who underwent posterolateral thoracotomy was investigated [34]. While examining TSH, fT3, and fT4 values, only fT3 data showed a statistically significant difference between the groups among postoperative results. However, in the study, it was observed that 4% concentration was applied for 5 min for the lavage process. These values were higher in terms of concentration and duration compared to the values obtained with the technique applied by us.

In our study, an increase was observed in the first postoperative urine iodine levels in the control group, and in the next urine iodine results, this difference decreased and lost statistical significance compared to the preoperative period. We thought that this result might be related to skin cleansing with PI. In the study of Nesvadbova et al., the relationship between the use of PI in skin antiseptics and time-dependent systemic iodine absorption was investigated [35]. In this in vitro study, healthcare workers were examined, and the results showed that there may be iodine absorption from the skin and an increase in systemic iodine levels in patients undergoing surgery. In the PI related dermal toxicity study of Eddy et al., experimental animals were evaluated in terms of serum iodine and thyroid functions after PI application [36]. In the results that were found to be safe in terms of thyroid functions, an increase in serum iodine values was also observed.

There are some limitations of the study. First, this study was not randomized, the hypothesis was presented in line with the surgical technique that changed over time, and the study was carried out for this purpose. However, as we mentioned, many parameters were considered while matching the patients, and patients who could not be matched were excluded from the study. Another limitation was the use of PI in skin cleansing. A statistically significant increase was observed in urine iodine values

in the early postoperative period in the patient group in which only isotonic solution was used for irrigation before closure. Therefore, a patient group in which PI was not used for skin disinfection could have been included in the study. However, not disinfecting the skin with PI, could increase the risk of possible periprosthetic infection. Due to this risk, this application was not taken as a variable. Another limitation can be noted regarding the short-term follow-up of the study. It could not be determined whether there was any deterioration in thyroid functions during long follow-ups. Although there is no information in the literature showing that thyroid function tests may deteriorate in the late period, studies with longer follow-up may provide information about the risks in this regard.

Conclusion

PI irrigation is a method used for local control of infection, but its systemic interaction in arthroplasty surgery has not been examined so far. Our study demonstrated early systemic absorption of iodine in patients irrigated with PI. In fact, in most patients, urinary iodine levels were at their highest measurable value in the early postoperative period. After a while, this effect disappeared and it was observed that it did not cause a significant difference in thyroid function tests. However, we think that the possible systemic effects of povidone-iodine on patients should be investigated in more detail and in prospective randomized studies with longer follow-up.

Author contributions

MBE: Conceptualization; Methodology; Writing – original draft; Software. KB: Methodology; Supervision; Resources. HK: Supervision, Writing – review & editing, Formal analysis. MYA: Data curation; Investigation; Software. EG: Resources; Data curation; Visualization.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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References

1. Zmistowski B, Restrepo C, Hess J, Adibi D, Cangoz S, Parvizi J. Unplanned readmission after total joint arthroplasty: rates, reasons, and risk factors. *JBJS*. 2013;95:1869–76.
2. Boraiah S, Joo L, Inneah IA, Rathod P, Meftah M, Band P, et al. Management of modifiable risk factors prior to primary hip and knee arthroplasty: a readmission risk assessment tool. *JBJS*. 2015;97:1921–8.
3. Kamath AF, Ong KL, Lau E, Chan V, Vail TP, Rubash HE, et al. Quantifying the burden of revision total joint arthroplasty for periprosthetic infection. *J Arthroplasty*. 2015;30:1492–7.
4. Kosashvili Y, Backstein D, Safir O, Lakstein D, Gross AE. Dislocation and infection after revision total hip arthroplasty: comparison between the first and multiply revised total hip arthroplasty. *J Arthroplasty*. 2011;26:1170–5.
5. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. *J Arthroplasty*. 2012;27:61–5.
6. Cahill JL, Shadbolt B, Scarvell JM, Smith PN. Quality of life after infection in total joint replacement. *J Orthop Surg*. 2008;16:58–65.
7. Parvizi J, Azzam K, Ghanem E, Austin MS, Rothman RH. Periprosthetic infection due to resistant staphylococci: serious problems on the horizon. *Clin Orthop Relat Res*. 2009;467:1732–9.
8. Van Meurs SJ, Gawlitta D, Heemstra KA, Poolman RW, Vogely HC, Kruijck MC. Selection of an optimal antiseptic solution for intraoperative irrigation: an in vitro study. *J Bone Joint Surg - Ser A*. 2014;96:285–91.
9. Quek AML, Ng MY, Teng O, Lim NA, Ng GJL, Yang SP, et al. Stable thyroid function despite regular use of povidone-iodine throat spray for SARS-CoV-2 prophylaxis. *Ann Med*. 2022;54:3299–305.
10. Cheng M-T, Chang M-C, Wang S-T, Yu W-K, Liu C-L, Chen T-H. Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery. *Spine (Phila Pa 1976)*. 2005;30:1689–93.
11. Slullitel PA, Dobransky JS, Bali K, Poitras S, Bhullar RS, Gofton WT, et al. Is there a role for preclosure dilute betadine irrigation in the prevention of postoperative infection following total joint arthroplasty? *J Arthroplasty*. 2020;35:1374–8.
12. Calkins TE, Culvern C, Nam D, Gerlinger TL, Levine BR, Sporer SM, et al. Dilute Betadine Lavage reduces the risk of Acute Postoperative Periprosthetic Joint infection in aseptic revision total knee and hip arthroplasty: a Randomized Controlled Trial. *J Arthroplasty*. 2020;35:538–e5431.
13. Shohat N, Goh GS, Harrer SL, Brown S. Dilute povidone-iodine irrigation reduces the rate of Periprosthetic Joint infection following hip and knee arthroplasty: an analysis of 31,331 cases. *J Arthroplasty*. 2022;37:226–e2311.
14. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis*. 2016;16:e288–303.
15. Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg*. 2017;152:784–91.
16. Lachapelle J-M, Castel O, Casado AF, Leroy B, Micali G, Tennstedt D, et al. Antiseptics in the era of bacterial resistance: a focus on povidone iodine. *Clin Pract*. 2013;10:579.
17. Russell AD. Introduction of biocides into clinical practice and the impact on antibiotic-resistant bacteria. *J Appl Microbiol*. 2002;92:S121–35.
18. von Keudell A, Canseco JA, Gomoll AH. Deleterious effects of diluted povidone-iodine on articular cartilage. *J Arthroplasty*. 2013;28:918–21.
19. Brown NM, Cipriano CA, Moric M, Sporer SM, Della Valle CJ. Dilute betadine lavage before closure for the prevention of acute postoperative deep periprosthetic joint infection. *J Arthroplasty*. 2012;27:27–30.
20. Weiss A-PC, Krackow KA. Persistent wound drainage after primary total knee arthroplasty. *J Arthroplasty*. 1993;8:285–9.
21. Kaysinger KK, Nicholson NC, Ramp WK, Kellam JF. Toxic effects of wound irrigation solutions on cultured tibiae and osteoblasts. *J Orthop Trauma*. 1995;9:303–11.
22. Tsunoda A, Shibusawa M, Kamiyama G, Takata M, Choh H, Kusano M. Iodine absorption after intraoperative bowel irrigation with povidone-iodine. *Dis Colon Rectum*. 2000;43:1127–32.
23. Below H, Behrens-Baumann W, Bernhardt C, Völzke H, Kramer A, Rudolph P. Systemic iodine absorption after preoperative antisepsis using povidone-iodine in cataract surgery - an open controlled study. *Dermatology*. 2006;212:41–6.
24. Tahirović H, Toromanović A, Grbić S, Bogdanović G, Fatušić Z, Gnat D. Maternal and neonatal urinary iodine excretion and neonatal TSH in relation to use of antiseptic during caesarean section in an iodine sufficient area. *J Pediatr Endocrinol Metab*. 2009;22:1145–9.
25. Mathew G, Agha R, Albrecht J, Goel P, Mukherjee I, Pai P, et al. STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. *Int J Surg*. 2021;96:106165.
26. Wang D, Huang X, Lv W, Zhou J. The toxicity and Antibacterial effects of Povidone-Iodine Irrigation in fracture surgery. *Orthop Surg*. 2022;14:2286–97.

27. Romano V, Di Gennaro D, Sacco AM, Festa E, Roscetto E, Basso MA et al. Cell toxicity study of antiseptic solutions containing povidone–iodine and hydrogen peroxide. *Diagnostics*. 2022;12.
28. Bartosz P, Marczyński W, Para M, Kogut M, Bialecki J. Comparative study of suction drainage placement in cementless hip replacement among patients undergoing extended thromboprophylaxis: a prospective randomized study. *BMC Musculoskelet Disord*. 2021;22:688.
29. Zhang Q, Liu L, Sun W, Gao F, Zhang Q, Cheng L, et al. Are closed suction drains necessary for primary total knee arthroplasty? *Medicine*. 2018;97:e11290.
30. Al-Farsi S, Oliva M, Davidson R, Richardson SE, Ratnapalan S. Periurethral cleaning prior to urinary catheterization in children: sterile water versus 10% povidone-iodine. *Clin Pediatr (Phila)*. 2009;48:656–60.
31. Iorio R, Yu S, Anoushiravani AA, Riesgo AM, Park B, Vigdorchik J, et al. Vancomycin Powder and dilute povidone-iodine lavage for infection Prophylaxis in High-Risk Total Joint Arthroplasty. *J Arthroplasty*. 2020;35:1933–6.
32. Buchalter DB, Kirby DJ, Teo GM, Iorio R, Aggarwal VK, Long WJ. Topical vancomycin powder and dilute povidone-iodine lavage reduce the rate of early periprosthetic joint infection after primary total knee arthroplasty. *J Arthroplasty*. 2021;36:286–e2901.
33. Kim CH, Kim H, Lee SJ, Yoon JY, Moon JK, Lee S, et al. The Effect of Povidone-Iodine Lavage in preventing infection after total hip and knee arthroplasties: systematic review and Meta-analysis. *J Arthroplasty*. 2020;35:2267–73.
34. Findik G, Gezer S, Aydogdu K, Öz G, Kucukbayrak A, Tastepe I, et al. Effect of intrapleural povidone-iodine lavage on thyroid hormones in thoracic surgery. *Thorac Cardiovasc Surgeon*. 2010;58:225–8.
35. Nesvadbova M, Crosera M, Maina G, Larese Filon F. Povidone iodine skin absorption: an ex-vivo study. *Toxicol Lett*. 2015;235:155–60.
36. Eddy EP, Shet MS, Cataldo M, Grob D, Bhaskar S. Evaluation of dermal toxicity and toxicokinetics of povidoneiodine in Göttingen minipigs. *Toxicol Appl Pharmacol*. 2024;482:116783.

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