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Research Article

Comparative Analysis of Dilute Povidone Iodine (Betadine) versus Normal Saline in Bilateral Knee Joint Replacement Surgery: A Retrospective Cohort Study

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Abstract

Background: One of the proposed methods to reduce the risk of infection after joint replacement is the use of disinfectant solutions at the end of the surgery. Differing results have been reported regarding the effects of diluted povidone-iodine (betadine) washing solution and normal saline in reducing the risk of periprosthetic joint infection (PJI). The purpose of this retrospective cohort study is to compare the outcomes of diluted betadine solution with normal saline in bilateral knee replacement surgery.
Methods: Patients who were referred to Ba'ath Hospital, Hamedan, Iran, from 2019 to 2021 for bilateral knee joint replacement were included. For each patient, one knee was washed with diluted betadine (35%), and the other with normal saline for 3 minutes before closing the wound. Demographic information, risk factors, and the rate of PJI three months after the surgery were collected and analyzed.
Results: Out of 320 patients, 177 (55.3%) were women, and the most common underlying disease was type 2 diabetes with a frequency of 20.0%. Out of 640 operated knees, 17 cases (2.7%) of PJI occurred after surgery, of which 11 (4.3%) were washed with normal saline (P = 0.326). The multivariate regression analysis showed that being male (P = 0.028), diabetes (P = 0.030), high blood pressure (P = 0.019), and an increase in each body mass index (BMI) unit (P = 0.030) increased the chance of infection.
Conclusion: Intraoperative irrigation with diluted betadine solution in bilateral knee replacement surgery can reduce the risk of infection, especially in patients with underlying diseases and obesity.

Keywords: Total Knee Replacement; Povidone Iodine; Prosthesis Related Infections

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Background

Periprosthetic joint infection (PJI) after total knee arthroplasty (TKA) and total hip arthroplasty (THA) is one of the most challenging complications for orthopedic surgeons, which can be associated with adverse consequences for patients, including increased costs, morbidity, and mortality (1). Recent studies estimate the incidence of PJI after TKA and primary THA from 0.3% to 2.4% (1). Two recent studies reported an incidence of 3.7% to 5.4% in sample sizes of 379 and 385 TKAs (2, 3). Although rare, PJI is associated with very high short-term mortality and devastating outcomes, with mortality rates ranging from 8% to 10.4% in one year after TKA and THA. In addition to the health consequences, it has a very high economic burden after surgery, being associated with a three-time increase or more in the total cost of care (4, 5).

With the introduction of new surgical methods and techniques, increasing preventive measures such as surgery only when the patient is in a stable condition, using antibiotics as prophylaxis, preparing the surgical site before cutting, and increasing the sensitivity of sterilization methods, however, a significant number of these patients are still at risk of infection around the prosthesis (6). One of the methods that have been considered to reduce the risk of infection is washing the surgical area with disinfectant solutions before suturing the skin and the surgical area. Among the solutions used for this approach, diluted betadine is a favorable choice due to its availability, cheapness, and low risk of side effects (7, 8).

Diluted betadine is a disinfectant solution containing iodine. This solution is a stable chemical compound that gradually releases iodine and has been proven to have a broad-spectrum bactericidal activity that is safe for host cells when used at appropriate dilutions (9). There are many techniques to reduce the risk of PJI, including prophylactic antibiotics, appropriate skin preparation, delaying elective procedures for patient optimization, and the use of topical antiseptics. Since various factors are effective in causing infection, we investigated and compared a number of these factors in this study. Specifically, we focused on comparing the infection-related outcomes of normal saline irrigation with diluted betadine.

Methods

In the current retrospective cohort study, infections occurring in bilateral knee replacement surgery were evaluated separately from 2019 to 2021 at Ba'ath Hospital in Hamedan, Iran. All patients were followed up and monitored for three months after the TKA operation. The studied patients underwent bilateral knee joint replacements. One knee was washed with normal saline solution, and the other was washed with diluted betadine solution (0.35%), both for 3 minutes (which were suctioned later on).

The study inclusion criteria included all patients with

indications of bilateral knee joint replacement in Hamedan Ba'ath Hospital in 2019-2021, aged 55 to 75 years, who completed the questionnaires, and access to the patient was available during the follow-up. The exclusion criteria included individuals' reluctance to cooperate, filling out the questionnaires incompletely, defects in medical records, sensitivity to iodine, chronic immunosuppression [history of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) or immunosuppressive drugs for cancer, organ transplant], and use of antibiotics two weeks prior to surgery.

Sampling was done sequentially and under stress. Considering the previous similar research (10), the sample size calculation was considered with a power of 80% and a coefficient of variation of 10% (α= 0.05, β= 0.02), necessitating a sample size of 320 cases in each group. Since the study subjects underwent bilateral surgery, 640 knees, corresponding to 320 subjects were included in the study.

The list of all patients undergoing bilateral knee joint replacement who aged 55 to 75 years was provided. After reviewing the cases, the eligible patients were included in the study after filling out the informed consent form. The information checklist prepared in this research for data collection and classification of patients included demographic characteristics, clinical information, and a clinical questionnaire for PJI and any other complications. Demographic information, including age, gender, and history of underlying diseases such as diabetes, high blood pressure, high blood glucose levels, heart disease, smoking history, etc., was extracted from the files and recorded. Besides, the type of washing solution used was recorded. Next, the patients were contacted and examined to investigate the development of PJI. The incidence of PJI was evaluated for 90 days after surgery. Acute PJI occurring within 90 days after surgery was diagnosed by meeting the main criteria (2 positive bacterial cultures or sinus-to-joint communication) or 3 of 5 minor criteria: increased C-reactive protein (CRP) (> 100 mg/l), increased synovial white blood cells (WBCs) (> 10000 cells/ml), synovial polynuclear count more than 90%, positive single bacterial culture, and pathological tissue containing more than five neutrophils in each field of view (11). Any major wound complication occurring within 90 days, including oral antibiotic use for superficial wound infection or suture abscess, wound dehiscence, prolonged discharge, or any other wound problem requiring a return to the operating room, was also recorded.

In this study, the JMP software was used for data analysis. A significance level of less than 5% was considered. The chi-square test (Fisher's exact test) was used to compare the outcome of the disease in terms of nominal and rank qualitative variables, and the t-test was used to compare in terms of quantitative variables. In addition, multivariate regression tests, Spearman's correlation, and graphic correlation were used to compare coefficients of determination and component correlation.

Results

In this retrospective cohort study, 320 patients who visited Ba'ath Hospital from the beginning of April 2019 to the end of 2021 for bilateral knee joint replacement were examined. The average age of the patients was 64.5 ± 6.1 years with a range of 55 to 77 years, and the average body mass index (BMI) was 27.7 ± 2.0 kg/m^2. 177 patients (55.3%) were women, and the most common underlying disease was type 2 diabetes (Table 1).

Table 1. Demographic characteristics and clinical symptoms

Variable	Value
Gender (female)	177 (55.3)
Type 2 diabetes	64 (20.0)
Increased blood pressure	57 (17.8)
Heart disease	54 (16.9)
Smoking	48 (15.0)
Drug use	45 (14.1)
Age (year)	64.5 ± 6.1
BMI (kg/m^2)	27.7 ± 2.0

Data are presented as number (%) or mean ± standard deviation (SD)
BMI: Body mass index

The moving average and the distribution of the data supported each other, indicating a reasonable data collection strategy (Figure 1).

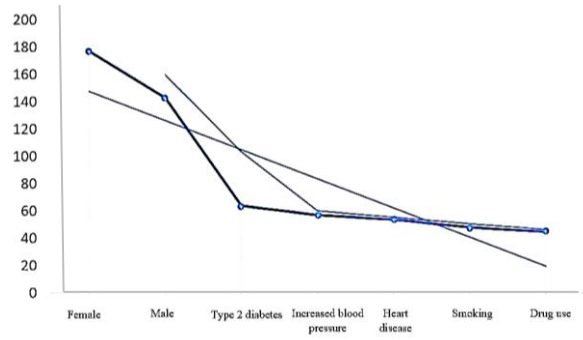

Figure 1. Abundance of demographic characteristics and risk factors in the study population

A total of 17 cases (2.7%) had a peri-prosthetic infection in the first three months after surgery, of which 6 (1.9%) were washed with diluted betadine solution and 11 (3.4%) were washed with normal saline.

These findings showed that the patients whose surgical site was irrigated with normal saline solution had a higher incidence of infection in the prosthetic area (64.7% vs. 35.3%). However, the difference was not statistically significant (P = 0.326). Male patients and individuals with diabetes had a higher chance of infection, with a statistically significant difference (P = 0.045). Moreover, patients with a higher average BMI had a significantly higher chance of infection (P = 0.010). Patients with a younger average age had a higher chance of infection, but it was not statistically significant (P = 0.485) (Table 2 and Figure 2).

Table 2. Frequency of infection around the prosthesis based on demographic variables and type of solution

Variable	Joint infection (n = 17)	No infection (n = 623)	P-value	OR (95% CI)
Washing solution (saline)	11 (64.7)	309 (49.6)	0.326*	1.86 (0.50-68.09)
Gender (male)	12 (70.6)	274 (44.0)	0.045*	3.05 (8.10-9.06)
Type 2 diabetes	8 (47.1)	120 (19.3)	0.010*	3.72 (1.40-9.85)
Increased blood pressure	6 (35.3)	108 (17.3)	0.094*	2.60 (0.95-7.18)
Cardiovascular disease	5 (29.4)	103 (16.5)	0.184*	2.01 (0.72-6.09)
Smoking	5 (29.4)	91 (14.6)	0.157*	2.43 (0.84-7.07)
Drug use	5 (29.4)	85 (13.6)	0.075*	2.63 (0.91-8.18)
Age (year)	63.52 ± 5.68	64.57 ± 6.10	0.485**	0.97 (0.89-1.05)
BMI (kg/m^2)	28.73 ± 1.26	27.66 ± 1.98	0.027**	1.31 (1.69-1.02)

Data are presented as number (%) or mean ± standard deviation (SD)
*Fisher's exact test; **T-test
BMI: Body mass index; OR: Odds ratio; CI: Confidence interval

To investigate the relationship of variances between dependent and independent variables, we measured their coefficient of determination. The coefficient of determination for each variable indicated the contribution of each desired variable, with a value varying between 0 and 1 (Table 3 and Figure 2).

Table 3. Determining factor in the investigated factors in the use of diluted normal saline and betadine serum in causing infection

Variable	Normal saline serum				Diluted betadine			
	T	β	F	Coefficient of determination	T	β	F	Coefficient of determination
Age	46.522	0.781	527.222	0.752	39.451	0.762	314.217	0.867
Gender	42.152	0.732	405.122	0.920	44.328	0.372	523.147	0.895
BMI	40.223	0.662	217.343	0.503	36.823	0.872	852.381	0.611
Type 2 diabetes	38.239	0.648	199.943	0.746	39.362	0.685	298.921	0.625
Increased blood pressure	8.958	0.664	201.612	0.681	18.958	0.597	247.257	1.000
Cardiovascular disease	11.134	0.662	643.623	0.816	16.644	0.436	644.321	0.656
Smoking	18.441	0.652	849.683	0.812	21.422	0.852	845.523	0.645
Drug use	19.144	0.665	349.603	1.000	19.144	0.665	754.254	0.645

BMI: Body mass index

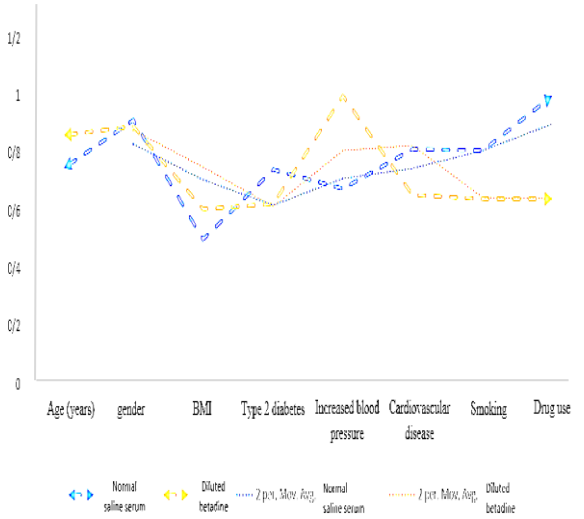

Figure 2. The coefficient of determination of investigated factors with post-operative infection

Based on the results of Kolmogorov-Smirnov's pre-test, data did not have a normal distribution; therefore, Spearman's correlation was used. Based on the results of Spearman's correlation, the correlation coefficients in the diluted betadine washing solution – the correlation coefficients between the factors causing infection –had lower values than the normal saline serum. Further, in the diluted betadine solution, the highest correlation was 0.856, and the lowest was related to age with a value of 0.245. On the other hand, in normal saline serum solution, the highest correlation coefficient was related to type 2 diabetes with a value of 0.882, while the lowest was related to age with a value of 0.472 (Table 4 and Figure 3).

Table 4. Spearman's correlation of investigated factors in the use of diluted normal saline and betadine serum in causing infection

Variable	Normal saline serum		Diluted betadine	
	P-value	Correlation coefficient	P-value	Correlation coefficient
Age	< 0.001	0.472	< 0.001	0.245
Gender	< 0.001	0.671	< 0.001	0.540
BMI	< 0.001	0.583	< 0.001	0.856
Type 2 diabetes	< 0.001	0.882	< 0.001	0.751
Increased blood pressure	< 0.001	0.795	< 0.001	0.517
Cardiovascular disease	< 0.001	0.511	< 0.001	0.485
Smoking	< 0.001	0.789	< 0.001	0.536
Drug use	< 0.001	0.695	< 0.001	0.656

BMI: Body mass index

To establish a relationship between the independent variables in the two washing groups with diluted betadine and normal saline, a graphical correlation was taken one by one. Based on these results, the independent variables in the two groups of irrigation with diluted betadine and with normal saline serum had a low correlation with each other, while the only variable with a significant correlation was age (0.77). However, in general, the results obtained from normal saline and diluted betadine serum were correlated (0.78) (Figure 4).

Discussion

The current retrospective cohort study was conducted to compare the outcomes of diluted betadine wash solution with normal saline in reducing the risk of PJI following bilateral knee replacement surgery. Our findings showed that 17 knees (2.7%) out of 640 operated knees had acute infections after surgery. Previous findings had estimated the incidence of infection around the prosthesis after joint replacement between 0.5% and 3% (12). The reason for the difference in prevalence in the studies can be the surgical technique, duration of surgery, type and number of operated joints, patient conditions, and care before and after surgery.

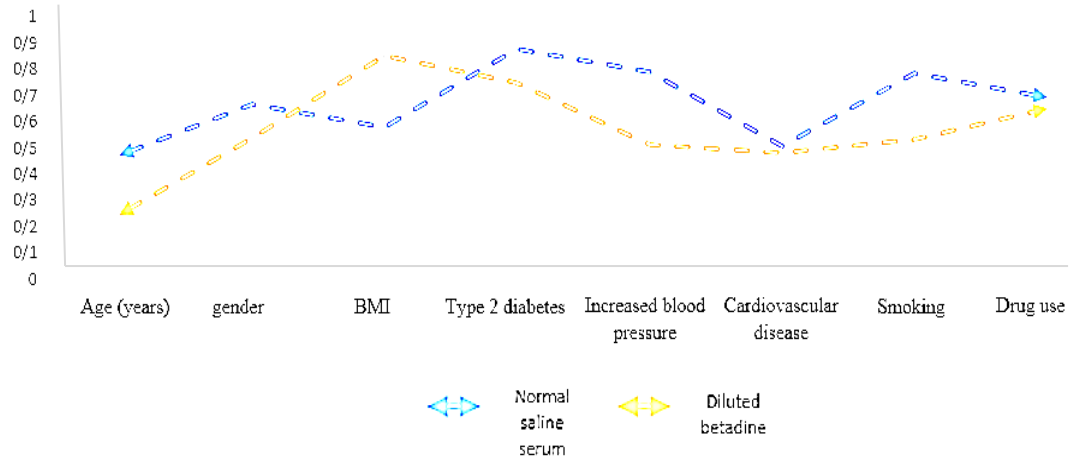

Figure 3. The correlation between investigated factors and post-operative infection

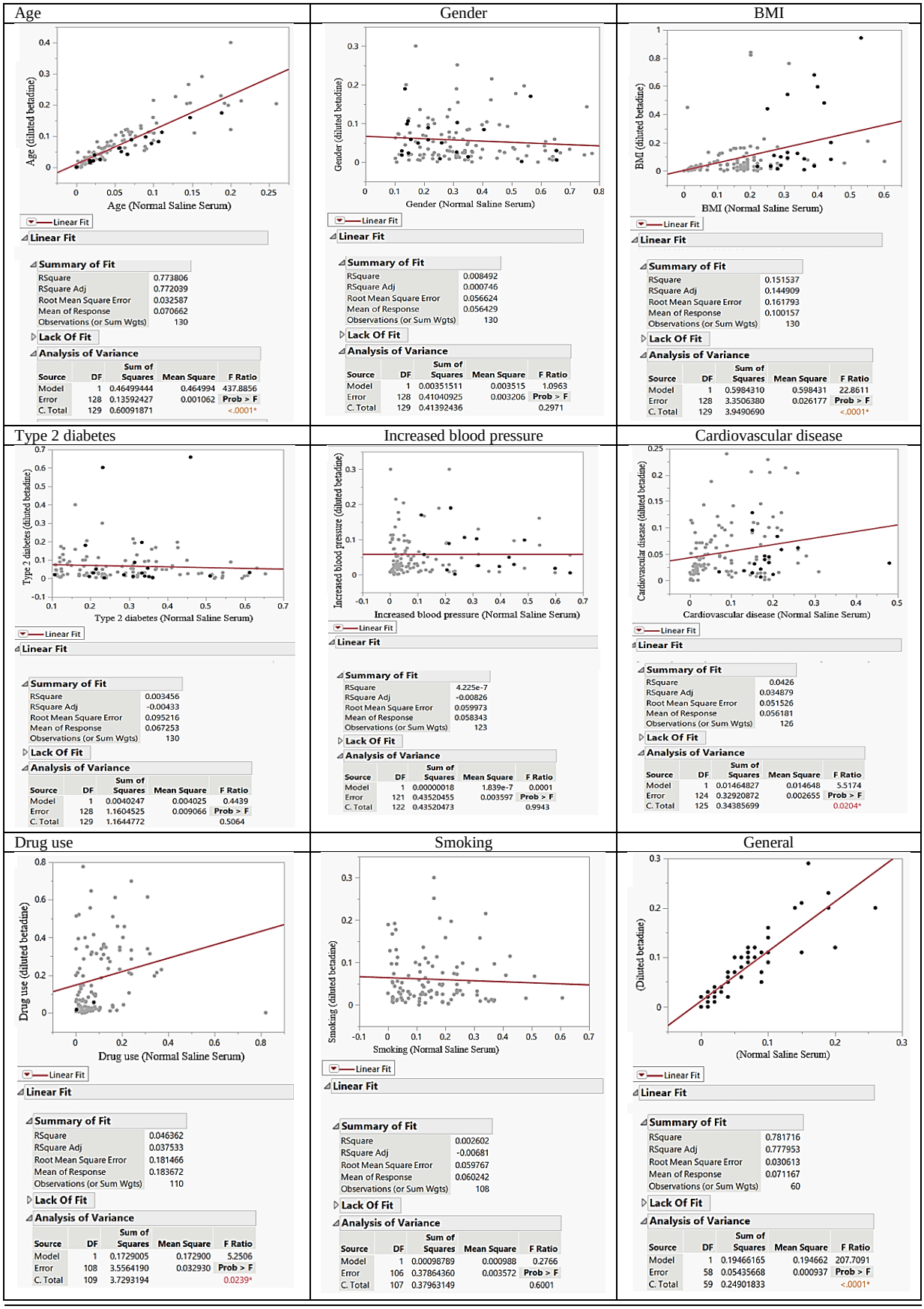

Figure 4. Graphical correlation between independent variables in two groups washed with diluted betadine and normal saline

The findings of this study showed that normal saline irrigation was 1.9 times more likely to develop an infection at the prosthesis site. Although the difference was not statistically significant, the small sample size may be accountable. Nevertheless, such a difference can be clinically important. Few studies have compared the effectiveness of diluted betadine and normal saline in preventing acute infections in these patients (13). Besides, to the best of our knowledge, no national study has been published in this regard. Considering that each patient's knee was compared with the other knee, this study is exempt from confounding variables that could affect the results of the study.

The results of the study related to the effect of diluted betadine on the PJI are controversial. In a study by Calkin et al. in the United States, 234 patients (153 knees, 81 hips) were flushed with normal saline, and 223 patients (144 knees, 79 hips) were flushed with diluted betadine lavage before final suturing. Eight cases of PJI in the saline group and one case in the diluted betadine group occurred in the first three months after surgery (3.4% vs. 0.4%, P = 0.038). The authors described diluted betadine lavage before surgical wound closure in TKA and THA as a simple, safe, and effective measure to reduce the risk of acute PJI (14). Ruder et al. also concluded that the use of diluted betadine in primary total joint arthroplasty (TJA) surgery reduced the risk of infection without any associated side effects (15). Muwanis et al. considered washing the surgical area in TKA and THA patients with diluted betadine as a simple and effective strategy to reduce infection in these patients (16). According to the findings of Shoha et al.'s study (17), the use of diluted betadine can reduce the risk of PJI by 73%. Based on the findings of the meta-analysis study by Kobayashi et al. (18), the results of 8 studies showed that diluted betadine reduced the chance of PJI compared to normal saline [odds ratio (OR) = 0.33, 95% confidence interval (CI): 0.16-0.71]; however, in the study by Slullitel et al. on patients with TJA surgery, 5588 cases were washed with normal saline and 2890 cases with diluted betadine (19).

The results of this study showed that the incidence of PJI was higher in normal saline, but the difference was not statistically significant (48 cases vs. 23 cases, P = 0.762). Based on the findings of a meta-analysis study by Wood et al. (20) in 2020, the results of 10 studies with a population of 29630 TJAs in 29596 patients were shown. In studies that used diluted betadine, although the risk of PJI was less when compared to saline, the difference was not statistically significant (OR: 0.62, 95% CI: 1.00-19.33).

Identifying patient-related infection risk factors in patients with joint replacement allows the treatment team to take additional precautions for these patients. The findings of the present study showed that the chance of infection increased with a statistically significant difference in male patients, overweight patients, and patients with underlying diseases. Previous findings also show that the male gender and having an underlying disease, especially diabetes, increase the risk of infection in patients requiring joint replacement (21). Obese individuals need joint replacement more than their thin counterparts; usually, the surgery time is longer in these patients, which is one of the risk factors for infection. In addition, obese patients may have more comorbidities. It is still not clear why male patients with a lower average age are at a higher risk of infection. It has been hypothesized that male patients with a lower average age are more active, and the risk of infection may increase due to pressure on the prosthetic area (22). Moreover, patients with diabetes have a higher risk of infection after surgery due to several reasons, such as defects in wound healing, concern about the use of antibiotics, and defects in fighting bacterial agents (23, 24). However, in some studies, different results have been reported about the underlying disease, obesity, and duration of surgery (24, 26).

This study had some limitations. The relatively small sample size, not checking the time of surgery, the class of anesthesia, the duration of tourniquet use, and the type and duration of the drainage in the patients. Based on the findings of this research, further studies observing the patients for a longer period are recommended (6 months, one year, and two years). We suggest conducting studies with larger sample sizes and investigating the effect of different concentrations of diluted betadine.

Conclusion

Infection after knee joint replacement is one of the debilitating complications in patients, which can be associated with increased costs, risks of re-surgery, and mortality. Several strategies have been introduced to reduce the risk of infection in these patients, one of which is the use of disinfectant solutions for washing at the end of surgery. There is still not enough certainty regarding the type of solution, concentration, and duration of its use. The findings of the present study showed that the use of diluted betadine compared to normal saline could reduce the risk of infection after knee replacement, while this difference was not statistically significant; however, patients who have an underlying disease are more at risk of infections and may benefit from using diluted betadine solution.

Conflict of Interest

The authors declare no conflict of interest in this study.

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