Effectiveness of chlorhexidine in preventing infections among patients undergoing cardiac surgeries: a meta-analysis and systematic review

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Abstract

Background: Although several meta-analyses reported the impact of chlorhexidine (CHX) use in patients undergoing various types of surgery, no meta-analysis summarized the overall effectiveness of CHX specifically for cardiac surgery. This meta-analysis aimed to examine the impact of CHX on infections after cardiac surgery compared with other cleansers or antiseptics.

Methods: PubMed, Embase, and the Cochrane Library were searched from inception up to October 2020 for potentially eligible studies: (1) population: patients who underwent cardiac surgery; (2) intervention or exposure: any type of CHX use in the treatment or exposed group; (3) outcome: number of patients with infections; (4) comparison: placebo or other antiseptic agents; (5) English. The primary outcome was surgical site infection (SSI).

Results: Fourteen studies were included, with 8235 and 6901 patients in the CHX and control groups. CHX was not protective against SSI (OR = 0.77, 95% CI: 0.57–1.04, P = 0.090). CHX was protective for superficial wound infection (OR = 0.42, 95% CI: 0.26–0.70, P = 0.001), but not with deep wound infection (P = 0.509). CHX was not protective against urinary tract of infection (P = 0.415) but was protective for bloodstream infection (OR = 0.36, 95% CI: 0.16–0.80, P = 0.012), nosocomial infections (OR = 0.55, 95% CI: 0.44–0.69, P < 0.001), and pneumonia (OR = 0.26, 95% CI: 0.11–0.61, P = 0.002).

Conclusions: In patients undergoing cardiac surgery, CHX does not protect against SSI, deep wound infection, and urinary tract infections but might protect against superficial SSI, bloodstream infection, nosocomial infections, and pneumonia.

Keywords: Chlorhexidine, Cardiac surgery, Wound infection, Surgical complications, Antiseptics, Meta-analysis

Background

Chlorhexidine (CHX) is a cationic bisbiguanide [1] and an antiseptic agent active against Gram-positive and -negative bacteria widely used in clean surgeries [2–5]. CHX binds to the negatively charged bacterial cell wall to disrupt the cell barrier [1]. CHX is bacteriostatic at low concentrations and bactericidal at higher concentrations [1].

In the past decades, CHX has been used to prevent surgical-related infections [6, 7], such as for decontamination of the oropharynx to avoid respiratory tract infection [8] or for gingival health [9], preoperative skin preparation to avoid surgical site infection [10, 11], or disinfection of medical appliances to avoid nosocomial infection [1, 9, 12–14]. CHX bathing is an effective measure in reducing the levels of pathogens on the skin, and it can also prevent catheter colonization and central line-associated bloodstream infection [15]. CHX is associated
with reduced postoperative surgical site infections (SSI) compared with povidone-iodine in clean-contaminated surgery [16].

Although several meta-analyses reported the impact of different types of CHX uses for patients undergoing various types of surgery [17–24], no meta-analysis summarized the overall effectiveness of CHX specifically for cardiac surgery. Indeed, cardiac surgery is highly invasive, usually long, and carries a high risk of infection. Infectious complications occur in 5–21% of the patients after cardiac surgery [25, 26]. After cardiac surgery, the risk of superficial wound infection is 0.5%-8%, and deep sternal wound infections occur in 0.4–2.0% of the cases [25, 26]. Infectious complications prolong the hospital stay, increase healthcare costs, and have dismal outcomes [25, 26].

Therefore, this meta-analysis aimed to examine the impact of CHX on infections after cardiac surgery compared with other cleansers or antiseptics.

**Methods**

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [27]. The relevant articles were searched based on the patient, intervention, comparison, outcome (PICO) principle [28], followed by screening based on the eligibility criteria: (1) population: patients who underwent open cardiac surgery, irrespective of the indication; (2) intervention or exposure: any type of application of CHX in the treatment or exposed group; (3) outcome: number of patients with infections (SSI, pneumonia, bloodstream infection, urinary infection, or nosocomial infection); (4) comparison: placebo, other antiseptic agents, or without CHX; (5) full-text article published in English. PubMed, Embase, and the Cochrane Library were searched from inception up to October 2020 for potentially eligible studies using the MeSH terms of “general surgery” AND “chlorhexidine”; as well as relevant key words such as cardiac or cardiovascular. The exact strategies for all three databases are presented in the Additional file. The literature search and selection of the studies were performed independently by two investigators (Fengxia Weng and Lingying He). Any discrepancy was solved by discussion.

**Data extraction**

Study characteristics (authors, year of publication, the country where the study was performed, type of the study design, and number, age, and sex of the patients), exposure parameters (method for the application of CHX, density, and frequency of the treatments); primary outcome (SSI), and secondary outcomes (superficial infection, deep wound infection, bloodstream infection, urinary tract infection, nosocomial infection, and pneumonia) were extracted independently by two investigators (Fengxia Weng and Lingying He). Any discrepancy was solved by discussion.

**Quality of the evidence**

The level of evidence of all articles was assessed independently by two authors (Fengxia Weng and Lingying He) according to the Cochrane Handbook for randomized controlled trials [29, 30] and the Newcastle–Ottawa Scale (NOS) criteria for observational studies [31]. Discrepancies in the assessment were resolved through discussion until a consensus was reached.

**Statistical analysis**

All analyses were performed using STATA SE 14.0 software (StataCorp, College Station, Texas, USA). The results were summarized as odds ratios (ORs) and 95% confidence interval (95% CI). Statistical heterogeneity among the studies was evaluated using Cochran’s Q-test and the I² index. A Q-test P-value < 0.10 and I² > 50% indicated high heterogeneity. Considering the different types of agents in the control group and the various CHX regimens among the included studies, the random-effect model was applied for all analyses to avoid an overestimation of the results. Possible publication bias was not evaluated by funnel plots and Egger’s test because the numbers of studies included in each quantitative analysis were less than 10, in which case the funnel plots and Egger’s test could yield misleading results [29].

**Results**

**Literature search**

Figure 1 and the Additional file present the literature search process. The initial searched yielded 513 records, and 424 were left after removing the duplicates. These records were screened, and 212 were excluded. The 212 full-text articles or abstracts were assessed for eligibility, and 198 were excluded (52 because of study design/aim, eight for the outcomes, 30 for the populations, 57 for the intervention/exposure, 21 for non-human studies, 10 for no accessible full-text, five for being meta-analyses, and 15 for being published in a language other than English). Finally, 14 studies were included.

**Characteristics of the studies**

Among the 14 studies (Table 1), there were five randomized controlled trials [32–36], six prospective cohort studies [37–42], two retrospective cohort studies [43, 44], and one case–control study [45]. Five studies examined the effect of an oral rinse [32–35, 37], four examined skin antiseptic [38–40, 43], and five examined the disinfection of surgical-related appliance [36, 41, 42, 44, 45]. There
were 8235 patients in the CHX group and 6901 in the control group.

Among the five randomized controlled trials [32–36], only one had an unclear risk of bias for two items [36] (Additional file 1: Table S1). Among the cohort studies [37–44], six studies scored 7 stars [37, 38, 41–44], one scored 8 stars [39], and one scored 9 stars [40] (Additional file 1: Table S2). The case–control study scored 9 stars [45] (Additional file 1: Table S3).

**Surgical site infection**

Eight studies could be included for the impact of CHX on SSI [34, 38–41, 43, 44]. CHX did not influence the risk of SSI compared with control interventions (OR = 0.77, 95%
| Author, year | Location | Design | Patients, n | Method of application | Intervention | Frequency of treatment | Age, year | CHX | Control |
|-------------|----------|--------|-------------|-----------------------|--------------|-----------------------|----------|-----|---------|
| DeRiso [32] | USA      | RCT    | 173         | Oral rinse            | 0.12% CHX gluconate | 2 times a day until ICU discharge | 64.1 ± 0.86 | 63.5 ± 0.84 |       |         |
| Houston [33] | USA      | RCT    | 270         | Oral rinse            | 0.12% CHX gluconate | \                        | \        | \   | \       |
| Segers [34] | USA      | RCT    | 485         | Oral rinse            | 0.12% CHX gluconate | 4 times daily until the day after surgery | 65.3 ± 10.4 | 66.4 ± 9.9 |       |         |
| Jacomo [35] | Brazil   | RCT    | 87          | Oral rinse            | 0.12% CHX gluconate | 2 times daily until discharge or death | 12.2(0–176) months | 10.8(0–204) months |       |         |
| Nicolosi [37]| Argentina| Prospective cohort | 150 | Oral rinse            | 0.12% CHX gluconate | Without CHX | Every 12 h for 3 days | 62.3 ± 12.4 | 63.1 ± 9.3 |       |         |
| Hannan [38] | Ireland  | Prospective cohort | 480 | Pre-operative Skin antiseptic | 2% CHX in 70% alcohol | 70% alcohol | \ | 68 (61–74) | 68 (61–75) |       |         |
| Madej [39]  | Germany  | Prospective cohort | 1523 | Pre-operative Skin antiseptic | 2% CHX combined with 70% IPA | 55% IPA | \ | 67.9 ± 9.9 | 68.1 ± 9.9 |       |         |
| Raja [40]   | UK       | Prospective cohort | 738  | Pre-operative Skin antiseptic | 2% CHX in 70% alcohol | 10% IPA | \ | \ | \ |       |         |
| Qintar [43] | USA      | Retrospective cohort | 1436 | Pre-operative skin antiseptic | CHX in alcohol | IPA | \ | 66 ± 14.14 | 65.69 ± 15.07 |       |         |
| Levy [36]   | Israel   | RCT    | 74          | CHX-impregnated sponge | CHX-impregnated sponge covered with a transparent polyurethane | \ | 21 ± 37 | 31 ± 43 |       |         |
| Kohler [41] | Switzerland | Prospective cohort | 646 | Whole-body shower | 4% CHX digluconate | Without CHX | Once daily | 64.4 ± 13.5 | 65.2 ± 13.0 |       |         |
| Yeo [42]    | Korea    | Prospective cohort | 960 | Pre-operative disinfection of circuits and hubs | 2% CHX + IPA | Without CHX | \ | 594 ± 15.2 | 56.7 ± 13.4 |       |         |
| Abboud [44] | Brazil   | Retrospective cohort | 82 | Bathing with CHX-impregnated washcloths | 2% CHX | Without CHX | Once-daily | \ | \ |       |         |
| Thompson [45]| USA      | Case-control | 1995 | Bathing with CHX-impregnated washcloths | 2% CHX | Without CHX | Once-daily | \ | \ |       |         |

CHX chlorhexidine, IPA isopropyl alcohol
Superficial and deep wound infections

Three studies could be included to analyze superficial/deep wound infection [38, 40, 41]. CHX was protective against superficial wound infection after cardiac surgery compared with control interventions (OR = 0.46, 95% CI: 0.22–0.94, P = 0.032; I² = 59.2%, P_{heterogeneity} = 0.061) (Fig. 3b). There was no difference between CHX and IPA, while the difference was driven by no intervention as control (Fig. 3a and Table 2). There was no difference between CHX and IPA, while the difference was driven by no intervention as control (Fig. 3a). No protective effect of CHX was observed for deep wound infection (OR = 0.79, 95% CI: 0.40–1.58, P = 0.509, I² = 51.7%, P_{heterogeneity} = 0.126) (Fig. 4a,b and Table 2).

Effect of the type of CHX intervention

Figure 5 and Table 2 show that the lack of association between CHX and SSI (OR = 0.77, 95% CI: 0.57–1.04, P = 0.090; I² = 63.5%, P_{heterogeneity} = 0.008) remained insignificant when considering only the oral rinse (OR = 0.88, 95% CI: 0.58–1.33, P = 0.549), skin antiseptic (OR = 0.82, 95% CI: 0.61–1.11, P = 0.201; I² = 51.4%, P_{heterogeneity} = 0.084), and disinfection of surgical-related appliance (OR = 0.20, 95% CI: 0.01–3.75, P = 0.279; I² = 86.9%, P_{heterogeneity} = 0.006).

Effect of CHX on infections other than surgical wound

The meta-analysis of four studies [32, 34, 37, 44] showed that CHX was not protective against urinary tract infection (OR = 0.80, 95% CI: 0.46–1.38, P = 0.415; I² = 18.1%, P_{heterogeneity} = 0.300) (Fig. 6 and Table 2). On the other hand, the use of CHX protected against bloodstream infection [32, 36, 42, 44] (OR = 0.36, 95% CI: 0.16–0.80, P = 0.012; I² = 16.3%, P_{heterogeneity} = 0.310) (Fig. 7 and Table 2), nosocomial infection [32, 34, 35, 37] (OR = 0.55, 95% CI: 0.44–0.69, P < 0.001; I² = 0.0%, P_{heterogeneity} = 0.520) (Additional file 2: Fig. S1 and Table 2), and pneumonia [32–35, 37, 44] (OR = 0.26, 95% CI: 0.11–0.61, P = 0.002; I² = 76.6%, P_{heterogeneity} = 0.001).

Sensitivity analyses

Additional file 3: Fig. S3 shows the analyses according to RCTs (A) and observational studies (B). The same conclusions were reached for the two study types for nosocomial infections, pneumonia, SSI, and urinary tract infections. The meta-analysis of RCTs showed no impact of CHX on bloodstream infection, while the meta-analysis of the observational studies showed an impact.

Discussion

Although several meta-analyses reported the impact of different types of CHX applications for patients undergoing various types of surgery [17–24], no meta-analysis summarized the overall effectiveness of CHX specifically for cardiac surgery, which carries a high risk of infections [25, 26]. Therefore, this study aimed to examine the impact of CHX compared with other cleansers or antiseptics used in cardiac surgeries. The results suggest that CHX was not protective for SSI, deep wound infection, and urinary tract infections but was protective against superficial SSI, bloodstream infection, nosocomial infections, and pneumonia.

The use of CHX before surgery is already well-documented and well-supported by a large amount of evidence, as revealed by many meta-analyses on the subject [17–24]. This meta-analysis adds further evidence by showing that CHX can decrease the risk of superficial SSI, bloodstream infection, nosocomial infections, and pneumonia, leading to poor outcomes in patients who are already affected by their cardiac condition, surgery itself, and often multiple comorbidities. This is supported by other meta-analyses and studies regarding superficial wound infection [12, 40, 41, 46, 47], bloodstream infection [15, 18, 48], nosocomial infections [17, 19, 24, 32–35, 37, 49], and pneumonia [8, 17, 18, 24, 33, 35, 37, 49–51]. Nevertheless, heterogeneity is observed in those previous studies and meta-analyses, mainly due to the different methods of using CHX, the different concentrations, and the different frequencies of use. Nevertheless, the studies agree that CHX generally contributes to the prevention of those infections. On the other hand, the present meta-analysis showed no significant impact of CHX for SSI, which is probably driven by the lack of association with deep wound infection. In addition, there was no association with urinary infections. Nevertheless, previous studies did report associations between CHX and lower odds of those infections [1, 6, 12, 13, 16, 17, 19, 20, 22, 23, 34, 38–41, 44–47, 49]. The discrepancies could be due to several factors such as the included studies, the study populations, and the CHX regimen. Nevertheless, previous meta-analyses that included cardiac surgery patients support the present meta-analysis [18, 24, 31, 52].

Mechanistically, the control of respiratory infection by CHX is probably due to the use of oral CHX [18, 52–56]. Nevertheless, pneumonia can also lead to bloodstream infection [57–59], and preventing one can prevent the other. Regarding the decreased odds of bloodstream infection, this is probably driven by using CHX for the skin and the medical devices since vascular devices are
Fig. 2  
a. Forest plot of surgical site infection (SSI) comparing patients treated with CHX vs. control (placebo, isopropyl alcohol (IPA), or without CHX).
b. Forest plot of surgical site infection comparing patients treated with CHX vs. control, according to the type of control (placebo, IPA, or without CHX).

Table 2: Subgroup analyses: CHX vs. control

| Subgroup                              | N  | OR (95% CI) | P     | I² (%) | P heterogeneity |
|---------------------------------------|----|-------------|-------|--------|----------------|
| Nosocomial infection                  | 4  | 0.549 (0.438, 0.687) | <0.001 | 0      | 0.520          |
| Pneumonia                             | 6  | 0.260 (0.110, 0.611) | 0.002  | 76.6   | 0.001          |
| Oral rinse                            | 5  | 0.259 (0.104, 0.643) | 0.004  | 81.2   | <0.001         |
| Disinfection of surgical-related appliances | 1  | 0.257 (0.010, 6.404) | 0.407  |        |               |
| Surgical site infection               | 8  | 0.757 (0.549, 1.045) | 0.090  | 63.5   | 0.008          |
| Oral rinse                            | 1  | 0.881 (0.582, 1.333) | 0.549  |        |               |
| Skin antiseptic                       | 5  | 0.824 (0.612, 1.109) | 0.201  | 51.4   | 0.084          |
| Disinfection of surgical-related appliances | 2  | 0.161 (0.006, 4.395) | 0.279  | 86.9   | 0.006          |
| Superficial infection                 | 3  | 0.422 (0.255, 0.696) | 0.001  | 19.4   | 0.289          |
| Deep infection                        | 3  | 0.792 (0.397, 1.580) | 0.509  | 51.7   | 0.126          |
| Bloodstream infection                 | 4  | 0.362 (0.164, 0.798) | 0.012  | 16.3   | 0.310          |
| Oral rinse                            | 1  | 0.256 (0.028, 2.312) | 0.225  |        |               |
| Disinfection of surgical-related appliances | 3  | 0.411 (0.138, 1.222) | 0.110  | 43.1   | 0.173          |
| Urinary tract infection               | 4  | 0.795 (0.459, 1.379) | 0.415  | 18.1   | 0.300          |
| Oral rinse                            | 3  | 0.746 (0.386, 1.442) | 0.384  | 40.6   | 0.186          |
| Disinfection of surgical-related appliances | 1  | 1.575 (0.140, 17.766) | 0.713  |        |               |

Fig. 3  
a. Forest plot of superficial infection comparing patients treated with CHX or control (isopropyl alcohol (IPA) or without CHX).
b. Forest plot of surgical site infection comparing patients treated with CHX vs. control, according to the type of control (IPA or without CHX).
among the first causes of bloodstream infection [60–62]. Of course, decreased superficial SSI is linked to skin disinfection [1, 12, 13, 40, 46]. Future studies could look at the interactions between specific uses of CHX with specific infections, but the present meta-analysis could not perform such analyses.

The conclusions of the meta-analysis must be considered in the light of its limitations. First, we included observational studies in our analysis due to the small number of RCTs in this study field, but at the price of introducing heterogeneity and bias. Second, the treatment regimens in the control group were variable among the studies. Accordingly, the random-effect model was applied to all quantitative analyses regardless of the results of Cochran's Q test and the I² index. Third, mortality could not be analyzed because it was not reported by enough studies. Finally, despite a relatively large number of patients, the numbers of patients and studies in each subanalysis were small. More studies are required.
Conclusions
In conclusion, in patients undergoing cardiac surgery, CHX is not protective for SSI, deep wound infection, and urinary tract infections but is protective against superficial infection, bloodstream infection, nosocomial infections, and pneumonia. Therefore, CHX can be useful in cardiac surgeries to prevent infections, especially superficial infection, bloodstream infection, nosocomial infection, and pneumonia. Future studies can work on a standardized protocol to determine the recommended concentration and frequency for different application methods of CHX in patients undergoing cardiac surgery.
Abbreviations
CHX: Chlorhexidine; SSI: Surgical site infection; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PICO: Patient, intervention, comparison, outcome; BSI: Bloodstream infection; UTI: Urinary tract infection.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1186/s13756-021-01009-3.

Additional file 1. Quality of the evidence assessment and the exact strategies for all three databases.
Additional file 2. Figure S1. Nosocomial infection, comparing patients treated with CHX or control (IPA or without CHX).
Additional file 3. Figure S2. Pneumonia, comparing patients treated with CHX or control (IPA or without CHX).
Additional file 4. Figure S3. Analyses of the outcomes according to randomized controlled trials (A) and observational studies (B).

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Authors’ contributions
Jianhua Wei contributed to the study design and concept. Lingying He and Fengxia Weng completed the article evaluation and data extraction and drafted the initial manuscript. Jianhua Wei and Fangfang Huang supervised the work. Peng Teng reviewed the manuscript. All authors contributed to the manuscript and revisions and approved the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References
1. Bednarek RS, Nassereddin A, Ramsey ML. Skin Antiseptics. StatPearls.
2. World Health Organization. WHO Model Formulary 2008. Geneva: World Health Organization, 2009.
3. British national formulary: BNF 69 (69 ed.). London: British Medical Association, 2015.
4. Leikin JB, Paloucek FP. Chlorhexidine gluconate. In: Leikin JB, Paloucek FP, editors. Poisoning and Toxicology Handbook (4th ed). London: Informa, 2008.
5. Milstone AM, Passaretti CL, Perl TM. Chlorhexidine: expanding the armamentarium for infection control and prevention. Clin Infect Dis. 2008;46:274–81.
6. 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.
7. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Awuаeааr PM, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70:195–283.
8. Rello J, Lode H, Cornaglia G, Masterton R. Contributors VAPCB. A European care bundle for prevention of ventilator-associated pneumonia. Intensive Care Med. 2010;36:773–80.
9. James P, Worthington HV, Pamell C, Harding M, Lamont T, Cheung A, et al. Chlorhexidine mouthrinse as an adjunctive treatment for gingival health. Cochrane Database Syst Rev. 2017;3:CD008676.
10. Donskey CJ, Deshpande A. Effect of chlorhexidine bathing in preventing infections and reducing skin burden and environmental contamination: a review of the literature. Am J Infect Control. 2016;44:e17–21.
11. Shah HN, Schwartz JL, Luna G, Cullen DL. Bathing with 2% chlorhexidine gluconate: evidence and costs associated with central line-associated bloodstream infections. Crit Care Nurs Q. 2016;39:42–50.
12. Wade RG, Burr NE, McCauley G, Bourke G, Ethimiou O. The comparative efficacy of chlorhexidine gluconate and povidone-iodine antisepsics for the prevention of infection in clean surgery: a systematic review and network meta-analysis. Ann Surg. 2020.
13. Durnville JC, McFarlane E, Edwards P, Lipp A, Holmes A, Liu Z. Preoperative skin antisepsics for preventing surgical wound infections after clean surgery. Cochrane Database Syst Rev. 2015:CD003949.
14. Sinha A, Saazwal S, Pradhan A, Ramji S, Opiyo N. Chlorhexidine skin or cord care for prevention of mortality and infections in neonates. Cochrane Database Syst Rev. 2015:CD007835.
15. Musuza JS, Guru PK, O’Horro JC, Bongiorni CM, Korobkin MA, Ganganon RE, et al. The impact of chlorhexidine bathing on hospital-acquired bloodstream infections: a systematic review and meta-analysis. BMC Infect Dis. 2019;19:416.
16. Noorani A, Rabey N, Walsh SR, Davies RJ. Systematic review and meta-analysis of preoperative antiseptics with chlorhexidine versus povidone-iodine in clean-contaminated surgery. Br J Surg. 2010;97:1614–20.
17. Pedersen P, Larsen P, Hikonsen SJ. The effectiveness of systemic perioperative oral hygiene in reduction of postoperative respiratory tract infections after elective thoracic surgery in adults: a systematic review. JBI Database System Rev Implement Rep. 2016;14:140–73.
18. Silvestri L, Weir WI, Gregori D, Taylor N, Zandra DF, van Saene JIM, et al. Impact of oral chlorhexidine on bloodstream infection in critically ill patients: systematic review and meta-analysis of randomized controlled trials. J Cardiothorac Vasc Anesth. 2017;31:2236–44.
19. George S, Leasure AR, Horstmanshof D. Effectiveness of decolonization with chlorhexidine and mupirocin in reducing surgical site infections: a systematic review. Dimens Crit Care Nurs. 2016;35:204–22.
20. Lee I, Agarwal RK, Lee BY, Fishman NO, Umscheid CA. Systematic review and cost analysis comparing use of chlorhexidine with use of iodine for preoperative skin antiseptics to prevent surgical site infection site. Infect Control Hosp Epidemiol. 2010;31:1219–29.
21. Solderer A, Kaufmann M, Hofer D, Wiedemeier D, Attin T, Schmidlin PR. Efficacy of chlorhexidine rinses after periodontal or implant surgery: a systematic review. Clin Oral Investig. 2019;23:21–32.
22. Davies BM, Patel HC. Systematic review and meta-analysis of preoperative antiseptics with combination chlorhexidine and povidone-iodine. Surg J (N Y). 2016;2:70–7.
23. Franco LM, Cota GF, Pinto TS, Ercolle FF. Preoperative bathing of the surgical site with chlorhexidine for infection prevention: systematic review with meta-analysis. Am J Infect Control. 2017;45:343–9.
24. Spreadborough P, Lott S, Pasquali S, Popplewell M, Owen A, Kreis L, et al. A systematic review and meta-analysis of perioperative oral decontamination in patients undergoing major elective surgery. Perioper Med (Lond). 2016;5:6.
25. Cove ME, Speilmann DW, MacLaren G. Infectious complications of cardiac surgery: a clinical review. J Cardiothorac Vasc Anesth. 2012;26:1094–100.
26. Gellinns NC, Moskowitz AJ, Acker MA, Angelozano M, Geller NL, Puskas JD, et al. Management practices and major infections after cardiac surgery. J Am Coll Cardiol. 2014;64:372–81.
27. Selcuk AA. A guide for systematic reviews: PRISMA. Turkish Arch Otorhino-laryngol. 2019;57:57–8.
