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Question 1: Does the type of administered anesthesia (general versus regional) influence the rate of surgical site infection /periprosthetic joint infection (SSI/PJI) in major orthopaedic surgery?[1]

Response/Recommendation

Based on current evidence and the delegate vote, regional anesthesia (RA) appears to reduce the risk of SSI and PJI in major orthopaedic surgery compared with general anesthesia (GA). While most available data are observational, the consensus strongly favors the use of RA whenever feasible, and further prospective studies are warranted to confirm these findings.

Strength of Recommendation: Weak

Delegate Vote: Agree: 68.4%, Disagree: 21.1%, Abstain: 10.5% (Majority Support)

Rationale

We conducted a comprehensive systematic review to evaluate the effect of administered anesthesia (general versus regional) on the rate of SSI/PJI in major orthopaedic surgery. Appropriate medical subject headings) terms were developed by the librarians to conduct a literature search in two databases, Medline and Embase publications, then screened by two experts to identify 13 final publications for inclusion in the systematic review.

Many orthopaedic surgical procedures can be performed with either RA or GA. The RA seems to reduce postoperative complications by minimizing sympathetic activation, inflammation, venous stasis, and the need for endotracheal intubation and positive pressure ventilation [1–3]. Postoperative complications, particularly SSIs, are a major concern in major orthopaedic surgery. The SSIs after knee and hip arthroplasty can significantly worsen surgical outcomes, increasing both morbidity and mortality [4].

In 10 studies, the superiority of RA in reducing the risk of SSI and PJI in arthroplasty and trauma surgeries was highlighted [5–14]. However, two studies did not observe significant differences between the two anesthesia methods [15,16].

A comprehensive registry study that included 779,491 patients who underwent total hip arthroplasty (THA) and total knee arthroplasty (TKA) found that RA was linked to a reduced risk of SSI, with odds ratios (ORs) of 0.87 for THA and 0.84 for TKA [8]. A systematic review comprising 15 studies demonstrated that patients receiving spinal anesthesia were 23% less likely to develop postoperative SSIs compared to those who received GA (OR: 0.77) [6].

An observational study involving 3,909 arthroplasties conducted by Scholten et al. showed an OR for PJI of 2.0 (95% confidence interval 1.0 to 3.7) for patients who had GA compared to those who received spinal anesthesia matched by propensity scores [5]. Another meta-analysis indicated that GA significantly raised the incidence of postoperative SSI compared to spinal anesthesia, with both unadjusted (OR: 0.77) and adjusted (OR: 0.84) analyses supporting this finding [12].

A population-based study of 3,081 patients undergoing THAs or TKAs reported that the odds of SSI for patients receiving GA were 2.21 times higher than those who underwent the procedures with spinal or epidural anesthesia. This finding was consistent even after adjusting for age, sex, comorbidities, surgeon experience, and hospital teaching status [11].

Not only is GA associated with an increased risk of SSI, but the duration of anesthesia itself is also considered an independent risk factor contributing to this increase [13]. Deep SSIs were notably less frequent in the RA group, with an OR of 0.38 compared to the GA group [14].

Also, it was observed that RA not only lowers the risk of superficial infections but also significantly reduces the risk of systemic infections, including sepsis [7]. In two separate studies focused on revision TKA, the risk of SSI was also found to be 1.43 and 1.32 times higher for patients under GA [9,10].

In the International Consensus Meeting 2018, the evidence either favored neuraxial anesthesia over GA or showed no difference in reducing the SSI risks after THA/TKA. No evidence supports

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GA, and neuraxial anesthesia is strongly recommended when feasible [17].

While two studies favored RA or reported no significant differences, the predominantly retrospective nature of the existing research highlights the need for high-quality prospective studies to validate these findings. Nevertheless, in the absence of evidence supporting GA and with a consistent trend favoring RA, RA should be prioritized as the anesthetic method of choice for major orthopaedic procedures, whenever clinically feasible.

Conclusions

This analysis demonstrates that RA offers major advantages over GA in major orthopaedic surgeries, particularly in reducing the incidence of SSI and PJI. The physiological benefits of RA, such as reduced sympathetic activation, minimized inflammation, and lower systemic infection risks, make it a compelling choice.

Question 2: Does intraoperative normothermia influence the rate of subsequent surgical site infection (SSI)/ periprosthetic joint infection (PJI) in major orthopaedic surgery?[2]

Response/Recommendation

Unknown. There is inconclusive evidence regarding the role of maintaining intraoperative normothermia for the prevention of SSI/PJI. However, we recommend that intraoperative normothermia be maintained to reduce complications.

Level of Evidence: Limited

Delegate Vote: Agree: 85%, Disagree: 9%, Abstain: 6% (Super Majority, Strong Consensus)

Rationale

Hypothermia is a difficult factor to assess in terms of periprosthetic infections in orthopaedics. Authors have described the negative effects of hypothermia after other major surgeries, like abdominal surgery. They have found that even mild perioperative hypothermia can increase the incidence of postoperative complications (e.g., increased mortality, increased bleeding, sepsis, stroke, SSI) [18–22]. In orthopaedics, one would not knowingly make a person hypothermic because of the potential other ill effects on our patients. In fact, one recent study showed increased 30-day mortality in major orthopedic surgeries, so the question of whether hypothermia leads to increased infection rates might be less relevant [23].

To compile this review of the topic, we conducted a systematic review to clarify the efficacy of normothermia over hypothermia in reducing SSI in major orthopaedic surgery, including spine surgery, fracture surgery, and joint arthroplasty. Following International Consensus Meeting guidance, we searched MEDLINE (via PubMed), CENTRAL, and Embase for all randomized controlled trials and observational studies, including longitudinal/cohort studies, case-control studies, controlled before-and-after studies, and cross-sectional studies published through November 2024 that reported the outcome of the surgical patients. We included all adult patients with primarily closed surgical incisions after spine surgery, trauma/fracture surgery, and joint arthroplasty of any joint, both with and without implants. We also included fracture fixation for open fractures if the wound was primarily closed, as well as outpatient, emergent, elective, and revision surgery. Of the 1,353 articles that were subjected to title and abstract screening, we shortlisted 49 articles for full-text screening. We excluded 38 articles and added three articles through a hand search. This left 14 observational studies that were included in our final analysis [23–36].

We found that four musculoskeletal surgery–related studies had patients who became hypothermic during surgery and were compared to normothermic patients and found to have an increased infection rate [24–27]. However, this was inconclusive because another seven studies have not shown that hypothermia led to an increased infection rate [28–32,35], and one study found that normothermia had a higher infection rate than the hypothermic group [33]. Other studies have found an increased incidence of other adverse events in hypothermic patients, including increased mortality [23,24,34,36].

For multiple reasons, tabulating this topic across studies and doing a true meta-analysis with a statistical analysis is not appropriate. This is because there were different operations (with different times of procedure, i.e., some over two hours, some shorter) and different hypothermia definitions or threshold temperatures (36.0 versus 35.5°C), as well as the retrospective nature and often incomplete data collected.

The fact that many studies routinely used cointerventions to prevent hypothermia, such as passive or active warming systems based on other physiological mechanisms (e.g., irrigation fluid or gas warming), as well as stricter temperature control in the study context compared with standard practice, may also explain the difficulty in observing a clinically relevant beneficial effect with normothermia. For instance, many studies do not control for the fact that obese patients, who are more prone to having an infection, are also more likely to retain normothermia. The total advantage of sustaining normothermia may have been underestimated as a result of these positive effects on the control group members. In addition, as stated earlier, the hypothermic threshold was re-established as 35.5°C by the Prevention of Operative Thermal Emissions and Complications by Thermoregulation Study [37], which was not used in prior studies (often 36°C).

As stated above, hypothermia has been linked to increased SSI and PJI rates in four studies, as follows: Frisch et al. reviewed 1,525 hip fracture cases and found a 17% rate of intraoperative hypothermia (< 36° C), which was significantly associated with deep SSIs (odds ratio 3.30, $P = 0.022$) [24]. Charles-Lozoya et al. reported a 25% mortality rate in hypothermic patients (< 35° C) with hip fracture cases (n = 300), with significantly higher SSI and transfusion rates [25]. Hu et al. (n = 2,692) identified intraoperative temperatures < 36.4° C as an independent infection risk in open fractures [26]. Dyck et al. analyzed 12,636 hip/knee arthroplasties and found that maintaining immediate postoperative temperatures between 36 and 38° C was linked to fewer SSIs [27].

Conversely, seven studies found no overall link between hypothermia and infection: Williams and El-Houdiri found that there was no increase in infection risk with hypothermia in primary arthroplasty patients [28]. Vicentini et al. [29] (n = 18,791) showed that normothermia, as part of a perioperative care bundle, did not reduce SSI risk. Frisch et al. [30] (n = 2,397) found no increase in complications despite greater blood loss with hypothermia. Liedl et al. [31] (n = 236) found no SSI increase from hypothermia alone, though risks were higher with elevated hemoglobin A1c patients. Yamada et al. [23] (n = 8,841) found no difference in SSI risk in hypothermic patients. Abugri et al. (n = 297) and Reina et al. (n = 941) found that hypothermia was not significantly associated with SSIs [32,35]. There was one study, Jildeh et al. [33] (n = 657), that found a higher risk of SSIs with normothermia in shoulder arthroplasty.

Other studies noted broader benefits of normothermia: Yamada et al. linked hypothermia with increased 30-day mortality in major orthopedic surgeries (as did Charles-Lozoya et al. [25]) (pooled odds ratio 4.55 (95% confidence interval 2.26 to 9.18). Pan et al. (n = 616) found that hypothermia increased blood loss and transfusion rates in total hip arthroplasty/total knee arthroplasty

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[34]. Charles-Lozoya et al. and Goel et al. also found that hypothermia increased transfusion rates [25,36].

There are several potential limitations to this review. All of the studies evaluated were observational studies with various definitions for SSI and normothermia with various follow-up periods. As stated, there are vast heterogeneities, and the nature of observational studies may affect the interpretation. In addition, although several studies linked increased risk of 30-day mortality with hypothermia, the number of observational studies evaluating mortality was very limited (n = two). Moreover, as we did not include a pediatric population, reproducibility and generalization of this population may be limited. Also, there are three important phases (pre-, intra-, and postoperative) for maintaining normothermia, but the association between these phases was not evaluated. Furthermore, there are several active body surface warming systems considered useful for preventing inadvertent hypothermia, but the effect of these different systems has not been evaluated.

Conclusions

Based on our results, we suggest maintaining normothermia as a measure to reduce the risk of 30-day mortality in adult patients undergoing major orthopedic surgeries. Maintaining normothermia reduced SSIs in the three fracture studies, but it was inconclusive for this outcome in the other orthopedic populations.

Question 3: Does administration of intravenous (IV) corticosteroids (dexamethasone) during major orthopaedic procedures increase the risk of subsequent surgical site infection (SSI)/periprosthetic joint infection (PJI)?[3]

Response/Recommendations

No. There is no concrete evidence linking intraoperative administration of low-dose IV corticosteroids to an increased risk of subsequent SSI/PJI.

Level of Evidence: Limited

Delegate Votes: Agree: (90.9%), Disagree: (2.2%), Abstain: (6.9%) (Total consensus, Unanimity)

Rationale

In recent years, there has been an interest in IV administration of corticosteroids during surgery to reduce the incidence of nausea and pain [38]. During the recent World Expert Meeting, administration of IV corticosteroids during surgery was discussed and strongly endorsed [39]. The use of IV corticosteroids has been shown to reduce the need for postoperative narcotics and pain medications after distal radius fixation, elbow fracture surgery, and total joint arthroplasty. Patients treated with taper doses of IV corticosteroids after these surgeries have been shown to have less postoperative pain and improved range of motion [40–42]. Recent studies have demonstrated the effectiveness of perioperative high-dose corticosteroid administration after total hip and knee arthroplasty in reducing postoperative inflammatory response, pain, nausea, and vomiting, and also accelerating postoperative rehabilitation [43–45]. However, there are insufficient data on the optimal dose of IV corticosteroids, considering side effects and the relation to SSI or PJI. Furthermore, contraindications for the administration of IV corticosteroids during surgery are not known [45]. A potential adverse effect of IV corticosteroids relates to the potential increase in subsequent SSI and/or PJI.

To evaluate the question posed here, we performed a comprehensive systematic review. All relevant literature was identified using medical subject headings terms and a search of PubMed and Scopus databases. A total of 5,980 articles were identified on initial screening. After excluding duplicates, 5,128 publications remained. After further review, 83 studies were found to meet the inclusion criteria and were selected for full review and data extraction. We subgrouped the studies into four groups: (1) single low-dose (up to 10mg dexamethasone) corticosteroids, (2) single high-dose (more than 10 mg dexamethasone) corticosteroids, (3) multiple low-dose corticosteroids, and (4) multiple high-dose corticosteroids.

Single Low-Dose Intravenous Corticosteroids

The review of 15 publications in this category that reported on the rate of SSI showed that the incidence was comparable between the corticosteroid group (one event in 740 patients) and the placebo group (one event in 737 patients), yielding a relative risk (RR) of 0.98 (95% confidence interval [CI]: 0.14 to 6.76) [46–60]. In addition, six studies focusing on PJI outcomes showed no events in either the corticosteroids group (zero of 272) or the placebo group (zero of 267) [51–53,56–58].

Single High-Dose Intravenous Corticosteroids

There were fourteen studies that reported SSI outcomes, with more events in the corticosteroids group (eight events in 607 patients) compared to the placebo group (three events in 611 patients) (RR: 1.99, CI: 0.71 to 5.60) [53,61–73]. Furthermore, nine studies on PJI reported an increased incidence in the corticosteroids group (nine of 384) compared to the placebo group (four of 358) (RR: 2.2, CI: 0.72 to 6.76) [53,65,67–73].

Multiple Low-Dose Intravenous Corticosteroids

There were 13 studies on SSI outcomes that observed a slightly higher number of events in the corticosteroids group (five of 640) versus the placebo group (three of 638), with an RR of 1.45 (CI: 0.45 to 4.66) [38, 48, 58, 72–81]. For PJI, three studies showed no events in the corticosteroids group (zero of 84) and two events in the placebo group (two of 92) (RR: 0.23; CI: 0.01 to 4.59) [37,72–81].

Multiple High-Dose Intravenous Corticosteroids

There were three studies on SSI outcomes that reported on one event in the corticosteroids group (one of 158) compared to none in the placebo group (zero of 160) (RR: 3.12, CI: 0.13 to 74.85) [82–84].

For the SSI and PJI outcome, we have downgraded the evidence one level due to indirectness and two levels due to imprecision, “insufficient number of events and short follow-up period,” so the evidence was downgraded from high to very low. Data from nonrandomized controlled trial and retrospective studies supported the results of our meta-analysis. Vournin et al. [85] studied 18,872 total joint arthroplasties and found no statistically significant difference in PJI rate at about 5-year follow-up between patients who received IV five to 10 mg dexamethasone and the nondexamethasone group (odds ratio 1.05, 95% CI 0.71 to 1.54, $P = 0.77$). Also, Klement et al. and Richardson et al. found no statistically significant difference in PJI risk after administration of eight to 10 mg dexamethasone with total joint arthroplasty [86,87]. Godshow et al. 2019 showed that, in their retrospective cohort, administration of IV dexamethasone did not increase the risk of PJI or affect the serum glucose level [88]. Jorgensen et al. [89], in a prospective cohort study including 1,442 patients who received a preoperative high-dose corticosteroid (125 mg methylprednisone), found no statistically significant increase in infections at 3-month follow-up.

Conclusions

Based on available data, administration of low-dose IV corticosteroids during major orthopaedic surgeries does not seem to result in an increase in the rate of postoperative SSI/PJI. There is low evidence that administration of a single or multiple high-dose IV corticosteroids during major orthopaedic procedures may

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increase the risk of SSI/PJI. However, all studies available have a relatively small sample size, are victims of type II statistical error, and carry immense heterogeneity. Thus, there is a need for large-sized randomized controlled trials investigating the risk of SSI/PJI as a primary outcome in patients receiving perioperative IV corticosteroids.

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