Authors: Mauro Jose Costa Salles, Mario Morgenstern, William T. Obremskey

QUESTION 4: Are there microorganism-specific risk factors for acute infection in trauma patients (i.e., does being a nasal carrier of methicillin-resistant *Staphylococcus aureus* (*S. aureus*), or MRSA, increase the risk for MRSA infection after trauma?)

RECOMMENDATION: The current evidence of an increased risk of infection is based on several risk factors, including MRSA colonization, presence of external fixator, anatomical location of surgery and severe open fractures. In these situations, alterations in antibiotic prophylaxis could be considered.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

MRSA colonization in the nares, axilla and other body sites has been associated with higher risk for MRSA surgical site infection (SSI) (cardiac and arthroplasties) [1]. Nasal topical decolonization, along with systemic antibiotic prophylaxis, has been shown to reduce the risk of MRSA prosthetic joint infections (PJIs) [2]. In a meta-analysis published by Schweizer et al. a bundle intervention consisting of nasal decolonization and glycopeptide prophylaxis showed a significant protective effect against MRSA PJI and cardiac surgical infection when all patients underwent decolonization (0.40, 0.29 to 0.55) and when only *S. aureus* carriers underwent decolonization (0.36, 0.22 to 0.57). Because only three randomized clinical trials (RCTs) assessed the risk associated with total joint arthroplasty, they also included seven studies assessing nasal decolonization for general orthopaedic surgeries. Most of decolonization regimens used mupirocin ointment into the anterior nares. In addition, seven studies assessed the bundle applied only for patients colonized with MRSA and found a significant protective effect against SSIs with gram-positive bacteria (0.41, 0.30 to 0.56) [3]. Therefore, there is a strong recommendation to perform nasal decolonization for those patients known to be at high risk for MRSA PJI.

However, nasal colonization with MRSA as an independent risk factor for MRSA infection after orthopaedic trauma and fractures has yet to be investigated. Taormina el al. prospectively assessed whether trauma patients with fracture nonunions who are colonized with nasal *S. aureus* (MRSA or methicillin-susceptible *S. aureus* (MSSA)) would be at greater risk of complications following surgeries, and if it would predict positive operative cultures. The study failed to demonstrate an association between MRSA or MSSA-colonized patients being treated for fracture nonunion of long bones with postoperative infectious complications. There was no significant difference in operative culture positivity or speciation between colonized or non-colonized patients [4]. On the other hand, in recent a non-randomized, 7-year prospective study in Japan, Nakamura et al. examined the role of preoperative nasal swabbing for *S. aureus* among patients who underwent several types of orthopaedic surgeries. One hundred and forty patients were MRSA nasal carriers (carriage rate 3.4%), even though only a minority of them (40) underwent osteosynthesis for fracture stabilization [5]. Nasal carriage of *S. aureus* or MRSA developed significantly more SSIs compared to non-carriers, suggesting that it may be a risk factor for SSI in orthopaedic surgery. Additionally, Croft at al. prospectively screened for MRSA colonization in 355 patients admitted to a trauma intensive care unit, of which 36 (10.1%) were colonized. Significantly higher rates of MRSA infection were diagnosed in the MRSA colonized group (33.3%) compared to those who were not (6.6%) ($p < 0.001$). Death rates were also higher among the colonized group compared to non-colonized patients, (22.2 vs. 5.% [$p < 0.001$]). Therefore, they recommended MRSA screening protocols at trauma units to identify these at-risk patients [6].

The current evidence that MRSA colonization predicts acute infection in trauma patients is scarce, but it suggests that assessment and decolonization may be beneficial in reducing fracture-fixation infection rates. Nixon et al. screened 1,122 trauma patients, of whom 3.8% were MRSA carriers, and after implementation of anti-MRSA policies the incidence of MRSA infection dropped by 56% [7]. The same group, in a retrospective study, identified 3.2% (79/2,473) MRSA carriage at admission in an acute trauma unit, and these patients were significantly more likely to develop MRSA SSI (7 of 79 patients, 8.8%) compared with 54/2,394 (2.3%) of MRSA-negative patients ($p < 0.001$). This difference was confirmed on multivariate analysis, in which the odds ratio for developing MRSA SSI among MRSA carriers was 2.5 ($p = 0.015$) [8].

Conversely, Kan et al. analyzed 66 patients with femoral neck fractures and rates of MRSA colonization and found no correlation between MRSA colonization and higher rates of postoperative infection. Nevertheless, this study presented several important limitations including the postoperative infection evaluation limited to the first immediate postoperative week and short follow-up evaluation no longer than four months [9].

Older patients with femoral neck fractures seem to be particularly prone to be colonized by MRSA. A large French retrospective multicenter cohort study identified an SSI rate of 5.6% in patients who had surgery for a proximal femur fracture, of which one-third involved MRSA. All infected patients received first-generation or second-generation cephalosporin for prophylaxis, whereas those who received antibiotics effective against MRSA (i.e., vancomycin or gentamicin) for prophylaxis had no MRSA SSI [10]. Similarly, a prospective cohort study assessed the MRSA colonization rates among patients with proximal femur fracture in a German trauma unit. Their conclusion and recommendation is to systematically search for MRSA colonization in patients presenting with known risk factors by swabbing them in the emergency room [11].

The role of MRSA carriage eradication among trauma patients admitted to the intensive care unit (ICU) as an independent measure to prevent MRSA infection was assessed in a large multi-center, patient-based RCT recently published by Maxwell et al. Those with positive nasal swabs were randomized to either daily chlorhexidine gluconate (CHG) baths and mupirocin (MUP) ointment to the nares or soap and water baths and placebo ointment (S + P) for five days. Upon admission, 13.3% (90/678) of patients were MRSA carriers, and clinical MRSA infection was significantly more often diagnosed in MRSA colonized patients (21.1%) than those who were not (5.4%, $p < 0.001$). Although underpowered to draw definitive conclusions regarding the role of MRSA decolonization with CHG + MUP to

reduce MRSA infection rates, due to the smaller number of recruited patients per treatment arm, the five-day treatment period resulted in only a trend towards the reduction of colonization, 13 (59.1%) vs. 9 (90%) for CHG + MUP vs. S + P (p = 0.114). There was no difference in the proportion of MRSA infections between CHG + MUP (seven [31.8%]) vs. S + P (six [60%], p = 0.244). CHG + MUP was ineffective in eradicating MRSA from the anterior nares, but may reduce the incidence of infection [12].

A pilot RCT evaluated SSI among patients with open fractures that received prophylaxis during 24 hours with cefazolin compared with vancomycin and cefazolin, depending upon their *S. aureus* colonization status. MSSA and MRSA carriers were 20% and 3%, respectively. Although underpowered with a sample size too small for a clinical efficacy analysis, no significant difference in the rates of SSI was observed between the treatment arms. A significantly higher rate of MRSA SSIs was observed among MRSA carriers compared with noncarriers (33% vs. 1%, respectively, p = 0.003) [13]. Other factors that raise the risk of MRSA infection include the use of external fixation and a prolonged time to intramedullary nailing of long bone fractures [14].

Torbert's retrospective study identified *S. aureus* and gram-negative rods (GNRs) as most commonly seen in deep postoperative infections. GNRs were seen more frequently in the pelvis acetabulum and proximal femur injuries even in closed fractures. Resistance to GNRs was lower than *S. aureus,* and the infection rates for combined surgical approaches were twice that of a single approach for acetabular or pelvic surgery [15].

Severity of open fracture plays a role in the choice of antibiotics. There was no statistically significant difference in infection rates between the group treated with ciprofloxacin and that treated with cefamandole/gentamicin for Types I and II open fracture wounds. A high failure rate for the ciprofloxacin only treated Type III open fracture group, with patients being 5.33 times more likely to become infected than those in the combination therapy group [16].

The anatomic location of surgery should be considered when administering preoperative antibiotics. Corynebacterium genera are frequently associated with implants when surgical incisions were made near the perineum [17]. *Cutibacterium acnes* is bacterial species that is often seen in the axilla and coverage for these organisms should be considered when operating near this anatomical location [18].

REFERENCES

[1] Bode LGM, Kluytmans JAJW, Wertheim HFL, Bogaers D, Vandenbroucke-Grauls CMJE, Roosendaal R, et al. Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. N Engl J Med. 2010;362:9–17. doi:10.1056/NEJMoa0808939.

[2] Diekema D, Johannsson B, Herwaldt L, Beekmann S, Jernigan J, Kallen A, et al. Current practice in Staphylococcus aureus screening and decolonization. Infect Control Hosp Epidemiol. 2011;32:1042–1044. doi:10.1086/661917.

[3] Schweizer M, Perencevich E, McDanel J, Carson J, Formanek M, Hafner J, et al. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease gram positive surgical site infections after cardiac or orthopedic surgery: systematic review and meta-analysis. BMJ. 2013;346:f2743.

[4] Taormina DP, Konda SR, Liporace FA, Egol KA. Can preoperative nasal cultures of Staphylococcus aureus predict infectious complications or outcomes following repair of fracture nonunion? J Infect Public Health. 2018;11:521–525. doi:10.1016/j.jiph.2017.10.007.

[5] Nakamura M, Shimakawa T, Nakano S, Chikawa T, Yoshioka S, Kashima M, et al. Screening for nasal carriage of Staphylococcus aureus among patients scheduled to undergo orthopedic surgery: Incidence of surgical site infection by nasal carriage. J Orthop Sci. 2017;22:778–782. doi:10.1016/j.jos.2017.03.005.

[6] Croft CA, Mejia VA, Barker DE, Maxwell RA, Dart BW, Smith PW, et al. Methicillin-resistant Staphylococcus aureus in a trauma population: does colonization predict infection? Am Surg. 2009;75:458–461; discussion 461-462.

[7] Nixon M, Jackson B, Varghese P, Jenkins D, Taylor G. Methicillin-resistant Staphylococcus aureus on orthopaedic wards: incidence, spread, mortality, cost and control. J Bone Joint Surg Br. 2006;88:812–817. doi:10.1302/0301-620X.88B6.17544.

[8] Shukla S, Nixon M, Acharya M, Korim MT, Pandey R. Incidence of MRSA surgical-site infection in MRSA carriers in an orthopaedic trauma unit. J Bone Joint Surg Br. 2009;91:225–228. doi:10.1302/0301-620X.91B2.21715.

[9] Khan T, Grindlay D, Ollivere BJ, Scammell BE, Manktelow ARJ, Pearson RG. A systematic review of Vancouver B2 and B3 periprosthetic femoral fractures. Bone Joint J. 2017;99-B:17–25. doi:10.1302/0301-620X.99B4.BJJ-2016-1311.R1.

[10] Merrer J, Pisica-Donose G, Leneveu M, Pauthier F. Prevalence of methicillin-resistant Staphylococcus aureus nasal carriage among patients with femoral neck fractures: implication for antibiotic prophylaxis. Infect Control Hosp Epidemiol. 2004;25:515–517. doi:10.1086/502432.

[11] Gessmann J, Kammler J, Schildhauer TA, Kaminski A. MRSA colonisation in patients with proximal femur fractures in a German trauma centre: incidence, infection rates and outcomes. Langenbecks Arch Surg. 2012;397:117–123. doi:10.1007/s00423-011-0847-y.

[12] Maxwell RA, Croft CA, Creech CB, Thomsen I, Soper N, Brown LE, et al. Methicillin-resistant Staphylococcus aureus in a trauma population: does decolonization prevent infection? Am Surg. 2017;83:1407–1412.

[13] Saveli CC, Morgan SJ, Belknap RW, Ross E, Stahel PF, Chaus GW, et al. Prophylactic antibiotics in open fractures: a pilot randomized clinical safety study. J Orthop Trauma. 2013;27:552–557. doi:10.1097/BOT.0b013e31828d92ee.

[14] Metsemakers W-J, Handojo K, Reynders P, Sermon A, Vanderschot P, Nijs S. Individual risk factors for deep infection and compromised fracture healing after intramedullary nailing of tibial shaft fractures: a single centre experience of 480 patients. Injury. 2015;46:740–745. doi:10.1016/j.injury.2014.12.018.

[15] Andersson AE, Bergh I, Karlsson J, Eriksson BI, Nilsson K. Traffic flow in the operating room: an explorative and descriptive study on air quality during orthopedic trauma implant surgery. Am J Infect Control. 2012;40:750–755. doi:10.1016/j.ajic.2011.09.015.

[16] Patzakis MJ, Bains RS, Lee J, Shepherd L, Singer G, Ressler R, et al. Prospective, randomized, double-blind study comparing single-agent antibiotic therapy, ciprofloxacin, to combination antibiotic therapy in open fracture wounds. J Orthop Trauma. 2000;14:529–533.

[17] Arciola CR, An YH, Campoccia D, Donati ME, Montanaro L. Etiology of implant orthopedic infections: a survey on 1027 clinical isolates. Int J Artif Organs. 2005;28:1091–1100.

[18] Levy PY, Fenollar F, Stein A, Borrione F, Cohen E, Lebail B, et al. *Propionibacterium acnes* postoperative shoulder arthritis: an emerging clinical entity. Clin Infect Dis. 2008;46:1884–1886. doi:10.1086/588477.

Author: Arjun Saxena

QUESTION 5: Is periprosthetic fracture a risk for the development of a periprosthetic joint infection (PJI)?

RECOMMENDATION: Infection rates from level III and IV evidence studies suggest an increased surgical site infection in patients who undergo re-operation for treatment of periprosthetic fracture of the femur after total hip and knee arthroplasty. There is limited literature available on periprosthetic acetabular and tibial fractures. Further study investigating the outcomes for treatment of periprosthetic fracture is recommended.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)