

infection risks of endoprosthesis implantation and immunosuppressive effects of neoadjuvant therapy, patient outcomes using synthetic mesh for abdominal hernia repair have been well studied and provide some insight regarding infection rates associated with the use of mesh. A recent meta-analysis of 10 randomized controlled trials comparing abdominal hernia surgery outcomes using mesh vs. surgical suture detected no significant difference in infection rates between the 2 groups. However, the mesh group did demonstrate significantly lower incidence of recurrent hernia than the surgical suture group, leading the authors to conclude synthetic mesh was a highly efficacious repair technique [12].

In summary, the published literature suggested little or no association between the use of mesh for soft tissue attachment with endoprosthetic reimplantation and development of subsequent PJI. Further study is needed before it can be conclusively determined that the use of soft tissue attachment meshes does not increase the risk for subsequent infection in patients undergoing oncologic endoprosthetic reconstruction. Future investigation should utilize larger cohorts and control for tumor type and location so that the use of mesh can be better isolated as the variable of interest.

REFERENCES

- [1] Cho W, Song W, Jeon D, Kong C, Kim J, Lee S. Cause of infection in proximal tibial endoprosthetic reconstructions. *Arch Orthop Trauma Surg.* 2012;132:163-169.
- [2] Gosheger G, Gebert C, Ahrens H, Streibueger A, Winkelmann W, Harges J. Endoprosthetic reconstruction in 250 patients with sarcoma. *Clin Orthop Relat Res.* 2006;450:164-171.
- [3] Rossi B, Zoccali C, Toma L, Ferraresi V, Biagini R. Surgical site infections in treatment of musculoskeletal tumors: experience from a single oncologic orthopedic institution. *J Orthop Oncol.* 2016;2:1. doi:10.4172/2472-016X.1000108.
- [4] Henderson E, Groundland J, Pala E, Dennis J, Wooten R, Cheong D, et al. Failure mode classification for tumor endoprostheses: retrospective review of five institutions and a literature review. *J Bone Joint Surg Am.* 2011;93:418-429.
- [5] Springer B, Cahue S, Etkin C, Lewallen D, McGrory B. Infection burden in total hip and knee arthroplasties: an international registry-based perspective. *Arthroplast Today.* 2017;3:137-140.
- [6] Lin J, Chen R, Yan W, Chen D. Enhancing soft-tissue reattachment with artificial mesh in joint endoprosthetic reconstruction for bone tumors. *Zhonghua Zhong Liu Za Zhi.* 2017;39:540-544. doi:10.3760/cma.j.issn.0253-3766.2017.07.013.
- [7] Dubina A, Shiu B, Gilotra M, Hasan SA, Lerman D, Ng VY. What is the optimal reconstruction option after the resection of proximal humeral tumors? A systematic review. *Open Orthop J.* 2017;11:203-211. doi:10.2174/1874325001711010203.
- [8] Gosheger G, Hillmann A, Lindner N, Rodl R, Hoffmann C, Burger H, et al. Soft tissue reconstruction of megaprotheses using a trevira tube. *Clin Orthop Relat Res.* 2001;393:264-271.
- [9] Maccauro G, Piccioli A, Barreca S, Fenga D, Rosa M. Local resections and prosthetic reconstructions in solitary bone metastases of the limbs according to histotypes. *J Integr Oncol.* 2016;5. doi:10.4172/2329-6771.1000161.
- [10] Schmolders J, Koob S, Schepers P, Kehrer M, Frey S, Wirtz C. Silver-coated endoprosthetic replacement of the proximal humerus in case of tumour—is there an increased risk of periprosthetic infection by using a trevira tube? *Int Orthop.* 2016;41:423-428. doi:10.1007/s00264-016-3329-6.
- [11] Nau P, J Clark C, Fisher M, Walker G, Needleman BJ, Ellison EC, et al. Modified rives-stoppa repair for abdominal incisional hernias. *Health.* 2010;2(2):162-169. doi:10.4236/health.2010.22024.
- [12] López-Cano M, Martín-Domínguez LA, Pereira JA, Armengol-Carrasco M, García-Alamino JM. Balancing mesh-related complications and benefits in primary ventral and incisional hernia surgery. A meta-analysis and trial sequential analysis. *PLoS One.* 2018;13:e0197813. doi:10.1371/journal.pone.0197813.

Authors: R. Lor Randall, Antonios I. Papadopoulos, John S. Groundland

QUESTION 6: Should endoprosthesis and/or allograft bone be soaked in antibiotic solution or antiseptic solutions prior to implantation in patients?

RESPONSE: Unknown. There is no evidence to suggest that the use of a pre-implantation antibiotic or antiseptic soak of an endoprosthesis or massive allograft would reduce the rate of surgical site infection/periprosthetic joint infection (SSI/PJI).

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

In the oncologic literature, infection rates following metallic endoprostheses and bulk allograft surgery are high. In a systematic review, Henderson et al. found the rate of infection-related failure of endoprostheses to be 7.4%, when all anatomic locations were taken into account. Proximal tibia replacements and total femur replacements were noted to be at particular risk for infection, requiring revision surgery in 19.7% and 17.5% of cases, respectively [1]. In a systematic review of pediatric oncology patients, Groundland et al. found an infection rate of 12.9% and 17.1% when bulk osteoarticular allografts were used to reconstruct the distal femur and proximal tibia, respectively [2].

While not fully understood or rigorously investigated, the causes of these high rates of infection are likely multi-factorial, including extensive surgical dissections and resections, substantial blood loss, implantation of large constructs with foreign material and, in the case of oncology patients, a potentially immunosuppressed host.

Any measure that leads to decreased infection rates of metallic endoprosthesis and massive allograft reconstruction would be desirable. Given the prevalence of the problem and the severity of the consequences of deep infection, even weak evidence supporting a decrease in infection rates would be worth considering. While a few interventions have been noted to be beneficial, as reported in retrospective case series, no rigorous, prospective studies have been completed in this population [3-8]. Regarding the question above, there is no evidence to support or reject the use of a pre-implantation antiseptic soak of the endoprosthesis (or allograft). Local application of an antibiotic solution (e.g., gentamicin) around prosthesis before closing the incision in conjunction with a parenteral agent as antibiotic prophylaxis is routine practice in some institutions [9]. However, antibiotic solutions have been found to offer no advantage over saline in the removal of bacteria from bone, titanium or stainless steel. In addition, there

are no efficacy data to support the use of antibiotic soaks in procedures with sterile prosthesis insertion [10,11]. There are no high quality trials testing the effectiveness of antiseptic soaking of prosthesis before implantation [12]. Moreover, antiseptics could exert changes in materials used for total arthroplasty (e.g., titanium alloy or hydroxyapatite), cause chondrolysis or pose cytotoxicity to human fibroblasts and osteoblasts [13,14].

Conceptually, a pre-implantation soak would decrease the bacterial load on the implant immediately prior to implantation, thereby reducing the risk of an infection caused by direct seeding of the wound bed by the implant itself. In an *in vitro* study bone fragments soaked with a solution of gentamicin or vancomycin for 30 minutes were loaded with an antibiotic concentration, 5-fold the minimum inhibitory concentration (MIC) values would be needed to provoke bacterial regression [15]. It has been also shown that *in vitro* decontamination of bone allografts contaminated with coagulase-negative Staphylococci is feasible after soaking bone with gentamicin or rifampicin for 60 minutes [16]. However, clinical studies are lacking, and there are no randomized controlled trials or systematic reviews that have evaluated soaking endoprosthesis or allograft bone in antibiotic or antiseptic solutions before implantation for the prevention of surgical site infections [17]. Two facts belie this practice. First, there is no published evidence that sterilized implants (endoprosthesis or allograft) routinely become colonized or contaminated from their unpackaging to implantation. Second, most infections in endoprosthesis and massive allograft surgery do not manifest in the perioperative period; rather, the average time to failure due to infection occurs years after the index surgery. In their report of 2,174 endoprosthesis surgeries, Henderson et al. reported an overall time revision surgery due to infection of 47 months, with a non-normally distributed standard deviation of 69 months [1]. The anatomic location with the fastest time to infection-driven revision was the elbow, occurring at a mean of 16 months, while the proximal humerus had an infection time of 80 months. A pre-implant soak would have no theoretical impact on these late infections.

REFERENCES

- [1] Henderson ER, Groundland JS, Pala E, Dennis JA, Wooten R, Cheong D, et al. Failure mode classification for tumor endoprostheses: retrospective review

- of five institutions and a literature review. *J Bone Joint Surg Am.* 2011;93:418–429. doi:10.2106/JBJS.00834.
- [2] Groundland JS, Ambler SB, Houskamp LDJ, Orriola JJ, Binitie OT, Letson GD. Surgical and functional outcomes after limb-preservation surgery for tumor in pediatric patients: a systematic review. *JBJS Surg.* 2016;4(2). doi:10.2106/JBJS.RVW.0.00013.
- [3] Lozano-Calderón SA, Swaim SO, Federico A, Anderson ME, Gebhardt MC. Predictors of soft-tissue complications and deep infection in allograft reconstruction of the proximal tibia. *J Surg Oncol.* 2016;113:811–817. doi:10.1002/jso.24234.
- [4] Campanacci M, Bacci G, Bertoni F, Picci P, Minuttillo A, Franceschi C. The treatment of osteosarcoma of the extremities: twenty year's experience at the Istituto Ortopedico Rizzoli. *Cancer.* 1981;48:1569–1581.
- [5] Donati F, Di Giacomo G, D'Adamio S, Ziranu A, Careri S, Rosa M, et al. Silver-coated hip megaprosthesis in oncological limb salvage surgery. *Biomed Res Int.* 2016;2016:9079041. doi:10.1155/2016/9079041.
- [6] Ghert M, Deheshi B, Holt G, Randall RL, Ferguson P, Wunder J, et al. Prophylactic antibiotic regimens in tumour surgery (PARITY): protocol for a multi-centre randomised controlled study. *BMJ Open.* 2012;2. doi:10.1136/bmjopen-2012-002197.
- [7] Zamborsky R, Svec A, Bohac M, Kilian M, Kokavec M. Infection in bone allograft transplants. *Exp Clin Transplant.* 2016;14:484–490.
- [8] Aponte-Tinao LA, Ayerza MA, Muscolo DL, Farfalli GL. What are the risk factors and management options for infection after reconstruction with massive bone allografts? *Clin Orthop Relat Res.* 2016;474:669–673. doi:10.1007/s11999-015-4353-3.
- [9] Song Z, Borgwardt L, Høiby N, Wu H, Sørensen TS, Borgwardt A. Prosthesis infections after orthopedic joint replacement: the possible role of bacterial biofilms. *Orthop Rev (Pavia).* 2013;5:65–71. doi:10.4081/or.2013.e14.
- [10] Guidelines on antibiotic prophylaxis in surgery: single dose before surgery. Montefiore Medical Center, Albert Einstein College of Medicine. [https://www.einstein.yu.edu/uploadedFiles/departments/medicine/Updated%20Surgical%20PPX%20Poster%2011%202017\(1\).pdf](https://www.einstein.yu.edu/uploadedFiles/departments/medicine/Updated%20Surgical%20PPX%20Poster%2011%202017(1).pdf). 2017.
- [11] McHugh SM, Collins CJ, Corrigan MA, Hill ADK, Humphreys H. The role of topical antibiotics used as prophylaxis in surgical site infection prevention. *J Antimicrob Chemother.* 2011;66:693–701. doi:10.1093/jac/ckr009.
- [12] George J, Klika AK, Higuera CA. Use of chlorhexidine preparations in total joint arthroplasty. *J Bone Joint Infect.* 2017;2:15–22. doi:10.7150/jbji.16934.
- [13] Shigematsu M, Kitajima M, Ogawa K, Higo T, Hotokebuchi T. Effects of hydrogen peroxide solutions on artificial hip joint implants. *J Arthroplasty.* 2005;20:639–646. doi:10.1016/j.arth.2005.01.010.
- [14] Lu M, Hansen EN. Hydrogen peroxide wound irrigation in orthopaedic surgery. *J Bone Joint Infect.* 2017;2:3–9. doi:10.7150/jbji.16690.
- [15] Shah MR, Patel RR, Solanki RV, Gupta SH. Estimation of drug absorption in antibiotic soaked bone grafts. *Indian J Orthop.* 2016;50:669–676. doi:10.4103/0019-5413.193486.
- [16] Saegeman VSM, Ectors NL, Lismont D, Verduyck B, Verhaegen J. Effectiveness of antibiotics and antiseptics on coagulase-negative staphylococci for the decontamination of bone allografts. *Eur J Clin Microbiol Infect Dis.* 2009;28:813–816. doi:10.1007/s10096-009-0715-7.
- [17] 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;152:784–791. doi:10.1001/jamasurg.2017.0904.



Authors: Muhammad Ather Siddiqi, A. Mazhar Tokgözoğlu

QUESTION 7: Should a coated prosthesis (silver/iodine) be used for reconstruction of patients undergoing primary bone tumor resection?

RECOMMENDATION: Yes, silver coating and iodine coating of prosthesis show good results in prevention of infection after reconstruction following primary tumor resection.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

Megaprosthesis has been used to reconstruct limbs and large skeletal defects after resection of bone tumors for many decades. A significant problem is the higher rate of infection as compared to an infection rate of < 1% after a standard primary arthroplasty procedure.

Many factors have been cited in literature which include length of surgery, OR environment, blood transfusions, soft tissue available for coverage and segment involved, e.g., tibia vs. femur. The average infection rate reported in literature is 10% (range 0–25%).