SH68: What type of spacer works best for elution of antibiotics? Does off-the shelf spacer versus custom antibiotic-tailored spacer affect outcomes?

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Recommendation: Unknown. While off-the-shelf spacers provide more predictable elution of antibiotics, custom antibiotic-tailored spacers yield higher peaks of antibiotic concentration. Both can provide favorable clinical outcomes, and they have not been shown to be superior to each other in the management of infection.

Strength of Recommendation: Limited

Rationale: A complete literature review was conducted to identify all studies that analyze off-the-shelf spacers and custom antibiotic-tailored spacers. Different combinations of search terms for "off-the-shelf spacers", "prefabricated spacer", "custom-tailored spacer", "custom antibiotic-tailored spacer", "personalized spacer", "customized spacer", "custom spacer", "custom-made spacer", "hand-made spacer", "home-made spacer" "antibiotic release", "antibiotic elution", "outcome", "hepatotoxicity", "nephrotoxicity" with different combinations of logical connectives were searched using the common medical search engines such as PubMed, Scopus, and Google Scholar through December 2024. Inclusion criteria for this systematic review were all English studies (Level I-IV evidence) published between 1996 and 2024 that included patients undergoing shoulder arthroplasty (primary or revision), included data about spacer types, evaluated the outcomes of spacer types, and utilized clinical study designs such as cohort, case-control, cross-sectional studies, meta-analyses, or systematic reviews. Exclusion criteria were non-English language studies (except one German study which was highly relevant to the topic), nonhuman studies (except one in vitro experiment which provides highly useful information), cohorts consisting of less than 7 patients, case reports, editorials, and technique papers without patient data. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) statement was followed for this review.

Namdari et al. (1) has conducted a systematic review of spacer types and their specific characteristics on periprosthetic shoulder infection. They state that there were 5 available retrospective studies (Level IV) analyzing spacer types for shoulder PJI. Their cohort size was ranging from 9 to 60 patients with mean follow-up period of 6 months to over 3 years. The first of aforementioned studies carried out by McFarland et al. (2) (Level IV, n=53 patients, 6-month-follow-up), and the authors analyzed off-the-shelf gentamicin-containing spacers (InterSpace Shoulder; Tecres, Verona, Italy) to custom antibiotic-tailored spacers and found no differences in infection control. Coffey et al (3) (Level IV, n=15, 20.5-months-follow-up) reported favorable outcomes by indicating the normalization of C-reactive protein in 8 of 12 patients, the erythrocyte sedimentation rate in 5 of 12 patients, interleukin-6 in 9 of 11 patients, and white blood cell counts in 12 of 12 patients using gentamicin containing off-the-shelf spacer (InterSpace Shoulder; Tecres, Verona, Italy). Stine et al. (4) (Level IV, n=30, 2.4-year follow-up) used custom antibiotic-tailored spacers containing vancomycin and tobramycin into PMMA (1 g of gentamicin, 1g of vancomycin and 1.2 g of tobramycin per 40-g bag of cement;), achieving 100% infection eradication. Strickland et al. (5) (Level IV, n=17, mean 35-months-follow-up) likewise used custom antibiotic-tailored spacers (described generally as vancomycin + gentamicin or vancomycin + tobramycin mixed into cement) between stages of a two-stage protocol and reported an 63% eradication rate. In the last study mentioned in Namdari et al's

review, Grubhofer et al (6) (Level III, n=48, 52-months follow-up) reported 95% infection control using custom antibiotic spacer made from gentamicin-loaded cement (PALACOS®) with an additional 1 g of vancomycin added per 40 g of cement. Consequently, from these reports, they have concluded that neither off-the-shelf nor custom antibiotic-tailored spacers clearly dominate each other in terms of infection eradication, both showing similar outcomes in infection eradication. However, they have shown some advantages of off-the-shelf spacers over custom antibiotic-tailored spacers. For instance, off-the-shelf spacers provide more anatomic design to permit for improved shoulder motion and function; they also yield more consistent release of antibiotics.(1-3) It has also been reported that off-the-shelf spacers are quicker to apply, safer and easier to remove (1). From these consensus findings, it can be assumed that off-the-shelf spacers yield more consistent release of antibiotics. For these reasons, off-the-shelf spacers may be preferable.

Next, Porcellini et al. (7) performed a retrospective study (Level IV) on the outcomes of off-the-shelf spacers (SpaceFlex Shoulder, G21-San Possidonio, Italy) spacers versus custom antibiotic-tailored spacers (cement containing a total of 2 g of gentamicin and added 2 g of vancomycin) in shoulder infections with a minimum 2-year follow-up. Their cohort had 48 patients who underwent two-stage revision arthroplasty for periprosthetic shoulder infections. It was reported that all patients in the study accomplished complete eradication of infection. However, eradication of infection is indicated by normal levels of C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) instead of cultures. In addition, neither clinical nor laboratory signs of infection recurrence were detected during the mean follow-up of 35.2 months. As a result, Porcellini et al. (7) stated that both off-the-shelf spacers and custom-tailored spacers have equal effectiveness in the eradication of periprosthetic shoulder infections. Additionally, they did not note any superiority between the two types of spacers.

On the other hand, Batailler et al. (8) reported that custom antibiotic-tailored spacers (premixed with gentamicin is used, with an additional 1 g of vancomycin per cement bag) have the highest peak concentration (Level V). They reported that after implantation, gentamicin concentrations begin around 21–22 μg/mL at 1 hour, dropping to 11–17 μg/mL at 1 week and 2–10 μg/mL by 6 weeks, while vancomycin peaks near 75 μg/mL at 48 hours, then declines to 15–20 μg/mL by day 7 and 5–10 μg/mL by day 14. It can be said that custom antibiotic-tailored spacers are less predictable in the elution of antibiotics, however, they give rise to higher antibiotic peak concentrations. They mention increased probability of acute kidney injury due to risk of excessive diffusion, however, they only point out this idea theoretically, do not provide any quantitative data. Additionally, Frew et al. (9) tested 18 cement discs, and compared the off-the-shelf spacers [Copal G+V (Haereus, Hanau, Germany), preloaded with 0.5 g gentamicin and 2 g vancomycin per 40 g mix] to custom antibiotic-tailored spacers [Palacos R+G (Haereus, Hanau, Germany) with 2 g vancomycin added by hand] in their in vitro experiment (Level V). They reported that the peak concentrations were dramatically higher in the custom antibiotic-tailored spacers (677 μg/ml for vancomycin and 756 μg/ml for gentamicin) than in the off-the-shelf spacers (149 μg/ml for vancomycin and 471 μg/ml for gentamicin). They reported that custom spacers showed 5-fold and 2-fold higher peak levels for vancomycin and gentamicin, respectively. Therefore, although high concentrations of antibiotics can be interpreted as beneficial in the treatment of infections, the risk of nephrotoxicity and hepatotoxicity should always be considered in the use of antibiotic-tailored spacers (1, 10,11). On the other hand, another issue in using these spacer types is that the ideal amount of antibiotic to be used is not certain. In the study by Slane et al, it was found that adding more antibiotics to the cement did not guarantee a higher level of elution (12). Additionally, it has been stated that the reported occurrence of acute nephrotoxicity due to elution of antibiotics (vancomycin, gentamicin, tobramycin) from a cement spacer ranges from 5% to 32% for custom antibiotic-tailored spacers used in hip and knee infections (13, 14).

Kim et al. (15) assessed short term outcomes of custom antibiotic-tailored spacers containing 4 g vancomycin on 11 patients with a mean follow-up of 29.9 months (12-48 months) on shoulder infection (Level IV). Nine out of eleven patients subsequently demonstrated negative culture. Hence, the main finding of this study emphasizes custom antibiotic-tailored spacers can be as successful as off-the-shelf spacers for infection control outcomes.

Another study that analyzes the outcomes of custom antibiotic-tailored spacers (tobramycin with no reported dosage) in shoulder infection was conducted by Torrens et al. (16) involving 21 patients with a 2 year-minimum follow-up up to 9 years (Level IV). In the second stage of the two-stage surgical procedure, they reported intraoperative negative cultures in 86.4% of the patients. These findings support that custom antibiotic-tailored spacers achieve similar clinical outcomes as off-the-shelf spacers.

A comprehensive review of the literature shows that both off-the-shelf and custom-made antibiotic-tailored spacers are equally successful in eradicating infection (1). The majority of systematic reviews and observational studies found that they were not superior to each other in treating infections. (1, 2, 7). In conclusion, both types of spacers provide similar outcomes in the infection management, however, while off-the-shelf spacers offer more consistent and predictable antibiotic elution, custom antibiotic-tailored spacers yield higher concentration.

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