SH61: What is the Optimal Timing of Second Stage Revision Surgery in the Treatment of PJI? Is this Dependent on Organism?

Liaison: Benjamin Zmistowski
Lead delegate: Joideep Phadnis
Supportive delegates: Jessica Seidelman, Jason Ho

Response: Based on the literature an optimal time to reimplantation (TTR) during two stage exchange to treat shoulder PJI cannot be recommended regardless of pathogen. However, there is evidence to suggest that increasing TTR is associated with adverse outcomes.

Strength of Recommendation: Limited

Delegate Vote: 49 (92%) agree; 3 (6%) disagree; 1 (2%) abstain

Rationale: While there is contention as to whether single or two stage revision is the optimal treatment for shoulder prosthetic joint infection (PJI), two-stage replacement remains the gold standard for many patients, particularly in the context of chronic and subacute infection[1].

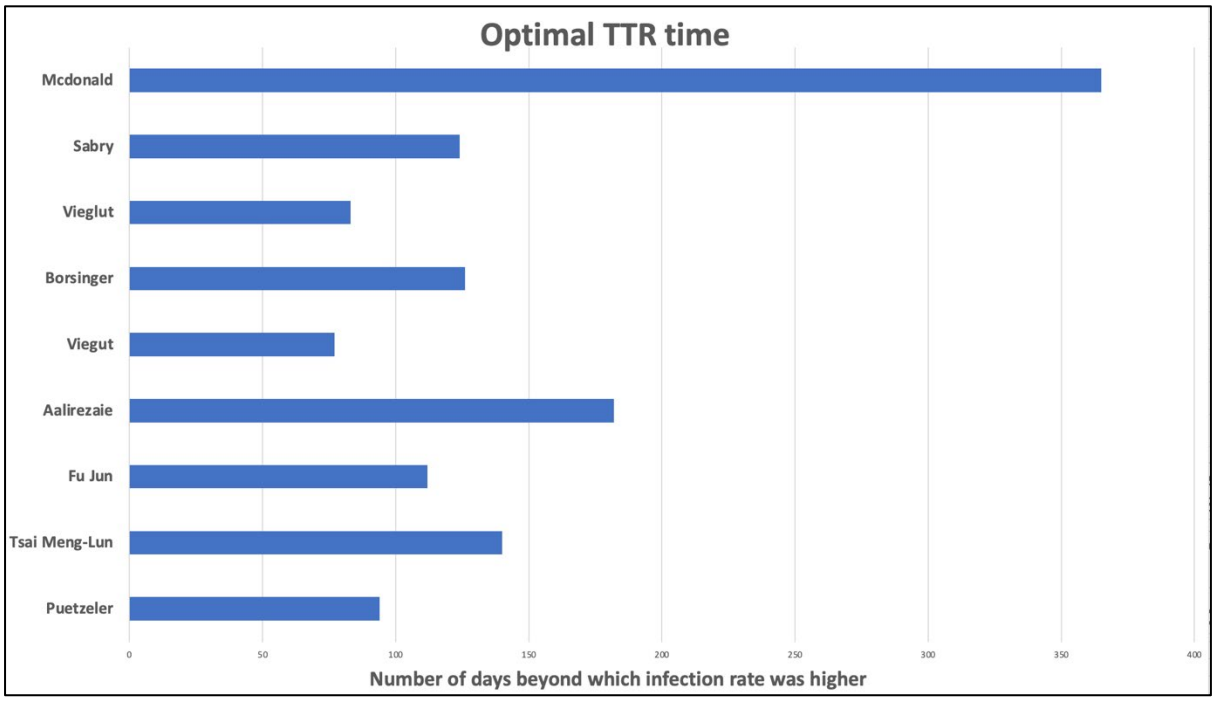
Multiple factors need to be considered when planning second-stage re-implantation. These include biochemical markers, soft tissue envelope, and virulence of the organism to name a few. Variation in time to reimplantation (TTR) has been suggested as a factor that may influence outcome, and because TTR is controllable in most cases, it is appealing to understand what the optimal TTR is for two-stage revision.

A clinical librarian performed a literature review using Embase, Ovid Medline, Pubmed and UpToDate databases to determine the answer to the question. The full search strategy is outlined in the appendix. There were no articles identified in the shoulder literature investigating the research question, hence relevant articles from the hip and knee literature were included in the literature synthesis to provide some guidance on TTR. Even these articles were all retrospective in nature with some case series and cohort studies, representing evidence subject to considerable bias.

Table 1 summarises articles of interest in the available literature and the below chart visually displays their recommended upper limit for TTR.

Article	**Number of Arthroplasties**	**Optimal TTR beyond which re-infection rate was higher**	**Magnitude of effect**	**Effect by organism**
Puetzler[2]	163	>94 days	2.8 x higher re-infection *p=0.004*	No
Tsai Meng-Lun[3]	361	112-140 days	1.27 odds ratio *Not significant*	No
Fu Jun[4]	81	84-112 days	7.5% vs 17% re-infection *p=0.001*	No
Aalirezaie[5]	282	>182 days	21% vs 44% re-infection *p=0.057*	No
Viegut[6]	76	28-77 days	90% success vs 0% (<28 days)	No

			and 52% (>77 days) *p=0.01*	
Winkler[7]	38	<28 days and >28 days equivalent outcome	5% vs 0% re-infection *No significant difference*	No
Borsinger[8]	101	>126 days	Odds ratio 7.0 *p=0.002*	No
Vielgut [9]	77	>83 days	Odds ratio 6.1 *p=0.007*	No
Sabry [10]	314	>96 days	Increased median TTR in re-infection group (124 vs 96 days) p=0.01	Gram negative higher failure but not assessed in relation to time to reimplantation
McDonald [11]	82	>365 days	27% vs 7% re-infection rate *p=0.05*	Gram negative higher failure but not assessed in relation to time to reimplantation



A common theme running through all studies was that increasing TTR was associated with an adverse effect on re-infection rate. However, the included studies are subject to bias because of their retrospective nature and due to the multiple confounding variables that influence failure after two-stage revision for PJI. An example, is that there is little information offered in any of the studies as to why some patients had longer TTR than others within the same series. It is likely that these patients may have had other reasons for delay in reimplantation that would have adversely affected their re-infection rate. Similarly, there is marked heterogeneity within and between studies regarding antibiotic treatment and reporting of bacterial virulence. This makes independently attributing variation in TTR with increased infection rates unreliable and determining the effect of bacterial virulence very difficult.
For clinical practice recommendation and accounting for the limitations of the evidence, the scattergram above suggests that surgeons should probably try to avoid extending TTR beyond 3-4 months following the first stage revision. Only two studies looked at the lower limit for safe TTR. Vielgut concluded that reimplantation at <4 weeks was associated with a higher re-infection rate than between 4 and 11 weeks[6], whereas Borsinger et al. found that the lowest risk of re-infection was between 0-12 weeks and highest >18 weeks in their series[8]. While these findings are far from conclusive, they do suggest that there is no advantage to very early re-implantation.

References

[1] Rangan A, Falworth M, Watts AC, Scarborough M, Thomas M, Kulkarni R, et al. Investigation and Management of Periprosthetic Joint Infection in the Shoulder and Elbow: Evidence and consensus based guidelines of the British Elbow and Shoulder Society. Shoulder & Elbow 2018;10:S5–19. https://doi.org/10.1177/1758573218772976.

[2] Puetzler J, Hofschneider M, Gosheger G, Theil C, Schulze M, Schwarze J, et al. Evaluation of time to reimplantation as a risk factor in two-stage revision with static spacers for periprosthetic knee joint infection. J Orthop Traumatol 2024;25:15. https://doi.org/10.1186/s10195-024-00745-7.

[3] Tsai M-L, Herng-Shouh Hsu A, Wu C-T, Lin P-C, Tan TL, Kuo F-C. Optimal reimplantation timing in two-stage exchange for periprosthetic joint infection: an observative cohort study in Asian population. BMC Musculoskelet Disord 2024;25:28. https://doi.org/10.1186/s12891-023-07129-8.

[4] Fu J, Ni M, Li H, Li X, Chai W, Zhou Y, et al. The proper timing of second-stage revision in treating periprosthetic knee infection: reliable indicators and risk factors. J Orthop Surg Res 2018;13:214. https://doi.org/10.1186/s13018-018-0885-z.

[5] Aali Rezaie A, Goswami K, Shohat N, Tokarski AT, White AE, Parvizi J. Time to Reimplantation: Waiting Longer Confers No Added Benefit. The Journal of Arthroplasty 2018;33:1850–4. https://doi.org/10.1016/j.arth.2018.01.073.

[6] Vielgut I, Sadoghi P, Wolf M, Holzer L, Leithner A, Schwantzer G, et al. Two-stage revision of prosthetic hip joint infections using antibiotic-loaded cement spacers: When is the best time to perform the second stage? International Orthopaedics (SICOT) 2015;39:1731–6. https://doi.org/10.1007/s00264-015-2751-5.

[7] Winkler T, Stuhlert MGW, Lieb E, Müller M, Von Roth P, Preininger B, et al. Outcome of short versus long interval in two-stage exchange for periprosthetic joint infection: a prospective cohort study. Arch Orthop Trauma Surg 2019;139:295–303. https://doi.org/10.1007/s00402-018-3052-4.

[8] Borsinger TM, Resnick CT, Werth PM, Schilling PL, Moschetti WE. Does Time to Reimplantation After Explant for Prosthetic Joint Infection Influence the Likelihood of

Successful Outcomes at 2 Years? The Journal of Arthroplasty 2022;37:1173–9. https://doi.org/10.1016/j.arth.2022.02.025.
[9] Vielgut I, Schwantzer G, Leithner A, Sadoghi P, Berzins U, Glehr M. Successful Two-Stage Exchange Arthroplasty for Periprosthetic Infection Following Total Knee Arthroplasty: The Impact of Timing on Eradication of Infection. Int J Med Sci 2021;18:1000–6. https://doi.org/10.7150/ijms.47655.
[10] Sabry FY, Buller L, Ahmed S, Klika AK, Barsoum WK. Preoperative Prediction of Failure Following Two-Stage Revision for Knee Prosthetic Joint Infections. The Journal of Arthroplasty 2014;29:115–21. https://doi.org/10.1016/j.arth.2013.04.016.
[11] McDonald DJ, Fitzgerald RH, Ilstrup DM. Two-stage reconstruction of a total hip arthroplasty because of infection.: The Journal of Bone & Joint Surgery 1989;71:828–34. https://doi.org/10.2106/00004623-198971060-00005.

Appendix 1

Search Strategy and Terms Used

Data bases searched: Embase, Ovid medline, Pubmed, UpToDate
Date of Search: September 30th 2024 performed by Lucy Wells (medical librarian).
52 Articles Identified in initial search

Full Search methodology:

Ovid MEDLINE(R) ALL <1946 to September 26, 2024>
1 Prosthesis-Related Infections/ 15299
2 (prosthe* adj2 infect*).ti,ab. 6338
3 ((periprosthe* or peri-prosthe* or peri prosthe*) adj2 joint infect*).ti,ab. 4218
4 1 or 2 or 3 20441
5 Reoperation/ 97842
6 ((two-stage or two stage or second-stage or second stage) adj2 revision).ti,ab. 1127
7 5 or 6 98385
8 ((optimal or proper or evaluat* or interval) adj5 (time or timing)).ti,ab. 129476
9 4 and 7 and 8 78
Embase <1974 to 2024 Week 39>
1 exp prosthesis infection/ 14536
2 (prosthe* adj2 infect*).ti,ab. 7969
3 ((periprosthe* or peri-prosthe* or peri prosthe*) adj2 joint infect*).ti,ab. 4330
4 1 or 2 or 3 19266
5 reoperation/ 111934
6 ((two-stage or two stage or second-stage or second stage) adj2 revision).ti,ab. 1191
7 5 or 6 112825
8 ((optimal or proper or evaluat* or interval) adj5 (time or timing)).ti,ab. 191723
9 4 and 7 and 8 44