High Infection Eradication of Two-stage Exchange Arthroplasty

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Two-stage exchange arthroplasty remains the gold standard in the United States for treatment of chronic periprosthetic joint infection (PJI). This technique resulted in a relatively high infection eradication, however, the mortality rate is alarmingly high. Antibiotic resistant organisms appear to be highest risk factor for failure.

two-stage exchange periprosthetic joint infection long-term

1. Introduction

Periprosthetic joint infection (PJI) remains as one of the most common major complications following joint replacement surgery ^[1]. PJI's will increase exponentially to 10,000 cases per year by 2030 ^[2]. With the almost exponential increase in joint replacement surgery, PJI will be costly and straining for the surgeon and healthcare system.

Two-stage exchange arthroplasty is the gold standard for the treatment of chronic PJI ^{[3][4]}. This process involves the placement of a temporary antibiotic spacer with a period of intravenous antibiotics followed by reconstruction when infection is determined to be eradicated. The reported success rates in the literature have varied between 65% and 95% depending on the definition of success as well as other factors. For example, many studies have chosen to exclude patients who died prior to 2-years of follow-up ^{[5][6]}, when high mortality rates have been reported following this treatment protocol ^{[Z][8]}. Factors such as host and extremity grade and organism virulence also affect the outcome of reinfection ^{[9][10][11][12]}. There are few studies ^{[Z][13][14]} reporting two-stage hip exchange outcomes. At many institutions, two-stage exchange remains the standard of care for the management of chronic PJI.

2. Current Studies

There is an infection eradication rate of 88.24% with an average 6.14-years follow-up. The infection eradication rate was 91.47% in subjects with more than five-year follow-up. The mortality rate was 41.1%. The most common organism was coagulase-negative staphylococcus.

Mortality remains relatively high despite overall excellent infection eradication rates. In 2018, life expectancy for males and females was 76.2 and 81.2 years, respectively, with overall death rates between ages 65–74 at 1783.3/100,000 population (1.78%) ^[15]. These rates are similar among patients with primary TJA and matched

cohorts with osteoarthritis in the first 10 years, but marginally rise thereafter ^{[16][17][18]}. To compare, overall cancer, uterine, breast, and prostate have a 5-year survival rate of 67.4%, 81.2%, 90.0%, and 97.8%, respectively. This compares to 80% in patients who underwent two-stage exchange for chronic PJI ^[19]. Higher probability of poorer hosts, morbidity of the treatment and nature of infection, and medical complications in this patient cohort may also play large role in the reported mortality rates.

There is paucity of data reporting long-term outcomes following two-stage exchange arthroplasty. Petis et al. described a reinfection rate of 15% and mortality rate of 56% in 164 hips with average follow-up of 12 years at a single institution [13]. However, there were 49% of the original cohort of patients that were excluded as they received prior treatment for PJI. This likely introduced selection bias. Researchers attempt to limit selection bias by not excluding patients with prior treatment for PJI and combining results of three large tertiary referral centers. A study out of the Danish Registry reported a 5-year reinfection rate after reimplantation of 14.6% (95% CI: 8.0–23.1) with overall survival rate of 68% (95% CI: 59–75) ^[20]. In a systematic review and metanalysis by Lange et al., they estimate risk of reinfection following two-stage exchange at 10.4% (95% CI: 8.5–12.7%) [21]. A single-surgeon retrospective review of 155 hips resulted in overall 91.7% survival rate with an average of 9.7 years follow-up and 16.1% mortality rate [14]. Overall, the results are similar, however there is a much higher mortality rate. This may be attributed to overall health of patients treated at the three large tertiary referral centers and geographic differences in overall health of patients in each study. Knutsor et al. revealed an unadjusted reinfection rate of 32.3% amongst pooled data of 1856 two-stage hips from 44 cohorts with average follow-up of 3.7 years. Infection rates for studies including over 50 hips is between 1.7-10.7% [22][23][24]. Triantafylloppoulos et al. reported 91.24% infected eradication rate in 548 patients treated with two-stage exchange with minimum two-year follow-up [25]. They identified heart disease, psychiatric disease, and female gender as a risk factor for failure. Despite previously reported comorbidity risk factors for failure, based on the multivariate regression analysis there are no identify any significant risk factors ^{[9][10]}. However, the results are similar to more recent literature suggesting polymicrobial and/or resistant organisms predict higher failure rates [12]. Most of the cohort (78.7%) had one or more major medical comorbidity with average of 2.55. Because many patients who unfortunately sustain PJI's have underlying major medical comorbidities, identifying one major comorbidity over another as a risk factor is often difficult.

There is a reinfection rate of 8.53% in patients with more than five-year follow-up. The ongoing risk of reinfection after five years should be further explored and re-iterated to patients. Despite the relative urgency to treat infection, patient optimization would likely decrease mortality risk and improve infection eradication. Future research investigating the routine use long-term antibiotic suppression is essential.

Patients with MRSA had a failure rate at 20.75%. This resistant organism has been previously reported as an independent risk factor with reinfection rates of 21–38% ^{[6][7]}. Suboptimal antibiotics and inability to maintain minimal eradication concentrations make these resistant organisms difficult to treat. Failure rate of polymicrobial infections was also high at 21.9% (including infections with MRSA) as has been reported ^{[26][27]}. This can be explained by difficulty maintaining treatment with broad spectrum antibiotics and increased risk of resistance. Although there is no data evaluating reinfection patterns, short-term failure may be resultant of more virulent bacteria while later failure by more indolent organisms. Researchers did not identify this pattern as there was a

mixed of more indolent and virulent bacteria despite the longevity of follow-up. Researchers report a relatively high success rate when treating culture negative infections (93.55%) similar to that reported by Haddad et al. (94%) with greater than five-year follow-up ^[28]. Researchers did report a high proportion of patients with culture negative infections. This may be explained by not excluding patients with prior PJI treatment or who were maintained on antibiotics prior to treatment. Without antibiotic sensitivity, these infections are difficult to treat; however, outcomes appear favorable with standardized two-stage exchange protocol and broad-spectrum antibiotics. Future endeavors to improve diagnostics and antibiotic sensitivity identification may improve success rates.

Aside from infection, researchers report a total complication rate following patients who underwent a first stage in a planned two-stage of 14.93% (33/221). Adjusting for subjects who did not proceed to reimplantation, we report a dislocation rate of 2.45% which is significantly lower than the one-year cumulative risk of dislocation of 9% (52/512) identified by McAlister et al. ^[29].

There was no standardized method to determine infection eradication prior to reimplantation. The study retrospectively spanned 25 years where perioperative management, diagnosis, and treatment techniques have evolved. The use of MSIS criteria was generally used to diagnose infection after 2011. Prior to this date, diagnosis was determined clinically by the treating surgeon. Despite the variability, the overall outcomes were similar between institutions. Researchers also attempted to limit selection bias with substantial follow-up until reinfection or death. Unfortunately, documentation of variables that have been reported as risk factors for reinfection such as extremity grade, duration and concentration of antibiotics, and interim time between stages were not recorded ^[11] ^[30]. The retrospective landscape of the report across three institutions inherently contains bias and may decrease the quality that is dependent on data reporting and mining. Functional outcomes were not reported. Reoperation was used to define failure. This likely overestimates success rates specifically if a complication, persistent pain, and/or debilitation did not have a surgical remedy. The results are likely best-case scenarios.

Periprosthetic hip infection remains as a morbid complication with a relatively high mortality rate despite the reported success rate. Polymicrobial and resistant organism infections are difficult to treat with high reinfection rates. Researchers reiterate the importance to educate surgeons and patients on the persistent long-term risk of reinfection in addition to the relatively high mortality rate. Improving patient optimization, decreasing surgical morbidity, and enhancing therapeutic and diagnostic regimens should be further explored in the patient cohort.

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