As mentioned earlier, one of the keys to the historical success of the one-stage exchange arthroplasty was the ability to deliver supra-therapeutic concentrations of antibiotics into the periarticular space, which is not feasible in standard cementless two-stage revision arthroplasty. Two authors have developed novel techniques to provide adjunct antimicrobials locally in the hopes of improving their infection-free survival.

Using antibiotic-impregnated allograft bone during single-stage revision for PJI, Winkler et al. showed no recurrence of infection in 34 of 37 (92%) of their patients at a mean follow-up of 4.4 years. They calculated supra-therapeutic concentrations of vancomycin in the drainage fluid up to three days postoperative without systemic adverse renal effects and demonstrated that the antibiotic-impregnated grafts had similar incorporation as the normal allografts [7]. Whiteside and Roy introduced a new concept of antibiotic infusion within the periarticular space after single-stage revision for PJIs using Hickman lines, and by this means they have achieved no reinfections and complete clinical eradications of infection in their 21 cases at five years mean follow-up [8].

Considering the fact that the evidence available to address this question is based on retrospective small case series with heterogenous methodologies, the level of recommendation is moderate at best. Taken as a whole, it appears that single-stage revision for acute PJIs may achieve eradication of infection in approximately 70% of patients, which is superior to many reported rates of success for irrigation/debridement and implant retention in the same setting [6]. Furthermore, this technique limits the perioperative morbidity, surgical complexity and healthcare costs associated with a two-stage exchange arthroplasty, and as such, should be strongly considered in the setting of acute PJIs of a THA.

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QUESTION 4: Does the morbidity and mortality differ between single-stage and two-stage exchange arthroplasty?

RECOMMENDATION: Putting aside the effect on successful treatment of periprosthetic joint infections (PJIs), it is logical that a single surgical procedure puts patients at lower risk for both mortality and morbidity compared to a two-stage exchange arthroplasty that involves two separate operations.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 83%, Disagree: 13%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

PJIs are associated with major patient morbidity and mortality. Browne et al. [1] put this in context with a contemporary comparison of two-stage revision hip arthroplasty to major non-orthopaedic surgery. In their study of over 10,386 patients, implant removal and spacer placementhad a 30-day readmission rate of 11.1% and a 90-day mortality rate of 2.6%. Major complications were found in 15.3% of the patients. Ninety-day mortality rates were significantly higher compared with carotid endarterectomy, prostatectomy and kidney transplant (odds ratio (ORs) between 2.1 and 12.5; $p < .0001$). Readmission rates at 30 days were significantly higher than all other groups including coronary artery bypass grafting and Whipple procedures (ORs between 1.4 and 8.2; $p < .0001$). A recent analysis of a large, prospectively collected, national database has also suggested that revision total knee arthroplasty (TKA) for PJIs is associated with increased postoperative morbidity and mortality in the first 30 postoperative days relative to non-infectious revisions [2].

Traditionally, it has been considered that a two-stage revision strategy may be the gold standardfor the management of PJIs as this allows for a more targeted antimicrobial plan; however, it also exposes the patient to the risks of an additional procedure [3]. Historically, studies have concentrated on the successful eradication of infection as an end-point for comparing one and two-stage surgery. Considering reinfection, several recent systematic reviews have been published that show equivalence in terms of infection eradication for single and two-stage exchange [4–8].

Morbidity

Putting the success of eradication of infection aside, morbidity other than reinfection has generally been rarely reported. Although there are limited qualitative studies that deal with the quality of life of the patients undergoing revision arthroplasty for PJIs, Moore et al. [9] found that deep PJIs impacted all aspects of patients' lives. Two-stage revision had a greater impact than one-stage revision on participants' well-being, because the time in between revision procedures led to long periods of immobility and related psychological distress. However, within the two-stage literature, there is marked difficulty in the interpretation of the data presented and what actually constitutes morbidity for the patient. Gomez et al. [10] raised several important points for discussion, and they highlighted the attrition of patients during the interval period in the two-stage process. Of their 504 cases of PJIs (326 knees and 178 hips), 18% failed to proceed to the second stage. The main reason given was that the patient was unfit for the surgical procedure. Clearly this sub-group represents a major morbidity for the patients concerned and may not be included in other reported results.

With regards to hip surgery, a recent systematic review and meta-analysis published by Kunutsor et al. [6] found that there have been no randomized controlled trials comparing one-stage and two-stage revision hip procedures. All included eligible studies were non-randomized longitudinal cohort studies, which were predominantly retrospective in nature. Very few studies in this systematic review contained morbidity (other than reinfection) as an outcome measure. De Man et al. sought to assess and compare functional outcomes in hip PJIs managed by both strategies [11]. They undertook a retrospective analysis and compared 22 single-stage and 50 two-stage revisions to a control group, who were revised for aseptic loosening. They demonstrated no statistically significant differences in Harris Hip Scores (HHSs), limping and use of support between the single-stage and control groups. Choi et al. performed a retrospective analysis of 17 single-stage and 44 two-stage revisions and found no significance differences in HHS or UCLA activity scores [12]. Klouche et al. found no significant differences in aretrospective analysis of 38 single-stage and 46 two-stage revisions between the two groups in terms of pre- and postoperative Merle d'Aubigné scores or complication rates [13]. Oussedik et al. performed a prospective study comparing 11 single-stage with 39 two-stage revisions and found that the HHS and visual analogue scale satisfaction scores were significantly higher in the single-stage group at a mean of five years postoperatively. They also found that the single-stage patients had a significantly greater improvement in their HHS scores and found that patient satisfaction was also statistically in favor of the single-stage procedure [14]. Reporting of morbidities in the remaining 98 individual studies was too infrequent to draw any significant conclusions.

With regards to knee surgery, the results of another systematic review of 10 single-stage and 108 two-stage studies comprising 5,552 participants also failed to find any studies which used morbidity as a primary outcome measure [5]. Using postoperative clinical outcomes from the studies, neither single- nor two-stage strategies for knee PJIs displayed superiority. Median postoperative range of motion for single-stage revision was 97.5 degrees (range, 93.8 to 100.5 degrees) and for a two-stage revision was 97.8 degrees (range, 93.7 to 104.0). Both median postoperative Knee Society knee scores and Knee Society function scores also showed no statistically significant differences.

Mortality

While clearly mortality is a very definite end-point, the causes for it can be multi-factorial and not always directly attributed to the PJIs and their treatment. When reanalyzing the papers from recent systematic reviews for hip and knee PJIs (with mortality as an outcome), establishing differences between a single- and two-stage approach is extremely difficult [5,6]. A minority of studies featured information about mortality. The upper limit of follow-up duration, where death was considered relevant, or was linked to the revision surgery in the manuscript, ranged from 14 days to 15 years [15,16]. Given that death was rarely a measured outcome, the variation in patient selection (some studies excluded patients who died), the absence of an "unrelated mortality" definition, and the variation in follow-up, meaningful pooled analysis from these studies was not possible. Comparison is also difficult even among studies using one revision strategy: Buchholz et al. found a mortality of 2% (patients) relating to "overall management" with up to nine-year follow-up in 640 single-stage hip revisions [15]. In contrast Raut et al. found an attributable mortality of 0% in their 183 single-stage hip revisions with an "unrelated mortality" of 7.7% (14 patients) [16]. One of the included papers by Wolf et al. used a Markov expected-utility decision analysis for which they derived a mortality rate of 0.52% (3 of 576) for single-stage and 2.5% (8 of 321) for two-stage revision based on 18 published papers [17]. The other reviewed articles were no clearer for two-stage revision or for either strategy in knee PJI revisions. Registry data may be a source of crude mortality; however, the joint registry annual reports of England (including Wales, Northern Ireland and the Isle of Man), Australia, Norway, Sweden, Finland, Canada and New Zealand currently do not publish mortality data for revision subgroups [18–23].

Another method of analyzing mortality rates following single and two-stage exchange, which clearly has some limitations, is to present a data summary of published reports that include 50 or more patients and where mortality is documented (see below). As can been seen in these series, there is marked overlap of the mortality ranges, but the highest mortality is evident with a two-stage exchange. The heterogeneity of the available data is far from robust to undergo meaningful meta-analysis.

One-stage mortality range - 4.4 to 11.4%

Buchholz et al. [24] N = 640 with 90 deaths recorded at mean 52 months follow-up = 8.1%

Loty et al. [25] N = 90 with 4 deaths reported at mean 47 months follow-up = 4.4%

Miley et al. [26] N = 100 with 11 deaths recorded at mean 48.5 months follow-up = 11%

Raut et al. [16] N = 123 with 14 deaths at mean 93 months follow-up = 11.4%

Two-stage mortality range - 2.9 to 25.7%

Chen et al. [27] N = 57 with 5 deaths at mean 67.2 month follow-up = 8.7%

Haddad et al. [28] N = 50with 2 deaths at mean 5.8 years follow-up = 4.0%

Hsieh et al. [29]N = 99 with 3 deaths at mean 43 months follow-up = 3.0%

Romanò et al. [30] N = 102 with 3 deaths at mean 48 months follow-up = 2.9%

Toulson et al. [31] N = 132 with 34 deaths at mean 64.8 months follow-up = 25.7%

Ibrahim et al. [32] N = 125 with 19 deaths at mean 5.8 years follow-up = 15.2%

In conclusion, based on the available studies to date, single-stage revision surgery (when suitable) is associated with lower morbidity and mortality rates. However, the data to support this statement is

weak and larger, prospective, multicenter clinical trials are needed. Of note, two prospective randomized trials are currently recruiting with the aim to compare single- and two-stage revision surgery in the United Kingdom and North America with outcome measures including reinfection, mortality and patient reported outcomes [33].

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5.4. TREATMENT: TWO-STAGE EXCHANGE, SPACER RELATED

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QUESTION 1: What are the indications for the use of non-articulating vs. articulating spacers during resection arthroplasty of the hip or knee?

RECOMMENDATION: Articulating spacers appear to provide better range of motion and less functional limitations to the patients undergoing resection arthroplasty and should be used whenever possible. The indications for the use of non-articulating spacers during resection arthroplasty include patients with major bone loss, lack of ligamentous integrity (knee) or abductor mechanism (hip) that places these patients at elevated risk for dislocation or periprosthetic fracture and patients who have major soft tissue defects in whom motion is protected to allow better wound healing.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 91%, Disagree: 7%, Abstain: 2% (Super Majority, Strong Consensus)