



Treatment options in PJI – is two-stage still gold standard?

Igor Lazic, Christian Scheele, Florian Pohlig, Rüdiger von Eisenhart-Rothe ^{*}, Christian Suren

Department of Orthopedics and Sports Orthopedics, Klinikum Rechts der Isar; Technical University of Munich (TUM), Ismaningerstr. 22, 81675, Munich, Germany



ABSTRACT

Total knee arthroplasty (TKA) is a successful treatment for osteoarthritis with good clinical outcomes ^{1,2}. Periprosthetic joint infection (PJI) in TKA has a low incidence between 0.5 and 3% but it is nevertheless one of the most dreadful complications ^{3–6}. Two-staged revisions are considered to be the gold standard for revision in chronic PJI with infection eradication rates of over 90% ⁷. Recently, similar infection eradication rates after one-staged revision arthroplasty have been reported ^{8–10}, raising the question whether the two-staged approach can still be considered the gold standard. We therefore performed a literature review to analyse the correlation of one-staged and two-staged TKA revisions with recurrent infection rates and functional outcomes. Studies concerning PJI treated by one- or two-staged revision published between 2000 and 2020 were retrieved by searching the databases PubMed/Medline and the Cochrane Database of Systematic Reviews. 29 studies were included in this qualitative synthesis. Mean follow-up was at 4.9 ± 2.6 years. The mean infection eradication rate after one-staged revision vs. two-staged revision in TKA was $87 \pm 8.8\%$ vs. $83 \pm 11.7\%$. The functional outcome measured by the mean Knee Society Score (KSS) of one-staged revision vs. two-staged revision in TKA was 80 ± 5.9 vs. 80 ± 3.9 points. One-staged revision arthroplasty in TKA appears to have similar infection eradication rates and functional outcomes compared to two-staged revision arthroplasty. However, these results should be interpreted with caution, since selection bias may have played a significant role. Several criteria to guide the surgeon in selecting the appropriate procedure have been described, but the current recommendations are based on poor evidence as randomized controlled trials are lacking ^{11,12}. Two-staged revision remains a successful treatment option which is rightly the gold standard. However, there is a variety of cases in which one-staged revision is a viable alternative, where similar success rates and functional outcome can be expected ^{7,13}.

Introduction

Total knee arthroplasty (TKA) is a highly reliable and successful treatment for severe osteoarthritis or other arthropathies. Good clinical outcomes have been widely reported, still the risk of complications remains. ^{1,2} Prosthetic joint infection (PJI) remains one of the most severe complications of arthroplasty procedures. After aseptic loosening, PJI represents the second most frequent indication for arthroplasty revision with 25% and the most frequent cause for TKA revision within the first two years. ^{3,14} The cumulative incidence of PJI after TKA ranges between 0.5 and 3% and is even higher after revisions. ^{3–6} Furthermore, the economic burden associated with PJI is tremendous. The costs for treatment of PJI in TKA for the year 2020 in the USA are estimated at over \$1.62 billion. ³ Management of PJI requires interdisciplinary therapy algorithms including surgical revision and antimicrobial treatment based on the duration of symptoms and causative organisms. There is a general consensus that in cases with chronic symptoms a mature biofilm has evolved and successful treatment requires the complete removal of the prosthesis. ¹⁵ One-staged revision for PJI was first described by Buchholz et al., in 1970. More detailed reports with success rates of over 70% followed within over the course of 20 years. ^{16,17} Insall et al. originally introduced the two-staged procedure in 1983, which at that time

already included a six-week interval with antibiotic therapy. ¹⁸ Important improvements to this strategy include the use of articulating or static spacers that were introduced in the early 2000s. ^{19–21} Infection eradication rates after two-staged exchanges of between 90% and 100% have been reported, so that two-staged revision is currently considered the gold standard for septic arthroplasty revision. ⁷ However, similar infection rates after one-staged revisions have been reported raising the question whether the two-staged approach can still be considered the gold standard. Randomized controlled trials (RCT) to compare these two approaches are needed, but they are difficult to implement for ethical and methodological considerations. Hence, the currently available literature is heterogeneous and the preferable approach still remains a matter of controversy. We therefore performed a literature review to analyse the correlation of one-staged and two-staged revision with recurrent infection rates and functional outcomes in TKA revisions.

Methods

In June 2020 we performed a review of the literature to identify articles reporting on one- or two-stage exchange in total knee arthroplasty for periprosthetic joint infection. Articles written in English published from 2000 to 2020 including the eradication rates and/or the

* Corresponding author.

E-mail address: eisenhart@tum.de (R. von Eisenhart-Rothe).

functional outcomes after either one-staged or two-staged revision were reviewed. 161 articles were identified by searching the international databases PubMed/Medline and Cochrane Database of Systematic Reviews. The Mesh terms consisted of:

(periprosthetic infection[Title]) AND knee arthroplasty[Title/Abstract], (single-stage[Title/Abstract]) AND knee arthroplasty[Title/Abstract], (two-stage[Title/Abstract]) AND knee arthroplasty[Title/Abstract].

The studies were evaluated independently by two researchers (I.L. and C.S.). Subsequently, a consensus on the included literature was reached. The criteria were the following:

- study population of at least 20 patients
- minimum follow-up of two years
- Reported number of persistent/recurrent infections after either single-stage or two-stage revision.
- reported functional outcomes of either single-stage or two-stage revision
- proportion of excluded patients/loss to follow-up < 20%

Results

29 articles reporting on one- or two-staged exchange in total knee arthroplasty for periprosthetic joint infection were included in the qualitative synthesis: two articles for one-staged exchange, 13 articles for two-staged exchange and 14 articles for both approaches. The number of included patients ranged from 17 to 291. Mean Follow up was at 4.9 ± 2.6 years. The mean infection eradication rate after one-staged revision in TKA was $87 \pm 8.8\%$. The mean infection eradication rate after two-staged revision was $83 \pm 11.7\%$. The results are demonstrated in Table 1.

The literature on the functional outcome after one- or two-staged surgical treatment of PJI in TKA was scarce and heterogeneous. Regarding one-staged revision, the mean Knee Society Score (KKS) improved from 32 to 80 ± 5.9 points. Tibrewal et al. reported a mean Oxford Knee Score (OKS) improvement from 15 to 35 points.²⁷ Zahar et al. demonstrated a mean Hospital for Special Knee Surgery Score (HSS) of 35 points preoperatively, which improved to 70 points post-operatively.²⁸ Regarding two-staged revision of TKA, the mean KKS was 40 ± 10.2 points. Postoperatively, the mean KKS increased to 80 ± 3.9 points. Two studies reported a mean HSS of 83 ± 0.5 points after two-staged revision in TKA. The results are summarised in Table 2.

Discussion

In 1995 Garvin and Hanssen et al. published a retrospective review and concluded that two-staged revision was superior in terms of infection eradication, establishing the two-staged strategy as the gold standard.⁴⁷ High eradication rates of over 90% were demonstrated for this approach.⁷ However, in the last decade, reported eradication rates from 50% to 70% after two-staged revision led to doubts about its superiority.^{24,29,45} Meanwhile, one-staged revision showed increasingly promising results. All this gives reason to questioning the dogma of two-staged revision in PJI. Hence, the purpose of this study was to review the eradication rates and functional outcomes after one- and two-staged exchange in PJI of TKA.

In this review, the pooled eradication rates after one- and two-staged revision in TKA were similar. One-staged revision yielded a slightly higher eradication rate in TKA without reaching significant differences (87% vs. 83%). Kunutsor et al. published a meta-analysis reviewing the efficacy of two-stage versus one-stage exchange arthroplasty for the treatment of PJI in TKA. This meta-analysis included 5129 patients treated with two-staged revision and 423 patients treated with one-staged revision. Likewise, the authors demonstrated lower re-infection rates for one-staged exchange (7.6%) compared to two-stage exchange (8.8%), albeit with overlapping confidence intervals.¹³ Similarly,

Table 1
Eradication rate after one- or two-staged revision in THA and TKA.

Author	Year	Patients [n]	Follow-up [years]	Eradication rate [% ± SD]
TKA, one-staged revision				
Silva et al. ²²	2002	37	4	89
Buechel et al. ²³	2004	22	10.2	91
Bauer et al. ²⁴	2006	30	4.5	67
Singer et al. ²⁵	2012	63	2	95
Jenny et al. ²⁶	2013	47	3	87
Tibrewal et al. ²⁷	2014	50	10.5	92
Zahar et al. ²⁸	2015	70	9	93
Haddad et al. ⁸	2015	28	6.5	100
Jenny et al. ⁹	2016	130	3.2	81
Massin et al. ²⁹	2016	108	3.5	77
Siddiqi et al. ¹⁰	2018	57	4.3	86
<i>Total</i>		642	$\mu = 5.5$	$87 \pm 8.8^*$
TKA, two-staged revision				
Fehring et al. ³⁰	2000	55	3	90
Emerson et al. ³¹	2002	48	5.6	92
Meek et al. ³²	2003	48	3.3	96
Haleem et al. ³³	2004	96	7.2	91
Durbakula et al. ³⁴	2004	24	2.8	92
Cuckler et al. ³⁵	2005	44	5.4	98
Hofmann et al. ³⁶	2005	50	6	88
Huang et al. ³⁷	2006	21	4.5	97
Jämsen et al. ³⁸	2006	34	2.8	85
Bauer et al. ²⁴	2006	77	4.5	67
Hsu et al. ³⁹	2007	28	2	87
Ghanem et al. ⁴⁰	2009	109	2.8	79
Westrich et al. ⁴¹	2010	75	4.4	73
Mortazavi et al. ⁵	2011	117	3.8	72
Choi et al. ⁴²	2012	47	3.6	68
Sabry et al. ⁴³	2014	291	3.3	72
Haddad et al. ⁸	2015	74	6.5	93
Lichstein et al. ⁴⁴	2016	121	3.7	94
Massin et al. ²⁹	2016	177	4.6	69
Ford et al. ⁴⁵	2018	56	3.3	54
Petis et al. ⁴⁶	2019	245	14	83
Siddiqi et al. ¹⁰	2018	137	4.6	76
<i>Total</i>		1148	$\mu = 4.6$	$83 \pm 11.7^*$

*p = 0.385.

Pangaud et al. reviewed 32 articles published between 1992 and 2018 including 687 patients with PJI in TKA after one- or either two-staged revision and calculated an eradication rate of 87% for one-staged revision and 85% for two-staged revision, respectively.⁷ However, methodological difficulties based on the heterogeneous literature have to be considered. Due to varying reported therapy regimes, especially in one-staged revisions, the results of some studies are of limited comparability.^{7,13} George et al. emphasized in this context the importance of a proper surgical technique. One-staged revision should be treated like two independent surgeries: First, a septic arthroplasty removal with closure and dressing followed by a cleaning of the operating theatre, a regowning of the team and new draping prior to the reimplantation with new sterile instruments.⁴⁸

Concerning functional outcomes after one- or two-staged revision in TKA, results of functional scores have also been comparable.^{7,42} Kunutsor et al. demonstrated no differences in functional outcomes with a Knee Society Score of 80.3 points in the one-staged group and 82.1 points in the two-staged group, respectively. On the other hand, Haddad et al. reported superior Knee Society Scores after one-staged revision in TKA analysing 102 TKA patients (88 vs. 76 points). Again, the evidence in this context is scarce and difficult to compare as various clinical scores have been used.^{7,49,50} Pangaud et al. therefore conclude that there is no clear benefit of either strategy in regard to functional outcomes.

However, one-staged exchange has been proposed as a viable alternative for infection control due to its potential advantages regarding morbidity, hospital length of stay, and healthcare costs.^{50–53}

Table 2

Functional outcome after one- or two-staged revision in TKA.

Author	Year	Patients [n]	Follow-up [years]	KSS praeop	KSS postop	OKS praeop	OKS postop	HSS praeop	HSS postop
TKA, one-staged revision									
Buechel et al. ²³	2004	22	10.2		79.5				
Bauer et al. ²⁴	2006	30	4.5		75.5				
Singer et al. ²⁵	2012	63	24		72				
Jenny et al. ²⁶	2013	47	3		85				
Tibrewal et al. ²⁷	2014	50	10.5			15	35		
Zahar et al. ²⁸	2015	70	9					35	70
Haddad et al. ⁸	2015	28	6.5	32	88				
<i>Total</i>		310	$\mu = 9.7$	32	$80 \pm 5.9 *$	15	35	35	70
TKA, two-staged revision									
Cuckler et al. ³⁵	2005	44	5.4	36	84				
Huang et al. ³⁷	2006	21	4.5	60	80				
Jämsen et al. ³⁸	2006	34	2.8	38	80				
Lichstein et al. ⁴⁴	2016	121	3.7	36	86				
Bauer et al. ²⁴	2006	77	4.5		75				
Haddad et al. ⁸	2015	74	6.5	31	76				
Durbhakula et al. ³⁴	2004	24	2.8					82	
Fehring et al. ³⁰	2000	55	3					83	
<i>Total</i>		450	$\mu = 4.2$	40 ± 10.2	$80 \pm 3.9 *$				83 [82; 83]

* $p = 0.377$.

Furthermore, the immense psychosocial distress of two-stage exchange has been described recently.⁵⁴ Izakovicova et al. concluded that for numerous patients, two-staged revision can be considered overtreatment.¹⁵

Several criteria to guide the surgeon in selecting the appropriate procedure have been described, yet are not precisely defined.^{7,11,55} The Infectious Diseases Society of America (IDSA) published guidelines in 2012, describing one-staged revision as a reasonable option in patients with a good soft tissue envelope and known pathogens susceptible to oral antibiotics with excellent bioavailability.¹¹

Similarly, Gehrke et al. postulated several criteria indicating the need for a two or multiple-staged procedure. In addition to the aforementioned IDSA criteria, Gehrke et al. described a history of failure of two previous one-staged procedures, infection spreading to the neurovascular bundle and the presence of a sinus tract as further contraindications for a one-staged revision.⁵⁵ Furthermore, it is generally assumed that one staged revision should not be considered in immunocompromised patients or in the presence of major medical comorbidities.⁵⁶ Several studies evaluating comorbidities have identified diabetes mellitus, coronary artery disease, pulmonary disease and obesity as risk factors, but in the context of two-staged revision.^{57,58} Abdelaziz et al. performed a single-centre retrospective analysis to detect risk factors associated with re-revisions after one-staged THA exchange and reported that in patients with prolonged wound discharge, a history of septic arthroplasty exchange or enterococcal infection, an alternative to one-staged exchange should be considered.⁵⁹ Citak et al. evaluated one-staged TKA exchange and identified prior septic exchange arthroplasty, isolation of enterococcus or streptococcus species and obesity (≥ 100 kg) as independent risk factors for re-revision due to reinfection.⁶⁰ Interestingly, Citak et al. highlighted that most of the risk factors they identified were not related to comorbidities.

While in the recent literature the one-staged approach is being increasingly endorsed, in 2018 the Musculoskeletal Infection Society (MSIS) confirmed the limitations of one-staged revisions mentioned above. The authors defined systemic infection with sepsis as a definitive contraindication, whilst the other criteria were specified as relative contraindications of one-staged exchange.⁹ A summary of these criteria is given in Table 3.

Both IDSA and MSIS authors emphasize that these recommendations are based on poor evidence (C-III) and that randomized controlled trials are lacking.^{11,12} Based on this limited evidence, surgeons are arguably

Table 3

Criteria advocating against one-staged revision arthroplasty in TKA.

- No good soft-tissue envelope (i.e. presence of fistula)
- No good bone stock
- No identified, nor susceptible pathogens
- septic patients
- prior failed septic revision arthroplasty
- immunosuppression
- body weight >100 kg or BMI >30
- No oral antibiotics with good bioavailability
- infection of neurovascular bundle
- isolation of enterococcus or streptococcus species

Criteria derived from ^{11,12,55,56,59,60}.

reluctant to indicate one-staged revision arthroplasty in TKA, so that it likely to have only been performed on a select group of patients so far. This suggests a possible selection bias which has to be considered regarding the literature of the past decades, especially in reports with outstanding infection control after one-staged exchange.⁶¹ Conversely, Jenny et al. reject the effectiveness of such a preselection in TKA revision. In a retrospective analysis they compared routine one-stage revision with one-stage revision in selected cases. The authors saw no significant difference in infection control between both groups after a mean follow-up of 38 months (85% vs. 78%) and concluded that patient preselection does not improve the success rate.⁹ Several limitations of their study, like the retrospective design, data inconsistencies and varying skills at different referral centres were discussed by the authors. Hence, it still remains unclear to which grade a selection bias affected the different success rates of one- and two-staged arthroplasty exchange.

In conclusion, the available literature does not prove the superiority of either one- or two-staged revision, in general. Moreover, the treatment of PJI depends on a variety of factors. Certainly, two-staged revision is a safe and successful treatment option which is rightly the gold standard. It is best suited for patients who have already undergone septic exchange arthroplastics, have poor bone quality or soft tissue conditions, or where the pathogen is unknown or unsusceptible to the antibiotic treatment of choice. However, there is a variety of cases in which one-staged revision is a viable alternative, where similar success rates can be expected. Therefore, there is a growing popularity of one-staged exchange.^{49,62} The most obvious merit is that patients do not have to undergo two surgeries at an interval in which the knee is largely

non-functional.³ In the end, either strategy remains complex and surgically and clinically demanding. Therefore, the choice of therapy should not only consider the patient's individual risk factors and the contraindications mentioned above, but also the surgical proficiency and experience with prosthetic joint infections of the team providing treatment.

Abbreviations

TKA	Total knee arthroplasty
PJI	Periprosthetic joint infection
KKS	Knee Society Score
OKS	Oxford Knee Score
HHS	Hospital for Special Knee Surgery Score
IDSA	Infectious Diseases Society of America
MSIS	Musculoskeletal Infection Society

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