



Infected total knee arthroplasty treatment outcome analysis

Analiza ishoda lečenja infekcije totalne artroplastike kolena

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Abstract

Background/Aim. Infected total knee arthroplasty (TKA) is a topic of great importance, because its diagnosing and treatment requires a lot of resources, and often has an unsatisfactory outcome. The aim of this study was to analyze the outcome of the treatment of infection developed following TKA. **Methods.** This retrospective study of infected TKAs was performed in the period from 1998 to 2008 in the Orthopedics & Traumatology Clinic of the Military Medical Academy (MMA) in Belgrade. A total of 654 primary and revised TKAs were performed in the said period. We registered and surgically treated 28 infected TKAs (primary TKAs: MMA – 22, other institutions – 6). The incidence of TKA infection in the MMA was 3.36%. The most common pathogens were: *Staphylococcus aureus* – 14 (50%) cases, and *Staph. epidermidis* – 3 (10.7%) cases. Other isolated pathogens were: *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Klebsiella spp.*, *Streptococcus viridans*, *Serratia spp.*, *Micrococcus luteus* and *Peptostreptococcus spp.* In one case we had mixed anaerobic flora, and in 3 cases cultures were negative. We analyzed diagnostic challenges, risk factors (such as age and previous viscosupplementation) and treatment outcomes in our series of infected TKAs. **Results.** In our series 2 infections healed after *in vivo* antibiotics and debridement, 1 patient responded to open debridement with component retention, 4 patients responded fully to one-stage reimplantation, 10 cases responded fully to two-stage reimplantation, 11 patients ended with arthrodesis and we had 1 patient with above knee amputation. **Conclusion.** Two-stage reimplantation remains gold standard for treatment of infected TKA, and we recommend it as treatment of choice for eradication of infection. The antibiotic loaded spacer prothesis concept in most cases allows infection eradication, good function and high patient satisfaction.

Key words:

arthroplasty, replacement, knee; bacterial infections; diagnosis; drug therapy; anti-bacterial agents; orthopedic procedures; treatment outcome.

Apstrakt

Uvod/Cilj. Infekcija totalne artroplastike kolena (TKA) je tema od velikog značaja, budući da dijagnoza i tretman zahtevaju značajne resurse sa često nezadovoljavajućim ishodom. Cilj ove studije bio je analiza ishoda lečenja infekcije nastale nakon totalne artroplastike kolena. **Metode.** Ova retrospektivna studija infekcije TKA obuhvatala je period od 1998. do 2008. godine u Klinici za ortopediju i traumatologiju Vojnomedicinske Akademije (VMA) u Beogradu. U navedenom periodu izvedene su 654 primarne i revizije TKA. Registrovali smo i hirurški lečili 28 infekcija TKA (22 TKA primarno izvedene u VMA i 6 TKA primarno izvedenih u drugim ustanovama). Incidencija infekcije u VMA bila je 3,36%. Najčešći uzročnici bili su: *Staphylococcus aureus* – 14 (50%) slučajeva i *Staph. epidermidis* – 3 (10,7%) slučaja. Ostali izolovani patogeni bili su: *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Klebsiella spp.*, *Streptococcus viridans*, *Serratia spp.*, *Micrococcus luteus* i *Peptostreptococcus spp.* Kod jednog bolesnika ustanovljena je mešovita anaerobna flora, a u tri slučaja kulture su bile negativne. Analizirali smo dijagnostičke izazove, faktore rizika (između ostalih godine života i prethodne viskosuplementacije) i ishod lečenja u našoj seriji TKA. **Rezultati.** U našoj seriji dve infekcije sanirane su nakon *in vivo* primene antibiotika i debridmana, jedan bolesnik izlečen je debridmanom sa zadržavanjem komponenta, četiri bolesnika izlečena su *one-stage* reimplantacijom, 10 bolesnika primenom *two-stage* reimplantacije, 11 bolesnika je rešeno artrodezom i urađena je jedna natkolena amputacija. **Zaključak.** *Two-stage* reimplantacija predstavlja zlatni standard u lečenju infekcije TKA, i preporučujemo je kao metodu izbora za eradikaciju infekcije. Koncept primene antibiotikskih *spacer* proteza u najvećem broju slučajeva omogućuje eradikaciju infekcije, dobru funkciju i visok stepen zadovoljstva bolesnika.

Ključne reči:

artroplastika kolena; infekcija, bakterijska; dijagnoza; lečenje lekovima; antibiotici; ortopedske procedure; lečenje, ishod.

Introduction

Average population in many countries is getting older, and total knee arthroplasty (TKA) is becoming more often performed. Infected TKA is a topic of great importance, because it is a diagnostic challenge, requires a lot of resources and often has an unsatisfactory outcome. Infection after TKA is catastrophic both to patients and surgeons. It can cause persistent pain, and loss of function. It can damage the peri-articular bone, causing prosthesis loosening and compromising further revision surgery, and may end up in septicemia, even life-threatening conditions. Reported rates of infected TKA in the literature are about 2%^{1,2} and about 0.4% for those ensuing within 3 months after operation¹. Risk factors have been identified^{1,2} and various methods have been devised to decrease the chance of this complication¹⁻⁴. In this study, we tried to determine the infection rate of TKA, the most common bacteria, and the success rate of various surgical treatment options in the Military medical Academy (MMA) in Belgrade. We also attempted to determine the risk factors for infection and ways of minimising the risk.

Numerous studies have shown the TKA infection incidence of less than 1% to 2%. The average annual cost of managing infected TKAs in the United States is \$150 to \$200 million⁵. Infected TKA requires 3 to 4 times the hospital resources when compared with primary TKA, and double the resources when compared with aseptic revision TKA⁵. An exact estimate of the costs in Serbia is not yet known since the data we have are only from our institution's arthroplasty register. We consider that primary uncomplicated TKA performed in MMA requires an average of 6.32 days of hospitalization, while infected TKA requires an average of 4.92 hospitalizations with a total of 39.2 days of hospital treatment.

The aim of this study was to analyze the outcome of the treatment of infection developed following TKA.

Methods

This is a retrospective study of all surgically treated infected TKAs in the MMA. Our team of orthopaedic surgeons reviewed all relevant medical records in the period from January 1998 to December 2008. A total of 654 TKAs were performed on 533 patients. There were 121 bilateral TKAs in single procedure, and others were unilateral TKAs or bilateral as two-stage procedure. Out of a total number, 386 patients were female and 147 were male. The mean patient age was 70.1 years ranging from 36 to 94 years. The mean patient age in the infected TKA group was 74.8 years while in the noninfected TKA cases the mean age was 69.7 years. We used different total knee prosthesis (Zimmer, Depuy-Johnson and Johnson, and Stryker models) and all TKAs were cemented. The mean follow-up period for infected TKAs was 39 months.

We define TKA as infected when there are: 2 or more cultures positive, or cultures negative (in less than 7%) but we have clinical and laboratory manifest infection, acute inflammation or purulence at the time of the surgery, sinus

tract. General signs of infection – fever, chills, malaise, wound erythema, are uncommon in the most infected TKAs. Sometimes the only presenting symptoms such as pain, swelling, warmth and synovitis are hard to distinguish from aseptic failure. TKA infections are primarily bacterial, although fungal ones were reported⁶. They are hematogenous or they occur after intraoperative contamination.

Diagnosis of infected TKA consists of: anamnesis – local status; laboratory findings (CBC, sedimentation, CRP, fibrinogen; knee aspirate – analysis of synovial fluid and culture); and imaging – radiography, scintigraphy.

Laboratory findings for infected TKA – sedimentation and CRP are highly sensitive but lack specificity. We noted increased sedimentation in 85% of cases CRP was elevated in 96%, fibrinogen was increased in 75% and leukocytosis was presented in 36% of cases. Silva et al.⁷ and Rand and Brown⁸ noted that only 28% of cases had leukocytosis greater than 11,000 in the presence of deep knee infection.

Knee aspirate serves for assessment: the color, clarity and, viscosity of the fluid – string test, cell count – Le > 20,000 with more than 65% polymorphonuclear leukocytes (PMN) (values are significantly lower than in septic arthritis of the knee that was not subjected to previous arthroplasty), culture and antibiogram (antibiotics should be discontinued two weeks before taking swab or aspirate). Histological examination of intra-operative tissue could also be taken as suggestive of infection, as could intraoperative findings of pus, turbid fluid, unhealthy granulation tissue, synovitis, bone destruction, and prosthesis loosening⁹.

Radiography is usually more useful in chronic infected TKAs. It can show the presence of radiolucent zones. In the presence of long lasting infections we can also see periosteal bone formation (indicating poor prognosis these knees have bad response to two-stage reimplantation), and loosening of components. Fistulography is rarely indicated for infected TKA.

Scintigraphy is used in the evaluation of infected knee arthroplasty with variable results. Indium scans have good sensitivity but poor specificity. Rand and Brown⁸ found that indium scans had a sensitivity of 83% and accuracy of 83%. We used scintigraphy in 2 cases (two cases with negative cultures). We had focal hot uptake around the prosthesis – positive results in all the cases, but we could not know for sure, in one case of failed TKA, if it was mechanical or septic loosening. We do not recommend routine use of radioisotope scanning since other diagnostic methods are cheaper, safer, faster and more reliable.

In the last two decades numerous studies have identified risk factors, and the immeasurable importance of adequate recognition. Immunocompromised host factors (leukopenia and malnutrition) and existing infections are of the utmost importance. Care should be taken to minimize risks for possible sources of contamination operating room (OR) environment, the skin of the patient or remote sources – dental infections, chronic ulcers, urinary tract infections, gastrointestinal, gynecological infections, even endocarditis. In order to minimize the risks of contamination, the necessary measures are: prophylactic antibiotics, sterile technique, drapes,

self contained exhaust suits, ORs with less traffic, laminar flow, careful closing.

Viscosupplementation as a risk factor – in the study on effect of intraarticular hyaluronic acid agents on subsequent rate of infection following TKA Petrella and Mahadeva¹⁰ recorded 18 infections after TKA in a group of 415 TKA, who had previously received intraarticular viscosupplementation injections, and 21 infected TKA in the group of patients who had not received viscosupplementation previous to knee arthroplasty. In our series we identified patients who had undergone previous knee viscosupplementation, there were 654 TKAs and 126 of them had undergone knee viscosupplementation previous to TKA. 28 patients had infected TKA only 2 of them were given viscosupplementation knee injections prior to TKA. Since there was no statistically significant relationship between viscosupplementation and infection after TKA we could not say that viscosupplementation injections promote infections.

Classification of TKA infection – Tsukayama et al.¹¹ presented a classification of infection based on clinical presentation (they differentiate between early, acute onset < 4 weeks post surgery, subdivided in superficial and deep, and late, chronic onset > 4 weeks post surgery). The two remaining categories are: acute hematogenous infection and infection based on positive intraoperative culture. We used this classification and we have registered 15 acute infections (< 4 weeks post surgery) two superficial and all other were deep infections. We noticed 13 late chronic infections (> 4 weeks post surgery).

Prophylactic measures in the MMA – one operating room is assigned for total joint replacements. We have not routinely used body exhaust suits, but water repellent paper gowns, drapes, and double gloves have been mandatory. We prepare the lower limb distal to tourniquet with iodine tincture twice: once by an assistant surgeon before gowning, and once more by surgeon, and routinely change the outer pair of gloves after draping. Prophylactic antibiotic has always been given (in most cases 1g of ceftriaxone or 1g of cefazolin) 1 hour preoperatively, antibiotic therapy continued in the same dose the next three days. In all cases we administered low molecular weight heparin (LWMH) once or twice daily (according to recommended dosage of specific product).

Results

In a period 1998–2008 in the MMA – Orthopaedics & Traumatology Clinic, 654 primary and revision TKAs were performed. During this period we registered and surgically treated 28 infected TKAs (MMAs primary TKAs – 22, other institutions primary TKAs – 6). The incidence of TKA infection in MMA was 3.36%. In our series of infected TKAs the most common pathogens were *Staphylococcus aureus* – 14 (50%) cases, and *Staph. epidermidis* – 3 (10.7%) cases. Other isolated pathogens were: *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Klebsiella spp.*, *Streptococcus viridans*, *Serratia spp.*, *Micrococcus luteus* and *Peptostreptococcus spp.* In one case we had *mixed anaerobic flora*, and in 3 cases cultures were negative. The most common bacteria in the study of

Silva et al.⁷ on 590 infected TKA were: *Staphylococcus aureus* 48.7%, *S. Epidermidis* 16.3%, *Pseudomonas* 5.1%, *Streptococcus* 4.8%, *Enterococcus* 4.5 %, *polimikroba flora* 5.4% *i others* 15.2%).

We registered 2 superficial and 26 deep infections. Superficial infections were treated by iv antibiotics and surgical debridement. Both healed well after the treatment, both patients enjoyed a painless knee without any signs of infection at the follow-up. A total of 26 deep TKA infections required a more serious approach. In the MMA we adopted the algorithm of treatment of TKA infections that all the MMA surgeons have to follow. Our strategy after clinical and microbiological confirmation of infected TKA was: debridement and, if found as viable option, retention of components or one-stage reimplantation, two-stage reimplantation, then if two-stage reimplantation fails the next option was arthrodesis, and finally if everything else fails above knee amputation.

In our series, 2 infections healed after iv antibiotics and debridement, 1 patient responded to open debridement with component retention, 4 patients responded fully to one-stage reimplantation, 10 cases were successfully treated with two-stage reimplantation, 11 patients ended with arthrodesis (9 external fixator, 2 plating technique) and we had 1 case of above knee amputation.

We performed two stage reimplantation in 21 cases. The rate of infection eradication in TKA with two-stage reimplantation was 76.19%.

Discussion

Infection eradication, alleviation of pain and restoration of function are goals of treatment of infected TKA. In effort to achieve the first two goals, we often have to sacrifice the function.

In general, treatment options for infected TKA are: treatment that retains prostheses – antibiotic suppression and open debridement with component retention; exchange arthroplasty (one- and two-stage reimplantation); salvage procedures – arthrodesis, resection arthroplasty and amputation.

Antibiotic suppression therapy if chosen is usually lifelong.¹² It is only adequate in the earliest and most benign infections and it can be considered if a patient is not suitable for surgery, if there is low bacterial virulence, no sepsis, no severe antibiotic side effects and if prosthesis is stable. In our series we did not have patients on lifelong antibiotic suppression.

Some authors recommend arthroscopy in management of infected TKA: and/or continuous irrigation^{13–16}. Arthroscopy theoretically has several advantages over open debridement: it is less invasive, has faster rehabilitation, but has also disadvantages to open debridement: poly change is not possible, debridement is less radical, possibility for eradication is worse than in open debridement.

We performed arthroscopic debridements and irrigations in five cases of infected TKA, but with poor results, which required further surgical treatment, so we cannot speak in favor of this kind of treatment.

Open debridement with component retention as a treatment option has few advantages, including reduced stress for a patient, less bone loss, better function of the knee, and less cost to the health care system¹⁷. Following criteria necessary for this treatment approach are: low-virulence organism (sensitive to antibiotics), acute infection (< 4 weeks), no signs of component loosening, no sinus tracts. Deirmengian et al.¹⁸ used open irrigation and debridement to treat 33 patients with acute gram-positive infected TKA with poor success. Of the 31 patients who underwent debridement with component retention, 20 (65%) experienced recurrent infection and eventual removal of components. We used open debridement with component retention in 8 cases, yet only one of them responded. It was the patient whose culture was positive to *Serratia species*, all the other infected TKA underwent further one- or two-stage reimplantation.

One-stage reimplantation as treatment option offers possibility to only one surgery, but there is no second chance, no second debridement, no local antibiotics, and it is not recommended if bacterium is not identified. One-stage reimplantation may be a viable alternative to the two-stage revision procedure. In one-stage surgery, incision and arthrotomy are performed in the usual way; and thorough irrigation and debridement are done, all infected total knee components are removed, and new total knee components are placed during the same session. In the study of Buechel et al.^{19–22} infected total knees were revised using single-stage resection and reimplantation. Out of 21 patients nineteen showed no signs of recurrent infection at an average of 10.2 years of follow-up.

In our series of infected TKA we had 50% rate of success with this approach, there were 4 successful one-stage reimplantations out of 8 performed. All the patients were then treated with 4 weeks of iv antibiotics, followed by 2 months of oral antibiotics, in all cases we consulted the infectious disease specialist.

Two-stage reimplantation consists of two stages. In stage one after confirming the diagnosis of infected arthroplasty, first steps are irrigation, debridement, and resection of components. Polyethylene, tibial, femoral, patellar components and bone cement are removed. Care must be taken to preserve as much bone stock as possible to allow a foundation for the reimplantation. The soft tissues are thoroughly debrided, the joint is then irrigated using antibiotic solution. The second part of stage one of the procedure is to place an antibiotic spacer in the joint to maintain the space for reimplantation of the components in the future and possibly to allow the patient to ambulate until component reimplantation can be completed. The spacers are made with bone cement impregnated with antibiotics. Cement allows antibiotics to elute into the joint and surrounding tissues over time, usually several weeks, to help eradicate infection. The goal of the spacer is to provide patient comfort and mobility, prevent the loss of joint space, enhance bone quality, and allow for treatment of the infection locally with time-released high local concentration of antibiotics²⁰. Spacers can be simple self-made block-shaped or articulating devices. Recent studies suggest that using an articulating antibiotic spacer allows

for better functioning for patients between the stage I and stage II procedures^{21–23}. Articulating spacers may be custom made – the components removed at debridement can be re-used to construct an articulating spacer. The femoral component is debrided, cleared of adherent bone and cement, autoclaved for 20 minutes, and coated with antibiotic-impregnated cement on its nonarticulating surface. A new polyethylene insert is open, and is coated, too, on its nonarticulating surface, and both are implanted with cement in a doughy stage, so that there is limited interdigitation with bone²². Or articulating spacers may be constructed from prefabricated cement molds. After an antibiotic spacer is implanted, a patient may be allowed to have at least partial weight bearing and range of motion of the joint. The patient is also treated with iv antibiotic therapy, with the choice of antibiotic dependent on microorganism culture and sensitivity results. Courses of antibiotics range from 14 days to 12 weeks^{24–26}.

The stage two occurs after the infection is eradicated. Indications for reimplantation are good bone stock, adequate soft tissues, immunocompetent patient and sensitive microorganism. Contraindications for reimplantation are persistent infection, immunocompromised host, extremely poor bone stock, poor soft tissues.

The lapse of time between the first-stage and second-stage procedures ranges from 4 to 58 weeks and depends on a patient's medical condition, a physical condition of the joint itself, and results of repeated aspiration/culture and tests for inflammatory markers^{22, 24–26}. Stage two consists of removal of antibiotic spacers, debridement, and reimplantation of total knee components, in some cases revision knee implants are needed. The two-stage revision procedure is generally considered to be the gold standard treatment for infected TKA. Cuckler²⁶ had no recurrence of infection with an average follow-up of 5.4 years for 44 infected TKA treated with two-stage revision using articulating spacers. In a study by Hirakawa et al.²⁴, a success rate of 66.7% was found when high-virulence organisms (*Staphylococcus aureus*, *Enterococcus* species, methicillin-resistant *S. aureus*) were involved. The success rate was 80% when infection was with low-virulence organisms (*Staphylococcus epidermidis*, *Streptococci*, *Proteus* species) and 71.4% with polymicrobial organisms²⁴.

We performed two stage reimplantation in 21 cases. When we closed follow-up in June 2010 and headed to the processing of data, we found 10 patients responding fully to two stage reimplantation and had good functional outcome, while the other 10 ended with arthrodesis and one patient had above knee amputation. The rate of good functional outcome with two-stage treatment was 47.6%. But we noticed that the mean follow-up period in the patients who had good functional outcome was 35 months, much shorter than in the group who ended with arthrodesis or amputation where the mean follow-up was 47 months. We must say that 6 of 10 patients who ended with arthrodesis did not undergo this procedure because of infection, they had mechanical problems due to instability and loosening of prosthesis components. We are under the impression that many patients after

two-stage reimplantation after a longer period of follow-up are in need for revision arthroplasty or arthrodesis due to loss of bone stock, or soft tissue problems. In our series only in 5 cases out of 21 of infected TKA, two-stage reimplantation failed to eradicate infection. So, the rate of eradication of infection in TKA with the two-stage reimplantation approach was 76.19%. In our series we have used self-made articulating spacers in all cases, and *iv* antibiotics from 2 to 4 weeks. In some cases we added orally rifampin 2×600 mg with *iv* antibiotics, and rifampin 600 mg $1 \times$ for 4 weeks orally after we discontinued *iv* antibiotics, based on infectious diseases consultants recommendations.

Salvage procedures for infected TKA are: resection arthroplasty arthrodesis and amputation.

Resection arthroplasty as a definitive treatment for infected TKAs is reserved for patients who are medically ill and sedentary. It results in a significant loss of function, instability, and potentially persistent pain. In most cases, arthrodesis require is eventually. In our series of infected TKA we did not perform resection arthroplasties. But in the MMA we found that it could be a viable option for some cases of infected total hip arthroplasty.

Arthrodesis is the treatment of choice when it is thought that reimplantation will have a high rate of failure, due to inadequate joint mechanics, soft tissue envelope, or immune system deficiency.

The relative contraindications to arthrodesis of infected TKA are: significant contralateral limb dysfunction, coexistent ipsilateral ankle or hip disease, inadequate bone stock for fusion. The available arthrodesis techniques are: intra-

medullary nailing, external fixation and plates and screws. We had 11 arthrodesis after infected TKA, in 9 cases we applied an external fixator (7 – type Mitković and 2 – Ilizarov), and in two cases we used the double plating technique.

Amputation is indicated when other attempts to salvage the knee have failed and when further salvage procedures would likely be ineffective. One patient in a 42-months-period from primary TKA, underwent multiple debridements, two-stage reimplantation and arthrodesis. Refractory infection (negative *Staph. aureus*) and severe bone defects compromised all reconstructive and salvage procedures. Above knee amputation was a definitive treatment.

Conclusion

Two-stage revision arthroplasty is the most commonly used treatment for infected TKA and had the best treatment results reported in the literature. However it is not almighty procedure, though numerous studies percentages of success are individually different.

Since success is not always guaranteed, a patient should be always aware of the back-up options and in best case scenario surgeons should expect some loss of function after two stage reimplantation.

Two-stage reimplantation remains gold standard for treatment of infected TKA, and we recommend it as treatment of choice for eradication of infection. The antibiotic loaded spacer prosthesis concept in most cases allows infection eradication, good function and high patient satisfaction.

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