CLINICAL OUTCOME AFTER TREATMENT OF INFECTED PRIMARY TOTAL KNEE ARTHROPLASTY

H. HUSTED, T. TOFTGAARD JENSEN

Twenty-six consecutive cases of infected primary total knee arthroplasties were treated at our institution from 1989 through 2000. Eleven patients had debridement and irrigation performed within 2 months of index arthroplasty or hematogenous spread ; only one infection was eradicated. Twenty-five patients had their prostheses removed ; 17 had two-stage revision arthroplasty, following which infection was eradicated in 15 ; one had a permanent spacer, 7 had arthrodesis (following failed revision arthroplasry in one) and 2 had a femur amputation (following failed revision arthroplasty in one) at follow-up of mean 24 months. Infections were cured equally well with revision arthroplasty and arthrodesis. Among the 15 patients who ended up with revision arthroplasty, 11 had a better range of motion compared to the index arthroplasty, but 8 had daily pain. We present our treatment protocol, which eradicated 15/17 (88%) infections in patients treated with two-stage revision arthroplasty.

Keywords : total knee arthroplasty ; infection.
Mots-clés : prothèse totale du genou ; infection.

Deep periprosthetic infection after total knee arthroplasty (TKA) is a serious complication with an unpredictable outcome. We report our experience in treating infected TKA's from 1989 through 2000.

MATERIAL AND METHODS

All patients operated with TKA and revisions of any kind following the primary procedure were recorded. Searching our database and scrutinizing each file, we found 26 cases of deep periprosthetic infection following TKA diagnosed and treated in the 12-year period from 1989 through 2000.

Twenty-four patients were operated for gonarthrosis and 2 for rheumatoid arthritis ; 23 were women, 3 were men. Sixteen patients had their primary TKA in our department ; 10 were operated at another institution and referred for treatment of infection. Mean age was 73 years (60-82 years) at the time of primary operation and 74 years (66-86 years) at diagnosis of infection. The mean interval from primary TKA to diagnosis of infection was 20 months (1-133 months).

The design of the primary prostheses used varied, but all were of posterior cruciate ligament retaining nonconstrained design, all components were cemented and the patella had been resurfaced in all cases. The definition of infection was based on one or more of the following : pus present in the wound and/or a positive culture of fluid or tissue from the knee joint and/or signs of infection at revision (pus and/or inflamed/necrotic tissue) and/or histopathological or scintigraphic evidence of infection (13).

Treatment

A total of 78 operations were performed on the 26 patients (mean 3 ; range 1-7) to eradicate the infection. The mean length of hospitalization due to infection was 121 days (19-406 days).

Eleven patients had debridement and irrigation with gentamycin in saline solution as initial treatment (1-2 months from detection of infection ; mean 1.5 months),

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Fig. 1a. — Loose infected primary TKA ; ***1b.*** — Genta-spacer ; ***1c.*** — revision TKA.

but this procedure eliminated the infection in only one patient. Twenty-five patients had their primary prosthesis removed, of whom 19 had gentamycin-loaded spacers (Palacos®) inserted. In one patient the spacer was left *in situ* for medical reasons ; she became pain-free (patient 16). Seventeen patients had revision arthroplasty performed, following which infection was cleared in 15, whereas the other two ended up with an arthrodesis (patient 26) or a thigh amputation (patient 23) ; 7 had an arthrodesis performed including one following failed revision arthroplasty and 2 were amputated above the knee owing to persistent infection with the formation of a sinus (patients 7 and 23, the latter following failed revision arthroplasty).

Revision TKA

In cases of revision TKA, all operations were two-staged, starting with removal of all components and cement, debridement and irrigation, opening of the medullary cavity and implantation of Gentamycin, – loaded beads into the medullary cavity followed by implantation of a Gentamycin, – loaded spacer (Palacos®). At the following operation, tissue samples were examined intraoperatively to exclude the continuing presence of bacteria. If no infection was found, the revision prosthesis was inserted and all components were cemented with Gentamycin, – loaded cement (fig. 1a, 1b, 1c).

The revision TKA's were performed with different types of prostheses (8 constrained, 8 posterior stabilized and one nonconstrained prosthesis) as two-stage operations with removal of the primary prosthesis and insertion of a spacer followed by approximately 5 weeks of antibiotics. Initially, antibiotics were administered intravenously for at least 2 weeks followed by oral administration when a clear decline in CRP, ESR and WBC was seen. After 5 weeks antibiotics were discontinued and if no rise in the blood parameters was seen after one week, a revision TKA was performed followed by antibiotics perorally until normalization of blood parameters. If the blood parameters rose at any time during these 6 weeks debridement was performed followed by another period on antibiotics (4 patients).

Arthrodesis

Arthrodesis was performed using intramedullary fixation (Grosse-Kempf, nail) in 6 patients, who healed uneventfully, while patient 26 had arthrodesis performed

by means of an Ilizarov fixator and did not heal ; she now wears an orthosis.

Treatment protocol

From 1992 a protocol was followed in our department : all infected primary TKA's with diagnosed infection ongoing for less than 2 months, either from primary operation or from late hematogenous spread, had initial debridement and irrigation with Gentamycin-loaded saline water performed. If the infection had persisted longer than 2 months, or the initial soft-tissue procedure had failed, all components and cement were removed with debridement and irrigation, with opening of the medullary cavity and implantation of gentamycin-loaded beads into the cavity followed by implantation of a gentamycin-loaded spacer (Palacos®). Surgery was followed by approximately 5 weeks of antibiotics, which were initially administered intravenously for at least 2 weeks followed by oral administration when a clear decline in CRP, ESR and WBC was seen. After 5 weeks antibiotics were discontinued and if no rise in the blood parameters was seen after 1 week a revision TKA was performed followed by antibiotics orally until normalization of blood parameters. If the blood parameters rose at any time during these 6 weeks, debridement was performed followed by another period on antibiotics. At the following operation, tissue samples were examined intraoperatively to exclude the continuing presence of bacteria (we had no positive intraoperative cultures in this material). If no infection was found, the revision prosthesis was inserted and all components were cemented with gentamycin-loaded cement.

RESULTS

The data on the 26 infected patients are shown in table I.

Organisms

The cultured bacteria were : *St. aureus* (11), *St. epidermidis* (10), *hemolytic Streptococcus* (2), *Cl. perfringens* (1), *Pseudomonas* (1), *Klebsiella* (1), *coryneform bacteria* (1), *Proteus mirabilis* (1) and *Enterococcus cloacae* (1) ; four patients had two different species of bacteria. Twenty-one of the patients were infected during their primary TKA, whereas in 5 patients the bacteria spread hematogenously from pyelonephritis (patient 2), a traumatic wound (patient 3), a pyarthron affecting the other knee (patient 9), infection after osteosynthesis of a supracondylar fracture of the ipsilateral femur (patient 17) and from a perianal wound (patient 20). The hematogenous spread occurred from 33 to 133 months after TKA, and identical bacteria were cultured from the primary wound and from the infected knee. In one patient (patient 10) no positive culture was obtained, but she was already receiving antibiotic treatment because of ongoing drainage from the wound after her primary TKA. All patients were treated with antibiotics according to the cultured bacterial species.

Clinical presentation

At time of diagnosis all patients had a painful, swollen knee with classic signs of infection (*rubor, dolor, calor* and functional impairment) - in 3 patients (patients 15, 17, 25) a leucocyte scintigraph was performed to aid in the diagnosis of infection 14 to 133 months after primary TKA. All patients had biplanar xrays of the affected knee with radiological loosening noted in four, but without signs of osteitis.

The C-reactive protein (CRP) and sedimentation rate (ESR) were elevated in all patients at the time of diagnosis of infection, whereas the white blood cell count (WBC) was indicative of infection in only 11 of the 26 patients. Mean CRP was 1069 mg/l (25-3108) (reference < 10 mg/l) and mean ESR was 83 mm. (24-125) (reference < 20 mm.).

Outcome

No patients died as a result of the infection. All infections were eradicated, and the patients were followed at least a few months after cessation of antibiotics, normalization of blood parameters and clinical clearance of infection. Follow-up ranged from 5 to 64 months after final operation (mean 24 months, table I). By checking the national database it was ensured that none of the patients had been admitted to another hospital owing to infection of the knee.

Thus, the various operative procedures eradicated 15 of 17 infections with two-staged revision

Table I. — Data on the 26 patients with periprosthetic infection

Pat./ Year	sex	age	time	bact.	cont.	CRP	SR	wbc	Treat	anti	op	out	hos	f-u	pain	rom	amb
1 1989	f	67	1	clost perfr	p	-	-	15.5	Deb rem	1+0	2	rtka	22	60	Yes	0/ 100	cane
2 1990	f	73	54	staph aure	h	-	98	13.9	deb rem	-	3	art	104	29	Yes	-	cane
3 1990	f	82	40	staph aure	h	-	86	8.4	deb rem	-	4	art	366	13	No	-	cane
4 1990	f	65	11	staph aure	p	-	117	6.1	rem	-	2	art	68	10	No	-	walk
5 1991	f	72	18	staph epid	p	500	90	4.3	deb rem+	-	5	art	169	5	No	-	cane
6 1991	f	72	1	staph epid	p	372	82	5.6	rem	-	2	art	107	12	No	-	2 crutc
7 1992	f	65	21	staph aure	p	623	26	11.0	rem	-	6	amp	406	9	No	-	unab
8 1992	f	69	5	staph epid	p	529	125	8.2	deb rem+	5+1	5	rtka	116	5	No	0/70	1 crutc
9* 1992	f	77	53	pseud	h	1286	55	9.0	rem+	-	2	art	88	64	Yes	-	2 crutc
10 1994	f	78	2	-	p	590	105	7.2	rem+	5+1	2	rtka	92	31	Yes	0/100	cane
11* 1994	f	66	2	staph aure	p	1720	105	11.7	rem+	6+1	2	rtka	79	5	No	0/110	ok
12 1994	f	77	1	s. aur strept	P	1300	47	11.0	deb rem+	5+1	3	rtka	77	56	No	0/100	cane
13* 1995	f	74	2	staph epid	p	746	120	8.6	deb rem+	5+1	4	rtka	84	26	No	0/100	cane
14 1996	f	71	1	staph aure	p	2300	90	9.5	rem+	5+1	2	rtka	61	62	No	5/90	walk
15* 1996	f	78	14	s. epi klebsi	p	236	82	7.4	deb rem+	5+1	3	rtka	114	40	Yes	0/100	1 crutc
16 1996	f	81	26	s. epi coryn	p	296	84	7.9	rem+ deb	-	1	genta space	74	38	No	0/30	unab
17 1997	f	60	133	strept	h	2873	96	6.3	rem+ deb	5+1	3	rtka	112	25	No	0/110	1 crutc
18* 1997	f	77	1	staph aure	p	1531	110	8.6	rem+	5+1	2	rtka	60	30	Yes	0/120	cane
19 1997	f	77	2	Prote mirab	p	1689	44	8.6	Deb	-	1	ptka	19	5	No	0/100	cane
20* 1997	f	70	33	Enter ocloa	h	3108	110	8.8	rem+	5+1	2	rtka	75	24	Yes	0/130	cane
21* 1998	m	76	10	staph epid	p	3100	70	15.2	rem+	5+1	2	rtka	141	9	Yes	0/70	2 crutc
22* 1998	f	76	1	s. aur s. epi	p	99	24	6.7	deb rem+	5+1	3	rtka	86	19	Yes	0/90	walk
23* 1998	m	67	48	staph epid	p	135	24	6.2	rem+	5+1	3	amp	91	5	No	-	2 crutc
24 1999	f	76	1	staph aure	p	242	100	9.5	deb rem+	5+1	4	rtka	121	19	No	0/90	walk
25* 1999	m	70	34	staph epid	p	25	81	9.5	rem+ deb	13+1	3	rtka	120	14	Yes	40/ 110	walk
26 2000	f	75	3	staph aure	p	208	94	5.7	rem+ deb	7+1	7	art	294	7	Yes	-	2 crutc

Table I, explanation :
Pat. = patient number ; * = primary total knee arthroplasty performed at other orthopedic departments.
Year = year when infection was diagnosed.
Sex (f = female ; m = male).
Age = age at primary total knee arthroplasty.
Time = time from primary total knee arthroplasty to diagnosis of infection (within full months).
Bact. = bacteria species cultured at time of infection.
Cont. = method of contamination (p = perioperative, h = hematogenous).
CRP = C-reactive protein at diagnosis of infection.
SR = sedimentation rate at diagnosis of infection.
WBC = white blood cell count at diagnosis of infection.
Treat = initial treatment of periprosthetic infection (deb = soft tissue debridement + antibiotics, rem = removal of prosthesis + antibiotics, rem+ = removal of prosthesis + spacer + antibiotics).
Anti = antibiotic regime following prosthesis removal before performing re-arthroplasty (number of weeks on antibiotics + number of weeks without antibiotics before revision arthroplasty).
Op = total number of operations due to periprosthetic infection.
Out = outcome (ptka = primary prosthesis *in situ*, rtka = revision prosthesis, art = arthrodesis of knee joint, amp = amputation above knee joint, gentaspace = gentaspacer).
Hosp = days of hospitalization due to periprosthetic infection.
F-u = months of follow-up after last operation due to periprosthetic infection.
Pain = pain at follow-up (no = no daily pain, yes = uses daily analgesics).
Rom = range of motion of knee joint at follow-up.
Amb = ambulatory outcome (ok = walks without support, cane = uses cane for walking, crutch = number of crutches used for walking, walk = uses walker for walking, unab = unable to walk/uses wheel-chair).

TKA, 7 of 7 infections with arthrodesis as opposed to only 1 of 11 infections with debridement and irrigation (Fisher test ; $p < 0.00005$).

At the final follow-up registered in the patient records, 11 of the 26 patients complained of daily pain and used analgetics ; 8 of 15 patients with revision TKA and 3 of 7 patients with arthrodesis had pain (Fisher test ; NS).

Of the 15 patients with revision TKA successfully performed, only 2 patients had decreased range of motion (ROM) compared to ROM after primary TKA, while 2 had identical and 11 had better ROM. Patient 25 had active 20/90° ROM after primary TKA and 40/110° after revision TKA - owing to a rupture of his quadriceps tendon. The mobility had increased in only one patient, who was now able to walk without support while 7 had the same walking capability as before and 7 had poorer ambulatory function needing more support to walk. Regarding the choice of prosthesis at revision, we used 8 constrained prostheses owing to instability after removal of the primary TKA. In the present study our material is too small to detect any differences (if present) in outcome between the different prostheses.

DISCUSSION

An infected TKA is a serious complication and presents a challenge to every orthopedic surgeon, who has to choose the best treatment for every individual patient among different surgical treatment options. It is estimated that surgical treatment of an infected TKA requires three to four times the resources of the hospital compared with a primary TKA and twice the resources for a nonseptic revision TKA (6).

The clinical presentation of the infected knees in this series left only little room for differential diagnosis to infection as all had elevated sedimentation rates and C-reactive protein values. The white blood cell count was elevated in only less than half, similar to the finding of others (4, 11). However, if a patient had been taking antibiotics prior to admission, the values could well be within the normal range as well as joint aspirates could show no growth of any bacteria (16). The three performed leucocyte scintigraphs in our study were all conclusive in favor of infection around the knee and thus can be very helpful to the clinicician when dealing with cases where infection presents in a less clear way.

The bacterial organisms cultured from the infected TKA's in our study group were largely staphylococci, both coagulase-positive and negative. This corresponds to all other studies on microbial agents responsible for periprosthetic infection, but only in 2 cases in our series were the staphylococci methicillin-resistant, and glycopeptides had to be used for treatment.

All patients were treated with antibiotics according to the specific cultured bacteria. There are a few reports on treatment of infected TKA with antibiotics alone or in conjunction with suction drainage, multiple aspirations or irrigations, but the chances of overcoming the infection this way are scarce (1, 9, 15). Almost always is surgery in some form indicated along with antibiotic treatment. The treatment modalities consist of surgical debridement, removal of the prosthesis and subsequent resection arthroplasty, arthrodesis or revision TKA or, when this fails, above-the-knee amputation.

We attempted a debridement and irrigation procedure in 11 patients (1 to 2 months after onset of symptoms of infection, mean 1.5 months), but were succesful in only one. Others have had success rates between 18-83% with this procedure, when applied to patients with signs of infection for less than one month and significantly poorer when longer periods of time had passed (3, 5, 10, 14). We attribute our poor result with 10/11 failures regarding survival of the primary prosthesis to the (too) late debridement as there seems to be a critical limit for success of approximately one month (14). Future infections in our department will only be debrided provided they have lasted shorter than one month. From 1989 to 1991 arthrodesis was the preferred method to treat infected TKA's in our department, but from that time on the manufacture of different revision prostheses suitable for almost every situation and the reports on successful management of the infection by two-stage revision TKA with maintenance of knee range of motion (1, 12) made it difficult to propose arthrodesis as the initial salvage procedure. We now always attempt a two-stage revision with a revision TKA as final outcome, and only in cases where this procedure fails or infection persists, is arthrodesis performed. However, the question arises : which is best for the patient ? A revision TKA with a good or fair ROM but possible accompanying pain or a rigid arthrodesis without pain ? It is often assumed, and we agree, that the outcome after revision TKA is more unpredictable compared to primary TKA with regards to both ROM and pain. However, in our series only 2 of 15 patients had decreased ROM after revision TKA compared to ROM after primary TKA ; 11 actually had increased ROM, but with daily pain in 8 of 15 patients. Clinically there were no signs of residual infection in any knee and ESR, CRP and WBC were normal. Radiographs showed well fixed and well positioned components. Pain was not associated with type of revision prostheses, age, number of days in hospital, ROM, mobility or the number of operations performed and we are unable to explain *why* half the patients experienced daily pain (in 6 of the 8 patients it was only mild pain treated with mild analgetics) in clinically well functioning revision knees. But the experienced pain may explain why half the patients had poorer ambulatory function after revision TKA compared to after primary TKA.

Regarding pain and comparing this to 6 of 7 patients with healed arthrodesis, but with daily pain in 3 of those including the nonhealed painful arthrodesis in patient 26 (Fisher test ; NS), it seems fair to assume that the overall outcome of the 26 patients answers the question in favor of revision TKA as the best treatment option when possible. In another study no patients with arthrodeses had an excellent Hospital for Special Surgery knee score and they scored significantly less than patients with revision TKA's (mean HSS-score 41 and 75, respectively) (17). However, in situations where revision TKA's become reinfected or have a persistent infection, arthrodesis seems to be the gold standard as it becomes more and more difficult to overcome soft tissue problems with draining sinus tracts if one plans for a re-revision TKA (4).

Eighty-eight percent of infections were eradicated with revision TKA following our treatment protocol. This compares favorably with other reports on two-staged revision TKA for infection, where 53 to 83% of infections were eradicated (1, 8, 9, 11, 12, 15). Some studies used no defined protocol of treatment, while others had 6 weeks of intra-

venously administered antibiotics followed by 2 weeks without antibiotics before reimplantation. Eradication rates from 89-100% were achieved with various protocols using from from 3 to 12 weeks of intravenously administered antibiotics, where rheumatoid arthritis, high-virulence organisms and the use of antibiotic-free cement were significantly associated with poorer outcome (2, 4, 7, 18). However, one author reports successful cementless revision arthroplasty in 32/33 TKA's (97%) at follow-up 2 to 8 years postsurgery, but he used antibiotic-soaked allografts for this (19).

Thus, in conclusion, our material reflects the various treatment modalities and also a shift in our treatment protocol from arthrodesis towards two-stage revision arthroplasty. Debridement, irrigation and antibiotics as sole initial treatment should be reserved for selected patients with ongoing infection less than a month, maybe even less. We managed to eradicate all infections with a mean follow-up of 2 years postsurgery and were able to maintain the revision prosthesis and a good ROM in 15/17 patients, who were initially treated with revision TKA. We believe this to be a result of a standardized treatment protocol, but also of the low incidence of resistant difficult-to-treat organisms in Denmark in general and in our material in particular.

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SAMENVATTING

H. HUSTED, T. TOFTGAARD JENSEN. Klinische resultaten van de behandeling van geïnfecteerde primaire totale knie protheses.

De behandeling van 26 primaire totale knieprotheses uitgevoerd tussen 1989 en 2000 en verwikkeld van infectie werd geëvalueerd.

Elf patiënten ondergingen een debridement met irrigatie binnen de twee maand na de primaire ingreep of de hematogene besmetting, maar slechts éénmaal betekende dit succes.Bij 25 patiënten werd de prothesis verwijderd : bij één bleef de spacer definitief, bij 17 werd een revisie in twee tijden uitgevoerd, bij 7 werd een arthrodesis uitgevoerd (waarvan één voor een gefaalde revisie) en twee eindigden met een dij amputatie (waarvan ook één na gefaalde revisie).
De follow-up bedroeg gemiddeld twee jaar. Revisie en arthrodesis waren even effectief in het bestrijden van de infectie (89.5% succes). De beweeglijkheid was bij 11 van de 15 gereviseerde knieën beter dan na de primaire ingreep, maar 8 hadden dagelijks pijn.
Het behandelingsprotocol wordt besproken.

RÉSUMÉ

H. HUSTED, T. TOFTGAARD JENSEN. Résultats cliniques du traitement des infections sur arthroplastie totale primaire du genou.

Les auteurs ont traité entre 1989 et 2000, 26 cas successifs d'infection sur arthroplastie primaire du genou. Onze patients ont subi un débridement – lavage réalisé endéans les deux mois de l'arthroplastie primaire ou de la contamination hématogène ; l'infection n'a été éradiquée que dans un seul cas. La prothèse a été enlevée chez 25 patients : 17 d'entre eux ont subi une réimplantation en deux temps, qui a éradiqué l'infection chez 15 d'entre eux ; un patient a reçu un spacer à demeure, 7 ont subi une arthrodèse (dont un après échec d'une reprise d'arthroplastie) et deux ont subi une amputation de cuisse (dont un après échec d'une reprise d'arthroplastie). Le suivi moyen est de 24 mois. L'infection a été guérie de façon aussi efficace par la reprise d'arthroplastie que par l'arthrodèse. Parmi les 15 patients qui ont subi avec succès une reprise d'arthroplastie en deux temps, 11 avaient une amplitude de mobilité meilleure qu'après l'arthroplastie initiale, mais 8 se plaignaient de douleurs quotidiennes.
Les auteurs présentent leur protocole de traitement, qui a éradiqué 15 infections sur 17 (88%) chez les patients qui ont subi une reprise d'arthroplastie.