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# Perioperative factors associated with septic arthritis after arthroplasty

## Prospective multicenter study of 362 knee and 2 651 hip operations

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Perioperative factors associated with late septic arthritis after knee and hip arthroplasties were prospectively investigated. All patients received a short course of perioperative cefuroxime. After a follow-up of 1 year, septic arthritis was diagnosed in 9/362 patients (2.5 percent) after knee arthroplasty and in 17/2651 patients (0.64 percent) after hip arthroplasty.

For the knee, factors associated with septic arthritis after arthroplasty were rheumatoid arthritis, wound infection, an unhealed wound, and a painful,

limited knee function at discharge from the hospital.

For the hip, corresponding risk factors were diabetes, failed fracture osteosynthesis, a breakdown of sterility during operation, wound infection, postoperative urinary tract infection, and an unhealed wound at discharge from the hospital or a difficult rehabilitation course.

Reoperation after knee and hip arthroplasty was also clearly associated with a higher incidence of septic arthritis.

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The purpose of this study was to identify patient-related factors associated with septic arthritis. Data from a prospective trial with 362 knee and 2651 hip arthroplasties were analyzed (Wymenga 1991). All patients were operated on in conventionally-ventilated operating theaters, with a short course of perioperative antibiotics.

### Patients and methods

From July 1986 to July 1988, this trial was performed at 27 hospitals, in order to establish the efficacy of one dose of cefuroxime (1500 mg i.v. at induction of anesthesia, or at least 20 minutes before inflation of the tourniquet in knee replacement); a three-dose regimen (additional doses of 750 mg i.v. after 8 and 16 hrs) served as a control. Only a short summary is given in this section, as details have been reported by Wymenga (1991) and Wymenga et al. (1991).

The most frequent reason for exclusion was the use of gentamicin-impregnated bone cement, which was often used in revision operations. This series therefore represents a rather homogeneous group of patients with relatively few revision operations (7 in the knee group and 66 in the hip group). Further exclusion cri-

teria were the use of other antibiotics and former or current sepsis in the joint. From 455 eligible knee cases, 58 were excluded, and from 3074 eligible hip cases, 278 were excluded. Approximately 80 percent of all consecutive arthroplasties of the participating hospitals were analyzed in the trial.

Reasons for withdrawal were: the wrong type and/or dose of antibiotics; the patient died (not sepsis-related) within 7 days of operation; or a second replacement was performed during the same hospitalization period. From the remaining 397 knee cases 35 were excluded and from the remaining 2796 hip cases 145 were excluded. This left for analysis 362 knee replacements in 345 patients and 2651 hip replacements in 2547 patients.

The end-point of patient participation in the follow-up was defined as reoperation or death. A separate analysis was done on the reoperations (not for infection). The mean follow-up was 12 to 13 months; 15 patients from the hip group were lost to follow-up. The majority (93 percent) of the patients were examined at the outpatient department of the hospital. The remaining patients were examined by their general practitioner or interviewed by telephone by one of the authors (ABW).

In the knee group, septic arthritis was diagnosed in 9 patients (2.5 percent). In the one-dose group (n 175),

3 patients suffered from septic arthritis (1.7 percent, 95 percent confidence limits [0.09 percent-3.33 percent]) and in the three-dose group (n 187) 6 patients (3.2 [0.63-5.77] percent). The difference between the one-dose group and the three-dose group was -1.49 percent (95 percent confidence upper limit 1.78 percent).

In the hip replacement group 17 patients suffered postoperative coxitis (0.64 percent). In the one-dose group (n 1327), 11 patients suffered coxitis (0.83 [0.33-1.32] percent) and in the three-dose group, 6 patients (0.45 [0.08-0.81] percent). The estimated difference between the one-dose group and the three-dose group was 0.38 [0-0.9] percent.

We could not establish that one dose of cefuroxime had the same prophylactic efficacy as a three-dose regimen in knee and hip arthroplasties. A longer follow-up, in cases of septic arthritis, is needed to provide more conclusive data (Wymenga 1991, Wymenga et al. 1991).

### Definitions

Confirmed septic arthritis was defined as a positive culture at reoperation or a draining sinus. Strong evidence of septic arthritis was defined as four or more possible signs of infection: pain on weight-bearing and/or at rest; wound tenderness; fever; abnormal radiography with periosteal reaction; progressive bone resorption; ESR increased 20 mm above the preoperative value or > 35 mm; positive culture of the joint fluid aspirate; arthrogram suggestive of infection; bone scan showing the typical signs of infection; or increased CRP. These two groups of conditions were analyzed together.

Wound infection in the postoperative period was defined as erythema more than one centimeter from the incision. Minor postoperative wound-healing problems were defined as erythema of the wound less than one centimeter from the incision; pus suture; small wound dehiscence; necrosis of the wound edge; and blisters. Distant infections were usually diagnosed on the basis of positive cultures. Urine cultures were considered positive with more than  $10^5$  bacteria per mL.

### Statistics

Septic arthritis rates within subgroups were estimated as crude ratios. Univariate analysis of all potential joint-sepsis-related-factors was performed by the chi-square test. Of all the factors tested, only those with a  $P \leq 0.1$  were considered significant. The number of times the risk for septic arthritis was increased can be expressed as the risk ratio (RR):

$$\text{Percent septic arthritis} = \frac{\text{with factor}}{\text{without factor}}$$

As it is possible for these factors to be related to each other, their importance can be overestimated in a univariate analysis. To overcome this problem, a multivariate logistic regression analysis was used. This method identifies factors that are independent of any other simultaneously occurring factors. In this way, we identified separate risk factors which have an additive effect on the risk of septic arthritis, i.e., the more factors a patient has, the higher the risk of septic arthritis. The relation of the identified factors with septic arthritis may be either causative (e.g., rheumatoid arthritis, due to immune suppression) or circumstantial (e.g., wound infection as a sign of deep infection).

## Results

### The knee

Septic arthritis was found in 9 patients, all of whom underwent reoperation.

### Preoperative and perioperative factors

In the univariate analysis, the following preoperative factors proved not to be associated with septic arthritis: sex, age, the cefuroxime dose (one dose versus three doses), overweight (the Quetelet index:  $\text{kg}/\text{m}^2$ ), physical condition, number of days in hospital before operation, preoperative infections of the urinary tract, lung or skin, a urine sediment with more than 5 leukocytes per field ( $\times 400$ ), the use of steroids, diabetes and previous surgery.

Rheumatoid arthritis was associated with an increased incidence of septic arthritis (Table 1). Analysis of the perioperative data showed that the use of (plain) bone cement versus cementless fixation, a breakdown of sterility, degree of difficulty, operation time, amount of blood loss, surgical experience (staff or resident) and the type of prosthesis (semi- or non-constrained), were not related to septic arthritis.

### Wound healing and other postoperative events

Unrelated to septic arthritis were the postoperative day of vacuum-drain removal, discharge from the vacuum-drain wound after removal of the drain, and indwelling urinary catheters. Conservatively treated orthopedic complications (9), such as nerve injury and fractures, were not related to septic arthritis. Nonorthopedic complications (11), the majority being cardiovascular, were not related either. 5 patients had nonorthopedic operations (urinary or gastrointestinal tract); none of them developed septic arthritis.

Table 1. Analysis of factors in total knee arthroplasty associated with septic arthritis

	Incidence		RR	95%-CI	
	+	-			
Rheumatoid arthritis	5.6	1.2	4.8	(1.2-19)	u
Wound infection	23	1.7	13	(3.8-48)	u
Antibiotics for wound	19	1.2	16	(4.6-57)	u
Wound not healed	31	1.4	20	(4.2-96)	m
Pain + limited function	15	1.6	7.0	(1.5-37)	m

Incidence of septic arthritis with (+) and without (-) factor

RR risk ratio

CI confidence interval

u univariate, m multivariate calculation

Severe hematoma was associated with an increased incidence of septic arthritis (14 percent), as were minor wound-healing problems (5.9 percent). Further analysis of this group showed that particularly patients with skin necrosis at the wound edge and, to a lesser extent, wound dehiscence carried a high risk for septic arthritis. Skin necrosis was not related to previous operations or rheumatoid arthritis. Other minor wound problems, such as erythema less than 1 cm from the incision, pus suture and blisters, were not associated with higher septic arthritis rates. Of 12 patients with skin necrosis, 3 underwent additional attempts to close the skin defect, which succeeded in 2 and failed in 1 patient. Wound drainage was associated with a higher infection incidence (5.9 percent), in the presence of serous drainage 3.9 percent, with blood 7.8 percent and with purulent drainage 25 percent. Wound infection was a strong predictor of septic arthritis (23 percent) as were antibiotics for wound-healing problems (19 percent).

Multivariate regression analysis of the problems in wound healing revealed that only wound infection was independently associated with an increased infection incidence (Table 1). Other wound-healing problems occurred often simultaneously with wound infection, which explains their relation with higher septic arthritis rates in the univariate analysis.

### Distant infections

Urinary tract infection occurred in 19 percent of the patients but there was no relation with septic arthritis. One of 6 patients with a skin ulcer developed septic arthritis. The 2 patients with bacteremia did not develop septic arthritis.

### Factors at discharge from hospital

An increased infection rate was found after the pres-

Table 2. Analysis of factors in hip arthroplasty associated with septic arthritis

	Incidence		RR	95%-CI	
	+	-			
Diabetes	2.0	0.6	3.7	(0.8-18)	m
Failed fracture osteosynth	3.2	0.6	5.4	(1.1-26)	m
Breakdown of sterility	1.9	0.6	3.4	(1.0-11)	m
Wound infection	16	0.3	52	(21-130)	u
Urinary tract infection	2.3	0.4	6.4	(2.5-17)	u
Wound not healed	11	0.6	22.2	(6.8-72)	m
Slow reconvalescence	2.9	0.5	5.2	(1.9-20)	m

See legends Table 1

ence of an unhealed wound (31 percent), elevated temperature (17 percent) and a painful knee with limited function (15 percent) at discharge from the hospital. A prolonged and difficult rehabilitation period was also predictive of septic arthritis (9.5 percent). The multivariate analysis revealed that an unhealed wound and, to a lesser extent, a painful knee with limited function, were independently associated with higher infection rates (Table 1).

### Mechanical reoperations

During the period of hospitalization and follow-up, reoperations were performed for patellofemoral problems (15), fractures (2), prosthetic fracture (1), medial ligament rupture (1), joint stiffness (2), hematoma evacuation (1), instability (1) and neurinoma (1). Septic arthritis was diagnosed after 2 of 24 reoperations (1 tuberositas transfer performed without perioperative antibiotics, 1 patellar tendon repair after traumatic rupture, and 1 arthrotomy for joint stiffness). The incidence without reoperation was 2.7 percent.

### The hip

Septic arthritis was confirmed by a positive culture. Confirmed septic arthritis was diagnosed in 14 patients. 3 patients had strong evidence of septic arthritis, of whom 2 underwent reoperation for septic arthritis but had negative cultures despite the clinical evidence. From the third patient, the joint aspirate grew *Staphylococcus aureus*.

### Preoperative and perioperative factors

In the univariate analysis, the following preoperative factors were not associated with an increased incidence of septic arthritis: sex, age, the cefuroxime dose (one dose or three doses), overweight, physical condi-

tion, number of days in hospital before the operation, preoperative infections of the urinary tract, lung or skin, a urine sediment with more than 5 leukocytes per field ( $\times 400$ ), the use of steroids, the orthopedic diagnosis and osteotomy. An increased septic arthritis incidence was found in patients with diabetes using medication for the disease (2 percent), after revision of a failed hemi- or total hip prosthesis (1.5 percent), and arthroplasty after failed fracture osteosynthesis (3.2 percent).

Among the perioperative factors, the surgical approach (lateral or posterolateral), the use of bone cement versus fixation without cement, the degree of difficulty of the operation, the operation time, the amount of blood loss, and the experience of the surgeon, did not display a relationship with septic arthritis, nor did positive cultures of the joint capsule, taken during arthroplasty. A breakdown of sterility, in more than 90 percent of the cases caused by a hole in the inner surgical glove, occurred in 6 percent of the operations and was associated with an increased incidence of septic arthritis (1.91 percent).

Multivariate analysis showed that diabetes, failed fracture treatment and a breakdown of sterility, were each independently associated with septic arthritis (Table 2).

### *Wound healing and other postoperative events*

Univariate analysis showed that minor wound-healing problems, the day of vacuum-drain removal and the use of an indwelling urinary catheter, were not related to septic arthritis nor were conservatively treated orthopedic (94) and nonorthopedic complications (88), which mainly occurred in the cardiovascular and gastrointestinal tract. Patients who underwent additional nonorthopedic surgery on the urinary tract (7), the gastrointestinal tract (10), pacemaker implantation (3), skin necrotomy (4) and lower leg amputation (1) during the period of hospitalization, did not develop septic arthritis either.

Moderate and severe hematomas were clearly related to septic arthritis (1.7 percent and 2.8 percent) as was early postoperative wound drainage (2.9 percent). The incidence after drainage of serous fluid was 1.4 percent, blood 6.9 percent, and pus 20 percent. The incidence of septic arthritis after discharge from the drain orifice arising more than 24 hours after removal of the drain was 1.3 percent, after wound infection 16 percent and after prescription of antibiotics for wound problems 98 percent.

The multivariate analysis revealed that wound infection was the only event that was independently related to septic arthritis (Table 2).

### *Distant infections*

Postoperative gastrointestinal and pulmonary infections (42) were not related to septic arthritis. Patients with skin infections, mainly decubitus sores on the sacrum and calcaneus, had an increased incidence (7 percent). The urinary tract was the most frequent site of distant infection (15 percent) and the septic arthritis incidence was 2.3 percent. One of 9 patients with bacteremia developed septic arthritis.

Multivariate analysis revealed that urinary tract infection was the only independently related factor (Table 2).

### *Factors at discharge from hospital*

Septic arthritis incidence was increased after discharge from the hospital of patients with an unhealed wound (11 percent), an elevated temperature (3.5 percent), a painful and limited function of the hip (2.1 percent), and a prolonged and difficult postoperative rehabilitation period (2.9 percent).

Multivariate analysis revealed that an unhealed wound at discharge from hospital and a prolonged and difficult period of rehabilitation were independently associated with septic arthritis (Table 2).

### *Mechanical reoperations*

The most frequent indications for reoperation were femoral loosening of a prosthesis which had been applied without cement, and dislocations. 4 out of the 64 patients with these complications developed septic arthritis versus 17 out of 2587 without reintervention. 3 infections occurred after reoperation for dislocation, and one after femoral stem revision.

## **Discussion**

Rheumatoid arthritis is an important risk factor for septic arthritis after knee and hip arthroplasty (Fitzgerald et al. 1977, Andrews et al. 1981, Salvati et al. 1982, Insall et al. 1984, Lidwell et al. 1984, Grogan et al. 1986, Johnson et al. 1986, Bengtson and Knutson 1991). We could not confirm this for hip arthroplasty in this series, perhaps due to the limited numbers or the relatively short follow-up; Poss et al. (1984) found an increased sepsis rate in rheumatoid arthritis only after a longer follow-up.

In knee arthroplasty, diabetes and previous operations were not identified as risk factors in contrast to others (Knutson et al. 1986, Rand et al. 1989), but the number of patients with these conditions was low. In

hip arthroplasty, diabetes was associated with septic arthritis (Nelson 1987), but not always (Fitzgerald et al. 1977). As in many other studies, failed fracture osteosynthesis was a risk factor for septic arthritis (Fitzgerald et al. 1977, Nelson 1980, Andrews et al. 1981, Surin et al. 1983, Poss et al. 1984), except in two large series (Salvati et al. 1982, Lidwell et al. 1984).

There is some evidence that gentamicin bone cement in combination with systemic antibiotics, reduces septic arthritis in hip replacement (Josefsson et al. 1981, Trippel 1986, Lynch et al. 1987). We therefore suggest its use in cemented knee and hip arthroplasty in all patients with rheumatoid arthritis, diabetes and previous operations. In view of the relatively high incidence of septic arthritis in knee replacement, as compared with hip replacement, even without risk factors, it might be beneficial for all cemented knee replacements. In patients who have undergone previous surgery, it is obvious that low-grade sepsis should always be excluded (Fitzgerald et al. 1977, Poss et al. 1984) using all the necessary diagnostic methods, including culturing of multiple biopsies from periprosthetic tissue (Kamme et al. 1981, Gristina et al. 1984).

We found an increased septic arthritis rate after a breakdown of sterility (more than 90 percent a ruptured inner surgical glove). It is logical to theorize that contamination with skin flora from the surgeon's hand may enhance septic arthritis. However, McCue (1980) found perforations in 15 percent of the inner gloves used in hip arthroplasty, but none of the gloves grew bacteria colonies. The clinical significance of our observation is therefore not clear.

Many authors have reported that delayed wound healing is related to septic arthritis in knee arthroplasty (Petty et al. 1975, Brodersen et al. 1979, Kaufer et al. 1981, Bliss et al. 1985, Johnson et al. 1986, Bengtson et al. 1989, Rand et al. 1989) but the relative importance of various wound-healing problems was not clear. In this prospective study, wound infection as well as skin necrosis or wound dehiscence were found to be important. In hip arthroplasty only wound infection was clearly associated with septic arthritis.

The 18 percent incidence of minor wound problems after knee arthroplasty in our series was high but comparable with the 5-25 percent mentioned in other reports (Insall et al. 1979, Jones et al. 1979, Kaufer et al. 1981, Johnson et al. 1986). Among the minor wound problems, only wound edge necrosis and wound dehiscence were clearly related to septic arthritis. Only patients who in addition also suffered from other wound problems such as erythema or drainage developed septic arthritis. Other authors (Brodersen et al. 1979, Knutson 1984, Bengtson et al. 1989)

have reported 10-33 percent septic arthritis in patients with skin necrosis and wound dehiscence. Vascularized musculocutaneous skin flaps should be used to salvage the joint if the necrosis is progressive (Sanders et al. 1981, Saliban et al. 1983, Bengtson et al. 1987). We could not confirm the relationship between necrosis and rheumatoid arthritis or previous surgery (Sanders et al. 1981, Saliban et al. 1983, Insall et al. 1984, Bengtson et al. 1987).

Secondary infection could have occurred through skin defects, as suggested by Bengtson and Knutson (1991), but this is in contradiction to the findings of the M.R.C. study (Lidwell et al. 1984) which revealed that the majority of wound infections in patients who developed later septic arthritis began during the operation.

An attempt should be made to reduce the incidence of septic arthritis in patients with wound infections (Fitzgerald 1977, Lidwell 1986) by early diagnosis and adequate antibiotic treatment. Treatment should be guided by the results of the wound culture, because when septic arthritis is preceded by wound infection, the organisms isolated from the joint are the same as those isolated from the postoperative wound in the large majority of cases (Lidwell et al. 1984). There is clearly no indication for antibiotic treatment in patients with a single minor wound problem, drainage or hematoma. We agree with Fitzgerald (1977) that, in the case of wound infection in combination with a draining hematoma, surgical evacuation hematoma is indicated. This procedure salvaged 3 out of the 4 hip replacements with these complications in our series.

A positive urinary tract culture was associated with septic arthritis, as has been reported in other series (Fitzgerald et al. 1977, Surin et al. 1983), although one other study did not find a significant relationship (Hill et al. 1981). Usually no clear correlation can be found between the pathogens of urinary tract infections and hip septic arthritis, so a causal relationship cannot be established. There are, however, a number of case reports with documented postoperative hematogenous seeding from the urinary tract (Benson et al. 1975, Donovan et al. 1976, Irvine et al. 1976, Wroblewski et al. 1980), and these infections should be treated adequately.

An unhealed wound at discharge from hospital was also associated with septic arthritis and undoubtedly mirrors the relation with wound infection. A prolonged and difficult convalescence period or a painful and limited function was also related to septic arthritis, as can be expected; many patients with low-grade septic arthritis stated that they were already suffering from pain immediately after the operation (van Rens et al. 1984). Such patients, who are also at risk, should have frequent check-ups at the outpatient department.

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