ORIGINAL ARTICLE

Infection in primary total knee replacement

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Objectives To determine the infection rate and identify the risk factors of primary total knee replacement in a general hospital and discuss possible preventive measure.

Design Retrospective study.

Setting Regional hospital, Hong Kong.

Patients All cases of primary total knee replacement performed between the period July 1997 and June 2006 were reviewed.

Main outcome measures Infection rate of primary total knee replacement and its relationship to risk factors.

Results In the defined period, 479 total knee replacements were performed in 353 patients (291 female and 62 male); 105 women and 21 men had bilateral replacements. The mean patient age was 69 (range, 40-88) years. In all, 447 knees had osteoarthritis, and 32 had rheumatoid arthritis. The mean follow-up period was 46 (range, 1-107) months; 345 knees were followed up longer than 24 months, but seven had no postoperative follow-up. Wound infection was defined by clinical, bacteriological, and/or histological examination. Primary total knee replacement was invariably performed in a theatre with vertical laminar flow, under prophylactic antibiotic cover, and body exhaust suits, water impermeable gowns, and double gloves were always used. The overall infection rate was 3.0% (14/472); the acute deep infection rate (within 4 weeks) was 0.2% (1/472), the delayed deep infection rate (4 weeks-2 years) was 0.6% (2/345). The superficial infection rate was 1.9% (9/472) and the late deep infection rate (after 2 years) was 0.6% (2/345). Diabetic patients had a three-fold higher risk of infection than non-diabetic patients, though this difference did not attain statistical significance (P=0.077).

Conclusions Our infection rates for primary total knee replacement were comparable to those encountered internationally.

Introduction

As the average population age in Hong Kong is getting older, total knee replacement (TKR) is becoming more common. Infection after TKR is catastrophic both to the patients and surgeons. It can cause persistent pain, especially at rest and at night. It also leads to recurrent knee swelling and affects the walking ability. Worse still, it destroys the periarticular bone and causes prosthesis loosening, and may end up in septicaemia and various other life-threatening consequences. Reported rates of deep infection in the literature are about 2%,[1,2] and about 0.4% for those ensuing within 3 months after operation.[1] Risk factors have been identified,[1,2] and various methods have been devised to decrease the chance of this complication.[1-4]

In this study, we aimed to determine the infection rate of primary TKR in the Alice Ho Miu Ling Nethersole Hospital (AHNH). We also attempted to determine the risk of infection in our local setting and ways of minimising the risk.

Methods

This was a retrospective review of all primary TKRs undertaken in the AHNH from July 1997 to June 2006 inclusive. One medical officer reviewed all relevant medical and computer records. A total of 479 primary TKRs were performed in 353 patients; 263 right knees and 216

Key words
Arthroplasty, replacement, knee; Infection

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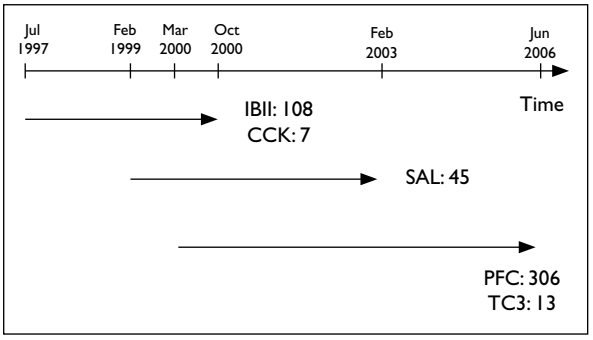

FIG 1. Models of total knee replacement changed with time

Number next to the model name indicates the number of total knee replacements performed with that model; IBII denotes Insall-Burstein II, CCK Constrained Condylar Knee, SAL Self-Aligning Knee, PFC Press-Fit Condylar, and TC3 Total Condylar III

首次全膝關節置換術後的細菌感染

目的 檢討在一所普通科醫院內進行首次全膝關節置換術後的感染率和確定其危險因素，並討論可行的預防措施。

設計 回顧研究。

安排 香港一所地區醫院。

患者 所有於1997年7月至2006年6月期間完成首次全膝關節置換術的個案。

主要結果測量 首次全膝關節置換術後的感染率與有關危險因素。

結果 研究期間為353名患者（291名女性和62名男性）進行共479次全膝關節置換術；105名女患者和21名男患者須進行雙側全膝關節置換。患者平均年齡為69（介乎40-88）歲。447個膝關節病變為退化性關節炎，32個為類風濕關節炎。平均術後覆診期為46（介乎1-107）個月，當中345個膝蓋手術後的覆診期超過24個月，但另外7個膝蓋手術則沒有隨訪。研究以臨床方法、細菌培植，以及/或者組織病理診斷關節感染；而手術過程亦以垂直式無塵操作台、消毒頭套、防水手術袍，雙重手套等來減低感染機會。整體感染率為3.0%（14/472）；其中急性深層感染率（4星期內）為0.2%（1/472），延遲深層感染率（4星期至2年）則為0.6%（2/345）。表面感染率為1.9%（9/472），而後期感染率（2年後）則為0.6%（2/345）。縱使未達統計顯著性（P=0.077），但研究顯示糖尿病患者的感染機會較非糖尿病患者高出3倍。

結論 首次全膝關節置換術的感染率與其他地方相若。

left knees. In all, 291 patients were female and 62 were male; 105 female and 21 male patients had bilateral TKRs (on separate operation sessions). Thus, about one in three patients had bilateral replacements. The mean patient age was 69 (range, 40-88) years. A total of 447 knees had osteoarthritis, and 32 had rheumatoid or seronegative arthritis.

Models of TKR changed with time (Fig 1). All TKRs were cemented. Insall-Burstein II (Zimmer, Warsaw, Indiana, US) and Press-Fit-Condylar Sigma (Depuy-Johnson and Johnson, Warsaw, US) were fixed bearing posterior stabilised models. Self-Aligning Knee (Protek-Sulzer Orthopedics CH-6341, Baar, Switzerland) was mobile bearing posterior cruciate ligament retaining model. Constrained Condylar Knee (CCK; Zimmer, Warsaw, Indiana, US) and Total Condylar III (TC3; Depuy-Johnson and Johnson, Warsaw, US) were semi-constrained models, which were used whenever there was significant collateral ligament insufficiency.

The mean follow-up period was 46 (range, 1-107) months. Seven TKRs in five patients (4 female and one male) had no postoperative follow-up as they might have moved to another geographical location or being followed up by family physicians; they all had osteoarthritis. A total of 127 TKRs had less than 24 months' follow-up, whilst 345 had longer follow-up. In all, 14 female and 4 male patients (with 24 TKRs) died during follow-up; all due to unrelated causes, and mean follow-up before death was 47 (range, 8-97) months. A further 33 females and 8 males (50 TKRs) were lost to follow-up; their mean follow-up was 31 (range, 2-81) months.

Statistical analysis was carried out by the Fisher's exact test. Statistical significance was defined as $P<0.05$. Relationships between infection, diabetes mellitus, the surgeon's status (trainer or trainee), operating time, and preoperative knee range and fixed flexion contracture were analysed.

Definitions in the study

Wound infection was defined by several means. The first depended on clinical signs (fever, wound erythema, and/or discharge), for which the responsible surgeon prescribed intravenous antibiotic treatment. Among imaging methods, X-rays showing evidence of radiolucency or osteolysis, bone scan and indium-labelled white blood cell scans showing focal hot uptake around the prosthesis were also taken to indicate infection. For bacteriological examination, blood culture, arthrocentesis and intra-operative granulation tissue culture that yielded organisms were also regarded as evidence of infection. Histological examination of intra-operative tissue could also be taken as suggestive of infection,[5] as could intra-operative findings of pus, turbid fluid, unhealthy granulation tissue, synovitis, bone destruction, and prosthesis loosening.

Infection involving skin and subcutaneous layer was termed 'superficial wound infection'. Infection involving bone and prosthesis was termed 'deep wound infection', which was further classified according to its onset after TKR:

FIG 2. Intra-operative prophylactic measures

- Acute deep infection: within 4 weeks, which marked the period within which salvage of the prosthesis by thorough debridement was feasible.[6]
- Delayed deep infection: presenting after 4 weeks but within 2 years of TKR.
- Late deep infection: presented more than 2 years after TKR, with primary wound healing without clinical symptoms and signs of infection for the first 2 years. This type of infection was considered haematogenous in origin.[7]

Preoperative assessment programme

Each patient scheduled to have TKR was admitted to our day ward 2 weeks before the index operation. A medical officer performed clinical examination, blood and urine tests to screen for septic foci. A dentist examined the teeth if necessary. Chest and knee X-rays were taken. The operation was postponed or cancelled if any septic source could not be cleared before the scheduled date of surgery.

A doctor, a nurse, and a physiotherapist undertook to educate the patient; a video-tape and pamphlet were provided. The importance of lifelong care for the prosthesis was reinforced. The need for promptly identifying and treating any septic lesion to prevent late prosthesis infection was explained. An anaesthetist also assessed the patient to determine their fitness for operation and explain the mode of anaesthesia.

Intra-operative prophylactic measures

One operating theatre was specifically assigned for total joint replacements, as it was equipped with vertical laminar flow unit (Fig 2). The air-flow was 5253 m^3 per hour. The air exchange rate was 29.2 m^3 per hour. The operating room temperature was set at 20°C and the humidity at 60%. Microbiological air sampling was last performed in August 2006 and 12 sampling sites studied. Bacterial counts were zero at 10 sites, 2 colony-forming units (CFU)/m^3 were found in the exhausted air damper and 4 CFU/m^3 in the scrub room centre. This fitted into the definition of ultraclean air (with <10 CFU/m^3) by Lidwell et al.[3]

We used body exhaust suits, water repellant paper gowns and drapes, and double gloves. We prepared the entire lower limb distal to tourniquet with betadine twice; once by an assistant surgeon before gowning, and once more by the chief surgeon, and routinely changed the outer pair of gloves after draping. Prophylactic antibiotic (1 g of cefazolin) was given at induction of anaesthesia before applying the tourniquet. Meticulous haemostasis and soft tissue handling were achieved at operation. Three more doses of antibiotic were given postoperatively over 24 hours.

Results

Wound infection

Table 1 details the different types of wound infections encountered, the year of operation, the operation, how the infection was diagnosed, the type of bacteria, and treatment method. Of the 472 knees in the 348 patients who were followed up, nine (1.9%) cases had superficial wound infections that all healed well after treatment. They enjoyed a painless knee without any sign of infection at the latest follow-up.

One (0.2%) of the cases had acute deep infection within 2 weeks of the operation and underwent wound debridement and intravenous antibiotic treatment. Because of persistent methicillin-resistant *Staphylococcus aureus* (MRSA) infection, two-stage revision surgery was performed about 3 months after the index operation. Recurrence of infection was found at about 5 months, after revision of the TKR. She refused further surgery and long-term suppressive antibiotics with rifampicin and fusidin were given. At her latest follow-up, she was wheelchair-bound.

Of the 345 knees that had longer than 2 years of follow-up, two (0.6%) cases developed delayed deep infection. One woman had had a TKR in 2002 and manifested recurrent knee swelling starting 6 months after the operation. Arthrocentesis yielded coagulase-negative *Staphylococcus*. She refused revision surgery, and started long-term antibiotic treatment with rifampicin and septrin. At her latest follow-up, she could walk with a quadripod for 20 minutes. Another man who had a TKR in 2003 developed a painful, erythematous, swollen knee 3 months after the operation. Arthrocentesis yielded methicillin-sensitive *Staphylococcus aureus* (MSSA). He was successfully treated with a 2-stage revision

TABLE 1. Types of infection and management

Infection	Year	Diagnosis*	Bacteria†	Treatment‡
Superficial wound	2000	C	-ve	IV ab
	2000	C	-ve	IV ab
	2001	C/B	MRSA	IV ab
	2002	C	-ve	IV ab
	2002	C/O	-ve	IV ab, wound debridement
	2002	C/B	Acinetobacter	IV ab, wound debridement
	2003	C	-ve	IV ab
	2004	C/B	MRSA	IV ab
	2004	C	-ve	IV ab
Acute deep	2001	C/O/B	MRSA	2-stage revision and ab
Delayed deep	2002	C/B	CNS	Long-term suppressive ab
	2003	C/R/B/H	MSSA	2-stage revision and ab
Late deep	2000	R (WBC scan)	-ve	Removal of prosthesis and cement spacer and ab in 2006
	2002	C/B/H	MSSA	Removal of prosthesis and cement spacer and ab in 2006

* B denotes bacteriological, C clinical, O operative finding, H histological, R radiological, and WBC white blood cell
† MRSA denotes methicillin-resistant *Staphylococcus aureus*, MSSA methicillin-sensitive *Staphylococcus aureus*, and CNS coagulase-negative *Staphylococcus*
‡ IV ab denotes intravenous antibiotics

TKR. He could walk unaided for more than an hour.

Two (0.6%) cases developed late deep infection. One woman had her TKR in 2000 and complained of progressive increase in knee pain since 2004, but defaulted follow-up until 2006. Knee aspiration revealed no bacterial growth. An indium-labelled white blood cell scan suggested low-grade infection. Removal of the prosthesis and insertion of antibiotic cement spacer was performed. She could not undergo second-stage TKR because she developed renal failure and congestive heart failure. At latest follow-up, she was wheelchair-bound. Another woman had a TKR in 2002. She enjoyed a painless functional knee until 2006, when she started experiencing recurrent leg cellulitis attributed to poor diabetic control. She then complained of a painful swollen knee. Knee aspiration revealed MSSA. Removal of prosthesis and insertion of antibiotic cement spacer was undertaken as a definitive procedure, because of the risk of recurrent infection due to her poor skin condition.

Risk factors

Five (6.1%) TKRs out of 82 in diabetic patients and 9/390 (2.3%) in non-diabetic patients developed wound infection, but this difference was not statistically significant (P=0.077). The greater the preoperative fixed flexion contracture (FFC) and the smaller the range of movement (ROM) of the knee, the more difficult was the operation. The preoperative FFC and ROM of the infected group of TKRs were similar to those in the non-infected group (Table 2), as were the operating times (about 120 minutes).

Nine (3.3%) of 271 knees in the trainer group and 3/201 (1.5%) in the trainee group of TKRs developed infection, but this difference was not statistically significant (P=0.251). None of the 32 rheumatoid arthritis patients (including none of the four who were Cushingoid) developed postoperative wound infection. None of the 20 TKRs using semi-constrained models (CCK, TC3) became infected.

TABLE 2. Mean preoperative knee fixed flexion contracture, range of movement, and operating time (according to development of postoperative infection)

Item	Total knee replacement, mean (range)		P value
	Infected	Non-infected	
Fixed flexion contracture	8.8° (0°-20°)	8.7° (0°-50°)	0.991
Range of movement	91.2° (40°-115°)	98.3° (0°-125°)	0.282
Operating time (mins)	117.5 (87-167)	122.3 (72-204)	0.508

Discussion

Prevention being better than cure, various methods were used to reduce the infection risk of TKR. The preoperative assessment programme was useful in identifying risk factors. Ayers et al[2] recommended open skin lesion should be treated promptly, and a 3-month interval of intact dermis over a previous ulceration should be present. Recurrent urinary tract infection and any associated structural causes should be identified and treated before TKR. For patients who had chronic uncorrectable urinary tract infection and accepted the higher risk of infection, lifelong antibiotic suppression to minimise the risk of immediate postoperative infection and late haematogenous seeding has been advocated.[2]

Prophylactic antibiotics administered immediately before the operation is one of the well-known interventions for this purpose, and can achieve adequate bactericidal levels in any haematoma that accumulates. The two most prevalent organisms responsible for infection in TKRs are *Staphylococcus aureus* and *Staphylococcus epidermidis*.[1,2,6] First-generation cephalosporins usually provide excellent cover for the staphylococcal species. In our study, we routinely used cefazolin for prophylaxis. In all, seven of 14 infected TKRs had positive cultures; MSSA caused two of the infections, and MRSA caused three. One patient acquired a late infection with MSSA, which was presumed to be unrelated to the use of prophylactic antibiotic.

Vertical laminar flow and body exhaust suits were also very important. In a multicentre study reported in 1982, Lidwell et al[3] described the effect of ultraclean air and body exhaust suits on deep sepsis in total joint replacement. Vertical laminar flow could reduce the number of bacteria-carrying particles in air close to the operation site from 164 CFU/m^3 to 2 CFU/m^3, even when the operating team was wearing conventional surgical clothing. When body exhaust suits were used, the bacterial count dropped to 0.4 CFU/m^3. The infection rate in the conventional ventilation group was 1.5% (63/4133), while that in ultraclean air group was 0.6% (23/3922). Blom et al[4] reported a drop in infection rate in primary TKR from 4.4% in 1986 to 1% in 2004 (after the introduction of stringent antibiotic prophylaxis, occlusive clothing, and vertical laminar flow). The excellent results of our microbiological air sampling and the low infection rate in our series are consistent with their results.

Diabetes mellitus is a significant risk factor for infection in TKR. Yang et al[8] reported a deep infection rate of 5.5% in 109 TKRs among 86 diabetic patients. England et al[9] encountered a 7% deep infection in 59 TKRs in 40 diabetic patients. Antibiotic-loaded cement was found to be effective in decreasing the infection rate in some studies only. In a prospective randomised study of 340 primary TKRs, Chiu et al[10] found no deep infection in 178 that had been fixed with cefuroxime-loaded cement, while 5/162 (3.1%) ensued after using plain cement (P=0.02). In another study, Chiu et al[11] found no deep prosthetic infection in 41 diabetic patients treated with cefuroxime-loaded cement, but 5/37 (13.5%) in diabetic patients treated with plain cement. Jiranek et al[12] recommended the use of antibiotic-loaded cement for primary total hip replacement (THR) and knee replacement in high-risk patients. We had to consider the disadvantages of its routine use, one being the emergence of drug-resistant organisms. In a group of 25 patients[13] with primary THR and TKR performed for up to 20 years with gentamicin-loaded cement, gentamicin could be detected in joint fluid from 9/15 TKRs and 4/10 THRs. Gentamicin released from cement around the failing implants appeared to lead to 'false-negative' cultures, yet provided selective pressure for the emergence of resistance. In our study, diabetic patients were found to have a three-fold higher risk of infection in their TKR. This difference was not statistically significant. This might have been due to the patient sample being too small, and the mixture of antibiotic-loaded and plain cements used our patients. Because the exact timing as to when these prophylactic practices commenced was not known, further analysis of the latter issue was not feasible.

Peersman et al[1] reported 0.39% for the rate of deep periprosthetic infection occurring within 3 months after primary TKR, and 1.06% for those presenting later than 3 months. The follow-up period was not mentioned in the study, and the cases reported were from patients operated on about 2 to 8 years earlier. By contrast, in our series, two (0.4%) cases of deep infection occurred within 3 months, and three (0.6%) occurred later than 3 months over a follow-up period of up to 107 months. Therefore, our infection control in primary TKR could be regarded as favourable compared to international standards.[1,2,6,7]

Conclusions

Prevention is better than cure; with proper standard practice, the infection rate of primary TKR is low. Diabetic patients have a higher risk of infection in TKR.

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