Decreased cancer risk in patients who have been operated on with total hip and knee arthroplasty for primary osteoarthrosis

A meta-analysis of 6 Nordic cohorts with 73,000 patients

Tuomo Visuri[1], Eero Pukkala[2], Pekka Pulkkinen[3] and Pekka Paavolainen[4]

[1]Department of Surgery, Central Military Hospital, P.O. Box 50, FI-00301 Helsinki, [2]Finnish Cancer Registry, Liisank. 21B, FI-00170 Helsinki, [3]Department of Public Health, University of Helsinki, PI 41, Helsinki, [4]Department of Orthopedics and Rheumaorthopedics, Surgical Hospital, Helsinki University Central Hospital, P.O. Box 263, Helsinki, Finland.
Correspondence: tuomo.visuri@helsinki.fi
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ABSTRACT **3 Nordic cohorts of total hip (THA) and total knee arthroplasty (TKA) in patients operated on for primary osteoarthrosis during 1967–1995 were partly adapted and combined for meta-analysis. THA was performed in 49,000 patients and TKA in 24,000 totaling 497,000 person years. The mean and maximum follow-up times were 6.8 and 30 years, respectively. Standardized incidence ratios (SIRs) with 95% confidence intervals (95% CI) were calculated for the observed and expected number of cancers. The expected numbers were based on national incidence rates. The overall SIRs as well as the site-specific ones were similar in the THA and TKA patients. The observed number of cancers at all sites was 7,639 and the expected one was 8,202 (SIR 0.93, 95% CI 0.91–0.95).**

The SIRs for lung cancer (0.69, 0.64–0.75) and laryngeal cancer (0.64, 0.44–0.92) were reduced. The incidence was also low for cancers of the stomach (SIR 0.76, 0.67–0.84), colon (SIR 0.86, 0.79–0.93) and rectum (SIR 0.89, 0.80–0.98).

Among TKA patients, the only increases in SIRs were seen in cancers of the endometrium (SIR 1.36, 1.05–1.74), prostate (SIR 1.19, 1.02–1.38) and, among both THA and TKA patients, in skin melanoma (combined SIR 1.21, 1.03–1.41).

Millions of osteoarthrotic patients regain the ability to walk without pain with the help of metal-on-metal or plastic-on-metal hip and knee prostheses. Corrosion and wear of the prostheses liberate polyethylene and metallic particles as well as soluble metallic compounds near the prostheses. These products are also widely dispersed throughout the body from hip and knee prostheses (Sunderman et al. 1989, Jacobs et al. 1991, 1996, 1998, 1999, Michel et al. 1991, Henning et al. 1992, Langkamer et al. 1992, Shinto et al. 1993, Case et al. 1994, Kreibich et al. 1996, Brodner et al. 1997, Urban et al. 2000). The modular interface of hip prostheses has been shown to be a specific source of metal release (Mathiessen et al. 1991, Cook et al. 1994, Urban et al. 1994, Jacobs et al. 1995). The corrosion products of the prostheses mainly affect the hemato- and lymphopoietic system and the urinary tract. However, implanted foreign bodies of metallic chromium or titanium and of cobalt-based, chromium-based and titanium-based alloys, stainless steel and organic polymeric materials have not been classified as carcinogenic to humans (IARC monographs 1999).

Hitherto, the site-specific incidences of cancers after total hip arthroplasty (THA) have been studied in 10 and total knee arthroplasty (TKA) in 4 cohorts (Gillespie et al. 1988, 1996, Visuri and Koskenvuo 1991, Mathiessen et al. 1995, Nyren et al. 1995, Lewold et al. 1996, Visuri et al. 1996, Olsen et al. 1999, Paavolainen et al. 1999, 2000). Most of the recent cohort studies show a lower total cancer risk than in the general population (Mathiessen et al. 1995, Visuri et al. 1996, Lewold et al. 1996, Olsen et al. 1999, Paavolainen et al. 1999, 2000).

Table 1. Gender, time of surgery, person-years and follow-up time among pooled patients with total hip and knee arthroplasties for primary arthrosis

Article	Time of surgery (years)	Date of follow-up	Men	Women	Total	Person-years	Mean follow-up time, years per patient
Total hip arthroplasty							
Visuri et al. 1996 [a] (69)	1967–79	1967–1997	516	881	1397	21000	15.1
Olsen et al. 1999 (45)	1977–89	1978–1993	10432	12423	22997	180000	6.9
Paavolainen et al. 2000 (48)	1980–95	1980–1995	9479	15159	24638	173000	7.0
Total			20427	28463	49032	374000	7.6
Total knee arthroplasty							
Lewold et al. 1996 (34)	1975–89	1975–1989	3184	6936	10120	40000	4.0
Olsen et al. 1999 (45)	1977–89	1978–1993	1262	3509	4771	31000	6.4
Paavolainen et al. 1999 (47)	1980–95	1980–1996	2001	7443	9444	52000	5.5
Total			6447	17888	24335	123000	5.1

[a] Updated 2000

Each Nordic country has a population-based cancer register with close to 100% coverage (Tulinius et al. 1992). This permits highly accurate, nationwide, analytical studies on the cancer risk of large populations exposed to possible carcinogens. THA and TKA patients can be traced through national hospital discharge or endoprosthesis registers with the help of personal identification numbers.

We combined the results based on 3 THA and 3 TKA cohorts from Denmark, Finland and Sweden to determine the combined cancer risk in patients operated on for primary hip and knee osteoarthrosis (Lewold et al. 1996, Visuri et al. 1996, Olsen et al. 1999, Paavolainen et al. 1999, 2000).

Material and methods

2 THA and 2 TKA cohorts were obtained from hospital discharge registers (Lewold et al. 1996, Visuri et al. 1996, Olsen et al. 1999) and one each from a national endoprosthesis registry (Paavolainen et al. 1999, 2000). Since the 2 Finnish cohorts (Visuri et al. 1996, Paavolainen et al. 2000) included some of the same persons, the older cohort (Visuri et al. 1996) was reanalyzed to prevent overlapping of person-years at follow-up. In the update analysis, the closing date was changed from 31 December 1993 in the original paper to 31 December 1997. The criteria for inclusion were that all patients were operated on for primary osteoarthrosis and that they all had a metallic hip or knee prosthesis. The types of prostheses were not reported, except in the first Finnish cohort, which consisted of 579 patients with a metal-on-metal McKee-Farrar and 818 patients with plastic-on-metal Brunswik and Lubinus prostheses (Visuri et al. 1996).

The combined THA series consisted of 49,032 patients and the TKA series of 24,335 (Table 1). The total number of patients was 73,367. The female-to-male ratio among THA patients was 1.4 and among TKA patients 2.8. THA patients were followed for 374,000 and TKA patients for 123,000 person-years or a total of 497,000 person years. The mean follow-up time per patient was 7.6 years for THA patients, 5.1 years for TKA patients and 6.8 years for all patients (Table 1). The follow-up of the Danish cohorts (Olsen et al. 1999) started 1 year after the date of hospital discharge and other cohorts on the date of THA or TKA. Follow-up ended at emigration, at death or on the general closing date, whichever occurred first. Closing dates for the newer Finnish THA and TKA cohorts were 31 December 1995 and 1996 (Paavolainen et al. 1999, 2000), respectively, for the Danish THA and TKA cohorts 31 December 1993 (Olsen et al. 1999), and for the Swedish TKA cohort 31 December 1989 (Lewold et al. 1996), respectively.

Lewold et al. (1996) analyzed the incidence of cancers in the respiratory tract, the female genital tract, urinary organs, sarcomas and lymphomas as a group, but reported the findings in all principal kinds of cancer in the other cohorts separately.

Table 2. Cancer incidence in combined Nordic series of hip and knee arthroplasties operated on for primary osteoarthrosis

Site	THA			TKA			ALL			
	Obs	Exp	SIR	Obs	Exp	SIR	Obs	Exp	SIR	95% CI
All sites	5860	6333	0.93	1763	1869	0.94	7623	8202	0.93	0.91–0.95
Upper digestive tract	395	495	0.80	97	118	0.82	492	613	0.80	0.73–0.88
Oral cavity, pharynx	116	123	0.94	17	19	0.90 [a]	133	142	0.94	0.78–1.10
Esophagus	60	74	0.81	7	10	0.70	67	84	0.80	0.62–1.01
Stomach	219	298	0.75	73	89	0.82	292	387	0.76	0.67–0.84
Colorectal	718	814	0.88	207	249	0.83	925	1063	0.87	0.82–0.93
Colon	453	519	0.87	133	162	0.82	586	681	0.86	0.79–0.93
Rectum	265	295	0.90	74	87	0.85	339	382	0.89	0.80–0.98
Liver, biliary tract	152	163	0.93	56	58	0.97	208	221	0.94	0.82–1.07
Liver	75	77	0.97	13	16	0.81 [b]	88	93	0.95	0.76–1.17
Gallbladder	77	86	0.90	18	21	0.86 [b]	95	107	0.89	0.72–1.09
Pancreas	210	232	0.91	71	74	0.96	281	306	0.92	0.81–1.03
Respiratory tract	572	833	0.69	133	172	0.66 [c]	685	1005	0.68 [c]	0.63–0.73
Larynx	30	45	0.67	1	3	0.30 [ba]	31	48	0.64	0.44–0.92
Lung	542	788	0.69	92	126	0.73 [b]	634	914	0.69	0.64–0.75
Breast	582	575	1.01	271	245	1.11	853	820	1.04	0.97–1.11
Female genital tract	306	284	1.08	153	142	1.08 [c]	459	426	1.08 [c]	0.98–1.18
Cervix uteri	49	52	0.94	14	15	0.93 [b]	63	67	0.94	0.72–1.20
Corpus uteri	141	127	1.11	64	47	1.36 [b]	205	174	1.18	1.02–1.34
Ovary	116	105	1.11	30	36	0.83 [b]	146	141	1.04	0.87–1.21
Prostate	478	456	1.05	172	144	1.19	650	600	1.08	1.00–1.17
Urinary tract	527	546	0.97	136	146	0.93 [c]	666	692	0.96 [c]	0.89–1.03
Kidney	176	189	0.93	37	41	0.90 [b]	213	230	0.93	0.81–1.05
Bladder	351	357	0.98	61	58	1.05 [b]	412	415	0.99	0.90–1.09
All skin	803	762	1.05	170	179	0.95 [c]	973	941	1.04 [c]	0.97–1.10
Skin melanoma	126	104	1.21	28	23	1.22 [b]	154	127	1.21	1.03–1.41
Other skin	677	656	1.03	117	127	0.92 [b]	794	785	1.01	0.94–1.08
Brain, nervous system	119	121	0.98	41	40	1.03	160	161	0.99	0.85–1.15
Thyroid gland	32	31	1.03	25	23	1.09	57	54	1.06	0.80–1.37
Bone/soft tissue	25	27	0.93	12	11	1.09 [c]	37	38	0.97	0.69–1.34
Bone	5	4	1.25	2	1	2.00 [b]	7	5	1.40	0.56–2.88
Soft tissue	20	23	0.87	6	5	1.20 [b]	26	28	0.93	0.61–1.36
All hematopoietic	392	372	1.05	130	118	1.10 [c]	522	490	1.07 [c]	0.98–1.16
Non–Hodgkin lymphoma	137	135	1.02	38	31	1.23 [b]	175	166	1.05	0.90–1.22
Hodgkin's disease	15	13	1.15	4	3	1.33 [b]	19	16	1.19	0.72–1.85
Multiple myeloma	90	82	1.10	33	27	1.22	123	109	1.13	0.94–1.34
Leukemia	150	142	1.06	41	41	1.00	191	183	1.04	0.90–1.20

[a] Missing data from Paavolainen et al. (45)
[b] Missing data from Lewold et al. (33)
[c] Includes data from Lewold et al. (33)

Statistics

All cohorts were analyzed, using the same statistical methods. The numbers of cancer cases observed in each of the implant cohorts were compared with the numbers expected on the basis of age-, sex- and calendar year-specific incidence rates from the cancer registers of each country. In this meta-analysis, we added together the observed and expected numbers from each study, and calculated the standardized incidence ratio (SIR)—i.e., the observed number of cases was divided by the expected number. The exact 95% confidence intervals for the SIRs were calculated on the assumption that the numbers of observed cases had a Poisson distribution.

Results (Table 2)

The overall incidence of cancer was lower in all cohorts—i.e., the SIR ranged from 0.86 (0.7–0.9) to 0.98 (0.91–1.05). The observed number of can-

cers was 5,860 for THA and 1,763 in TKA patients and the expected number 6,333 in THA and 1,869 in TKA patients. The SIR was 0.93 (0.90–0.95) in THA and 0.94 (0.90–0.99) in TKA patients. The sex-specific SIRs for all types of cancer were reported in 1 THA cohort (Visuri et al. 1996) and in 2 TKA reports (Lewold et al. 1996, Paavolainen et al. 1999). The combined SIR of these cohorts for males was 0.92 (0.84–0.99) and in females 0.94 (0.88–1.00).

Latency did not increase the risk of cancer in all sites in Finnish cohorts. In the first THA cohort during a 30-year follow-up: the SIR was 0.86 (0.66–1.10) during the first 4 years, 0.92 (0.77–1.08) during 5–14 and 0.98 (0.78–1.22) after 15 years of follow-up (Visuri et al. 1996).

A statistically significant reduction in the risk of stomach cancer was observed in all of the THA and in one of the TKA cohorts; SIR ranged from 0.46 (0.20–0.91) to 0.82 (0.69–0.96). In one TKA series, we found only a 2% reduction in the incidence of stomach cancer (Paavolainen et al. 1999). Both the THA and TKA patients had a significantly lower combined incidence of cancer in the upper gastrointestinal tract.

All 3 TKA and 2 THA cohorts (Olsen et al. 1999, Paavolainen et al. 2000) showed a slight reduction in colon cancer—i.e., SIRs ranged from 0.67 (0.5–0.9) to 0.96 (0.73–1.24). In one THA cohort (Visuri et al. 1996), the SIR was 1.20 (0.76–1.80). A slight reduction was also noted in rectum cancer—i.e., SIRS from 0.78 (0.5–1.2) to 0.94 (0.61–1.37) in 5 cohorts, but in 1, it was slightly increased (SIR 1.27, 0.74–2.02) (Visuri et al. 1996). Thus, colorectal cancers were decreased by 12% among THA, by 17% among TKA patients and by 13% in the combined series.

The effects of the follow-up time on stomach and colon cancer were reported in 2 THA and 2 TKA cohorts (Olsen et al. 1999, Paavolainen et al. 1999, 2000). The combined SIRs of these cohorts for stomach cancer were low before and after a 10-year follow-up—i.e., being 0.77 (0.67–0.87) and 0.73 (0.48–1.07), respectively, but not those of colon cancer after 10 years—i.e., 0.85 (0.78–0.94) and 0.94 (0.74–1.18), respectively.

All cohorts showed a lowering incidence of lung cancer—i.e., SIRs ranging from 0.45 (0.27–0.71) to 0.78 (0.57–1.04). The combined SIRs in all THA patients were 0.69, and 0.73 in TKA patients. A very low incidence of lung cancer was seen in the first Finnish THA series among men over 60 years of age (SIR 0.45, 0.24–0.74). In this cohort, the SIR remained low throughout the entire follow-up period of 15 years (Visuri et al. 1996). This was also noted among Finnish TKA patients (Paavolainen et al. 1999). In the combined large Finnish THA and TKA cohort, the SIRs for the incidence of lung cancer during the first 10 years were 0.64 (0.56–0.73) and thereafter 0.75 (0.48–1.12) (Paavolainen et al. 1999, 2000). We found a significant reduction in laryngeal cancer with a combined SIR of 0.64.

The incidence of female genital cancer was increased by 8% due to a significant excess of endometrial cancer, especially among all the TKA patients (SIR 1.36 (1.05–1.74)).

The incidence of prostate cancer was close to the expected value or slightly increased in all cohorts; in the Finnish TKA series, it was significantly increased—i.e., SIR 1.48 (1.19–1.84) (Paavolainen et al. 1999).

There was a higher incidence of skin melanoma in both for the THA (SIR 1.47 (1.17–1.83)) and TKA (SIR 1.53 (0.85–2.52)) patients in the Olsen et al. series (1999), but in the Finnish cohorts, the incidence of melanoma remained close to the expected values (Paavolainen et al. 1999, 2000). In the combined series, it increased significantly by 21%.

Bone and soft tissue sarcomas were uncommon. The incidence of bone sarcomas was slightly increased and of soft tissue sarcomas slightly decreased, but the findings for all sarcomas were in line with the expected values.

All forms of combined hematopoietic cancers, except that of leukemia in TKA patients, were slightly, but not significantly increased.

Discussion

Osteoarthrosis was chosen for the preoperative diagnosis, because it has not been known to be related to cancer (Lindberg et al. 1985, Typpö 1985), although no large epidemiological studies have been done.

The only cohort hitherto reported to have no reduction the incidence of cancer at all sites was the large Swedish cohort by Nyren et al. (1995), which included patients operated on for late or acute fracture (26%), for rheumatoid arthritis (5%) and for causes other than osteoarthrosis (5%). Their patients had a 3% excess of total cancer, which was due to an increase in kidney (SIR 1.31, 1.13–1.51) and prostate cancers (1.13, 1.04–1.22) and melanoma (SIR 1.23, 1.00–1.50).

Cohorts including diagnoses other than primary osteoarthrosis were excluded (Gillespie et al. 1988, 1996, Visuri and Koskenvuo 1991, Mathiessen et al. 1995, Nyren et al. 1995). Rheumatoid patients from Nordic countries have had higher incidences of lymphomas, lung cancer and non-melanoma skin cancer and lower incidences of stomach, colon and rectum cancers (Isomäki et al. 1978, Gridley et al. 1993, Mellemkjaer et al. 1996a).

Bias caused by differences in the incidence of cancer among social classes is supposed to be eliminated by the fact that all Nordic citizens have an equal right to undergo THA and TKA operations (Nyren et al. 1995, Paavolainen et al. 2000). However, preoperative selection of patients who have no severe illnesses probably causes a bias towards a cohort with healthier life habits (even as regards the cause of cancer)—i.e., to those in the upper classes.

THA and TKA patients who are operated on for primary osteoarthrosis have a longer life expectancy than the general population (Holmberg 1992, Visuri et al. 1994, Garelick et al. 1998, Ritter et al. 1998, Schröder et al. 1998, Lie et al. 2000). The effect of including healthy patients has been used to explain the total reduction in the incidence of cancer among THA patients. However, this effect was seen in only certain types of cancer in our series, which may indicate other causes of the reduction in these cancers.

A decrease in the incidence of cancer at all sites among THA patients has reduced cancer mortality (Visuri et al. 1997, Paavolainen et al. 2002). Decreases in lung and stomach cancers, that have a high mortality, reinforce this effect. An increased in life expectancy of THA and TKA patients operated on for primary osteoarthrosis may be due to the reduction in cancer mortality.

Common risk factors for severe osteoarthrosis and cancer

About 80% of the etiology of idiopathic coxarthrosis requiring endoprosthetic surgery was caused by a heavy physical workload, sports and overweight (Olsen et al. 1994). Much physical activity, sports and strenuous work are etiological factors for severe osteoarthrosis of the hip and knee in both men and women (Vingård et al. 1993, 1997, 1998, Olsen et al. 1994, Sandmark and Vingård 1999).

Little physical activity may increase the risk of colon cancer and possibly also of cancers related to changes in endogenous hormones, such as cancer of the breast (Winther et al. 1997). Therefore, much physical activity increases the risk of severe hip ostearthrosis, but at the same time reduces that of colon cancer.

Obesity is an established risk factor for endometrial cancer, renal cancer in both men and women and gallbladder cancer in women (Winther et al. 1997). It is also a significant risk factor for bilateral osteoarthrosis of the knee, but not for bilateral hip osteoarthrosis (Stürmer et al. 2000). Consequently, the incidence of endometrial cancer was significantly higher among TKA patients, but not among THA patients. Both groups had a slightly lower incidence of renal and gallbladder cancer.

Gastrointestinal cancers

In the present meta-analysis, the SIR for stomach cancer was 0.76 (0.67–0.84). In the Swedish THA cohort (Nyren et al. 1995), the relative risk of gastric cancer declined among men and women, to a total SIR of 0.58 (0.39–0.84). The incidence of cancer in the upper gastrointestinal tract was also slightly lower in another Swedish THA series (SIR 0.88, 0.68–1.11) (Mathiessen et al. 1995). On the other hand, the incidence of stomach cancer in the unoperated patients with hip or knee osteoarthrosis was similar (SIR 1.0, 0.9–1.2) to that in the general population in the Danish series (Olsen et al. 1999). A reduction in the incidence of gastric cancer among implant patients may therefore be due to patient selection or the implant or the adjuvant treatment of these patients.

Helicobacter pylori infection is an established risk factor for stomach cancer (IARC Monographs 1994). Early use of antibiotics for prophylaxis and treatment of respiratory infections might be

of value in reducing infections with H. pylori. Both long-term antibiotic treatment before surgery and prophylactic antibiotic treatment reduced the incidence of gastric cancer in THA patients. This effect seemed to be more marked after 5 years than after a shorter follow-up, although the reduction in the level of H. pylori antibody was not much greater among THA than control patients (Akre et al. 2000).

Patients with pernicious anemia run a higher risk of gastric cancer (Brinton et al. 1989, Hsing et al. 1993, Mellemkjaer et al. 1996b). An increase in the levels of serum cobalt is the commonest after THAs and TKAs using cobalt chrome (Sunderman et al. 1989, Michel et al. 1991, Henning et al. 1992, Jacobs et al. 1996, 1998, Kreibich et al. 1996, Brodner et al. 1997, Schaffer 1999). Cobalt is an essential trace element for vitamin B12. We do not know whether the human body can use the cobalt ions released from implants to form vitamin B12 and to prevent pernicious anemia followed by gastric cancer.

We found a reduction in the incidence of colon and rectum cancer although, since the cohort is thought to have a bias towards the upper social classes, somewhat higher SIRs would have been expected (Pukkala 1995). Some experimental and epidemiological evidence suggests that nonsteroidal anti-inflammatory drugs (NSAIDs), especially aspirin, can prevent the development of colorectal cancers by increasing apoptosis (Muscat et al. 1994, Agarwal et al. 1999, Hawk et al. 1999). In the elderly population, long-term use of NSAIDs nearly halved the risk of colon cancer (Smalley et al. 1999). Most of the osteoarthrotic patients have taken these drugs for long periods before surgery. THA effectively relieves hip pain and the use of these drugs decreased significantly after the operation (Visuri et al. 1985). The preventive effect of NSAIDs may persist, despite their reduced use after surgery. This effect was most marked when they had been taken 11–15 years before the diagnosis of cancer (Collet et al. 1999). The incidence of colorectal cancer in the unoperated Danish patients with knee or hip osteoarthrosis was not reduced (Olsen et al. 1999).

Respiratory tract cancers

The most striking feature was the low incidence of lung cancer, observed in all analyzed cohorts. A slight or moderate reduction in this incidence was also observed in two Swedish cohorts: among men (SIR 0.84, 0.72–0.97) (Nyren et al. 1995) and among all patients (SIR 0.76, 0.58–0.98) (Mathiessen et al. 1995). Less smoking by those with a prosthesis than in the general population has been thought to be one reason for this. Other tobacco-associated malignancies include cancers of the larynx, oral cavity, pharynx, esophagus, pancreas, renal parenchyma, renal pelvis and the urinary bladder (Dreyer et al. 1997). Not all of these cancers showed a decrease in the cancer risk in the combined cohort.

Recently, a serological association between Chlamydia pneumoniae infection and lung cancer has been found (Laurila et al. 1997, Koyi et al. 1999). THA and TKA patients are easily treated with antibiotics for respiratory tract and other infections to prevent hematogenous spread of the bacteria to the prosthesis. These antibiotics may control Chlamydia infections.

Physical activity—perhaps even independent of smoking—lowers the risk of lung cancer (Lee et al. 1999). Formerly active athletes in Finland had 65% and those who had taken part in endurance sports even an 88% lower incidence of lung cancer than the general population (Pukkala et al. 2000). The lower risk of lung cancer among THA and TKA patients may reflect the physical activities of these patients before the development of arthrosis. THA and TKA permit resumption of physical activity and an improvement in the cardiovascular fitness of the patients (Ries et al. 1997).

Urinary tract cancers

Nyren et al. (1995) reported a significantly increased risk of renal cancer. SIRs of renal cancer and of all urinary tract cancers in the present combined cohort were slightly below 1.0. The stress produced by metallic ions does not seem to increase malignant degeneration of the urinary tract in THA or TKA patients with primary osteoarthrosis.

Prostate cancer

The incidence of prostate cancer was slightly, but significantly, increased among THA and TKA patients giving a total SIR of 1.08. Nyren et al.

(1995) also reported a significant increase in the incidence of prostate cancer. The patients with endoprostheses are more carefully and regularly followed than the normal population. Survey bias may enhance the detection of this cancer, which commonly occurs in an occult form. Such small increases may also be due to selection of patients from the upper social classes (Pukkala 1995).

Skin cancers

We found an increase in the risk of malignant melanoma in THA and TKA patients. Olsen et al. (1999) reported the highest SIRs in Denmark. An increase in the risk of melanoma was also reported by Nyren et al. (1995). This may reflect an increase in the number of patients examined or in selection of certain social classes. Persons in the upper classes tend to sit more in the sun, which increases the risk of skin melanoma (Pukkala 1995).

Sarcomata

Despite the accumulation of wear debris around the prosthesis, only 38 cases of local sarcoma at the site of the hip or knee prosthesis have been reported (IARC monographs 1999, Stephensen et al. 1999, Rana et al. 2001). In large Nordic cohorts, only one local malignant fibrous histiocytoma has been reported (Mathiessen et al. 1995).

Hematopoietic cancers

We found that the total risk of the hematopoietic cancers in our combined series was slightly increased. Some early findings have suggested that THA entails an increased risk of hematopoietic cancers (Gillespie et al. 1988, Visuri et al. 1991). Long-term exposure to the metallic ions could be expected to increase this risk. However, the SIRs of the leukemia and lymphomas in association with the McKee-Farrar prosthesis were reduced from 3.01 (1.11–6.56) to 1.43 (0.74–2.50) in some of the same cohort of patients after a longer follow-up (Visuri and Koskenvuo 1991, Visuri et al. 1996). In the series by Mathiessen et al. (1995), the risk of lymphoma and leukemia also increased (SIR 2.66, 1.49–4.39) during the first year after surgery but declined to 1.00 thereafter. Gillespie et al. (1996) did not confirm an increase in the risk of hematopoietic cancers in their two studies of THA and TKA patients. None of their cohorts showed a significant increase in the risk of any of these forms of cancer.

Stress as well as lower resistance of the immune system caused by the large amounts of wear and corrosion products from the prosthesis have been thought to encourage tumor growth among patients with endoprostheses (Friedman et al. 1993). Major changes in the functioning of the immune system are associated with a marked increase in the risk of non-Hodgkin's lymphoma (NHL) (Hardell et al. 1998). Nevertheless, the total risk of NHL entailed in THA patients was about 1.00 and in TKA patients, only slightly higher (SIR 1.23, 0.87–1.69).

The 5 largest cohorts have an average follow-up time of 6.6 years per patient. Modern hip and knee prostheses may last for 30 years. The latency period had to exceed 20 years before the risk of lung cancer increased among metal workers exposed to nickel or chromium compounds (Rosenman and Standbury 1996, Anttila et al. 1998). No significant increase in cancer at all sites was found in the Finnish THA cohort after 30 years' use of implants or single metal-on-metal THAs (Visuri et al. 1996, Visuri and Pukkala 2001).

Type-specific analyses of various prostheses, carefully adjusted for the way of life of patients with THAs and TKAs are needed to assess the factors for reducing the risks of cancer. Our findings do not suggest that there is any oncogenic risk from the components of hip and knee prostheses and their degradation products.

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