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Long-term risk of receiving a total hip replacement in cancer patients

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ABSTRACT

Aim: To investigate whether cancer patients have an increased risk of receiving a total hip replacement compared to the standard population of Norway. *Materials and methods*: By linking of The Cancer Register of Norway and The Norwegian Arthroplasty Register we obtained information on cancer diagnoses (type, date of diagnosis), total hip arthroplasties and date of death for all patients living in Norway. This includes 741,901 patients categorized into three groups: 652,197 patients with at least one cancer diagnosis but no hip arthroplasties, 72,469 patients with at least one hip arthroplasty but no cancer diagnosis and 17,235 patients who have at least one cancer diagnosis and at least one hip arthroplasty. Within this latter group, 8563 individuals had been diagnosed with cancer prior to a total hip arthroplasty. Statistical methods applied in this study were Cox interval censored regression models and standardized incidence ratios (SIR). *Results*: Cancer patients had a slightly increased risk of receiving a total hip arthroplasty compared to the Norwegian population (SIR = 1.15 (95% CI, 1.12–1.17)). For primary tumours located cranially to the pelvic area there was no significant increase in risk for hip arthroplasty. An exception was breast cancer (SIR = 1.13 (95% CI 1.08–1.18)). Cancer located in the pelvic region (SIR = 1.20 (95% CI 1.16–1.24)), malignant lymphoma (SIR = 1.30 (95% CI 1.15–1.46)) and leukaemia (SIR = 1.17 (95% CI 1.01–1.34)) had an increased risk for receiving a total hip arthroplasty. *Conclusion*: Cancer survivors, mainly those with pelvic and lympho-hematological malignancies, have a small statistically significant increase in risk for receiving total hip arthroplasty.

1. Introduction

Approximately two thirds of cancer patients survive more than 5 years [1] and research on cancer survivorship has gained increasing interest during the last decade. Much focus has been on second cancer [2] and cardiovascular complications, and psycho-social sequelae after cancer [3] whereas the relation between cancer and musculo-skeletal disorders and their treatment has barely been investigated.

Radiation and chemotherapy for cancer may negatively influence the normal bone-formation and thereby give rise to structural and functional alterations of the skeleton and joints. For example will long-term treatment with corticosteroids, as used in childhood cancer and Hodgkin's lymphoma, reduce osteoblast activity and thus increase the risk of osteoporotic fractures [4]. Premature menopause in patients with gynaecological cancers or breast cancer, chemotherapy and aromatase inhibitors are associated with an increased risk of osteoporosis [5,6] as is androgen deprivative therapy in men with prostate cancer [7]. During recent years it has furthermore been shown that high-dose pelvic irradiation is followed by micro-fractures in the sacrum [8]. Similar bone alterations may occur in the hips, which are irradiated during so-called box technique of pelvic malignancies. In addition to the primary alterations of irradiated bone, radiotherapy of soft tissues around major joints may lead to increased fibrosis and sciatic changes leading to abnormal functional conditions with premature development of arthrosis [9]. Finally, hip replacement may represent an excellent modality of palliative treatment in selected patients with metastatic spread to the hip. All these conditions may also lead to an increased risk of hip fractures which may require hip prostheses.

We therefore wanted to assess the risk of total hip replacement in cancer patients with adult-onset cancer diagnoses as compared to that of the general population. Using two national registries with an almost 100% compliance we identified a cohort of cancer patients who had undergone total hip replacement after their malignant diagnosis. Our hypothesis was that increased incidence

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rates for hip prosthesis would be observed in cancer survivors as compared to the general population.

2. Materials and methods

2.1. Patient selection

The Cancer Registry of Norway (CRN) was established in 1953. Registration of each new cancer case is compulsory. The CRN has records on 99% of all cancer patients in Norway [10]. For each cancer patient the CRN contains information on type of malignancy, date of diagnosis and initial treatment together with demographics.

The Norwegian Arthroplasty Register (NAR) started its registration of total hip replacements in 1987, with the aim of monitoring quality of total hip prostheses used in the country [11]. This voluntary register has a compliance rate exceeding 95% [12].

By using the 11-digit unique national personal identification number of each Norwegian inhabitant we linked all cancer cases and all hip prosthesis (primary and revisions), and the date of death for each patient. Of the 741,901 cancer patients, 652,197 patients had one or more cancer diagnosis but no hip prosthesis, 72,469 patients had one or more hip prosthesis but no cancer, and 17,235 patients had one or more cancer diagnosis and one or more hip prosthesis. To be included in this study patients had to fulfil 3 eligibility criteria: Age 16–90 years at the date of their first cancer diagnosis, no hip prosthesis prior to the first cancer diagnosis, and alive per September 1st 1987. 403,809 patients were selected and 8563 of these had received a primary total hip replacement.

Eligible patients were grouped into 8 different subgroups based on their International Classification of Diseases [ICD] 7 code and the anatomical site of the first primary cancer; 1. Above the shoulders (ICD7 codes 140–148, 160, 161, 192–194), 2. Shoulders to diaphragm without breast (ICD7 codes 150, 162, 163), 3. Diaphragm to pelvis (ICD7 codes 151–153, 155–157, 180), 4. Pelvis (ICD7 codes 154, 171, 172, 175–179, 181), 5. Breast (ICD7 code 170), 6. Malignant lymphoma (ICD7 code 206), 7. Leukaemia (ICD7 code 207) and 8. Others (ICD7 codes 190, 191, 196, 197, 199) (Table 1).

There may be several ways to categorize the cancer diagnoses. The main argument for our categorization was due to the type of treatment that cancer patients may receive, such as radiation located to an area close to the hip. Thus, our categorization is arbitrary based on the distance from the hip.

Table 1
Number of patients alive after September 1st 1987, age and gender for the different locations of cancer.

Location group	*N*	Age (std)	Sex % male
Above the shoulders[a]	23783	58 (16)	58
Shoulders to diaphragm, without breast[b]	35234	67 (11)	68
Diaphragm to pelvis[c]	75750	69 (12)	51
Pelvis[d]	133418	65 (15)	63
Breast[e]	55158	60 (14)	1
Lymphoma[f]	14513	58 (18)	54
Leukemia[g]	14495	67 (15)	56
Others[h]	51458	64 (17)	50
Total	403809	65 (15)	50

[a] ICD7 codes 140 (lip), 141, 143, 144 (tongue, floor of mouth and other parts of mouth, and of mouth, unspecified), 142 (salivary gland), 145 (tonsils), 147, 148 (hypopharynx, and pharynx, unspecified), 160, 146 (nose, nasal cavities, middle ear and accessory sinuses and nasopharynx), 161 (larynx), 192 (eye), 193 (brain and other parts of nervous system), 194 (thyroid gland).
[b] ICD7 codes 150 (oesophagus), 162, 163 (bronchus and trachea, and of lung specified as primary, and lung, unspecified as to whether primary or secondary).
[c] ICD7 codes 151 (stomach), 152 (small intestine, including duodenum), 153 (large intestine, except rectum), 155 (liver), 156 (galblader, ductus and papilla), 157 (pancreas), 180 (kidney).
[d] ICD7 codes 154 (rectum), 171 (cervix uteri), 172 (corpus uteri), 175 (ovary, fallopian tube and broad ligament), 176 (other and unspecified female genital organs), 177 (prostate), 178 (testis), 179 (other and unspecified male genital organs), 181 (bladder).
[e] ICD7 code 170 (breast).
[f] ICD7 code 206 (lymphatic system).
[g] ICD7 code 207 (haematopoetic system).
[h] ICD7 codes 190 (skin), 191 (other malignant neoplasm of skin), 196 (bone), 197 (connective tissue), 199 (other and unspecified sites).

Table 2
Standardized incidence ratios (SIR) showing the incidence for cancer patients receiving a total hip prosthesis compared to the incidence in the general population.

	N	Observed prosthesis	Expected prosthesis	SIR (95% CI)
Gender				
Male	201568	2539	2230	1.14 (1.09–1.18)
Female	202241	6024	5230	1.15 (1.12–1.18)
Age when diagnosed cancer				
16–49	66639	1382	1197	1.15 (1.09–1.22)
50–59	64583	1690	1555	1.09 (1.04–1.14)
60–69	96493	2696	2397	1.12 (1.08–1.17)
70–79	112749	2327	1941	1.20 (1.15–1.25)
80–89	63345	468	370	1.26 (1.15–1.38)
Cancer location				
Above the shoulders	23783	396	413	0.96 (0.86–1.05)
Shoulders to diaphragm, without breast	35234	118	171	0.69 (0.57–0.81)
Diaphragm to pelvis	75750	1195	1128	1.06 (1.00–1.12)
Pelvis	133418	3282	2734	1.20 (1.16–1.24)
Breast	55158	1907	1691	1.13 (1.08–1.18)
Lymphoma	14513	274	210	1.30 (1.15–1.46)
Leukemia	14495	189	161	1.17 (1.01–1.34)
Others	51458	1202	952	1.26 (1.19–1.33)
Year of cancer diagnose				
Earlier than 1970	11245	618	551	1.13 (1.03–1.21)
1970–1979	24861	1237	1072	1.15 (1.09–1.22)
1980–1989	86530	2498	2288	1.09 (1.05–1.13)
1990 and later	281173	4210	3549	1.19 (1.15–1.22)
Total	403809	8563	7460	1.15 (1.12–1.17)

Table 3
Standardized incidence ratios (SIR) showing the incidence for receiving a total hip prosthesis for patients diagnosed with cancer in different periods.

	1: Cancer diagnosed earlier than 1970				2: Cancer diagnosed in 1970–1979				3: Cancer diagnosed in 1980–1989				4: Cancer diagnosed in 1990 or later			
	N	Obs[a]	Exp[b]	SIR (95% CI)	*N*	Obs[a]	Exp[b]	SIR (95% CI)	*N*	Obs[a]	Exp[b]	SIR (95% CI)	*N*	Obs[a]	Exp[b]	SIR (95% CI)
Gender																
Male	2475	69	61	1.13 (0.86–1.40)	8462	203	187	1.09 (0.94–1.23)	42194	689	660	1.04 (0.97–1.12)	148437	1578	1322	1.19 (1.13–1.25)
Female	8770	549	490	1.12 (1.03–1.21)	16399	1034	885	1.17 (1.10–1.24)	44336	1809	1629	1.11 (1.06–1.16)	132736	2632	2226	1.18 (1.14–1.23)
Age when diagnosed cancer																
16–49	6841	473	431	1.10 (1.00–1.20)	8083	432	386	1.12 (1.01–1.22)	14466	257	246	1.04 (0.92–1.17)	37249	220	134	1.64 (1.42–1.86)
50–59	2976	124	106	1.17 (0.96–1.38)	6656	481	435	1.11 (1.01–1.20)	12409	574	530	1.08 (0.99–1.17)	42542	511	483	1.06 (0.97–1.15)
60–69	1262	19	13	1.46 (0.80–2.12)	6452	282	218	1.29 (1.14–1.44)	23585	995	929	1.07 (1.00–1.14)	65194	1400	1236	1.13 (1.07–1.19)
70–79	160	2	1	2.00 (0.00–4.77)	3237	41	32	1.28 (0.89–1.67)	24815	591	523	1.13 (1.04–1.22)	84537	1693	1387	1.22 (1.16–1.28)
80–89	6	0	0	No estimat	433	1	1	1.00 (0.00–2.96)	11255	81	61	1.33 (1.04–1.62)	51651	386	308	1.25 (1.13–1.38)
Cancer location																
Above the shoulders	1063	41	43	0.95 (0.66–1.25)	2243	85	78	1.09 (0.86–1.32)	5810	123	139	0.88 (0.73–1.04)	14667	147	152	0.97 (0.81–1.12)
Shoulders to diaphragm, without breast	92	0	3	No estimat	356	10	12	0.83 (0.32–1.35)	5115	26	41	0.63 (0.39–0.88)	29671	81	115	0.70 (0.55–0.86)
Diaphragm to pelvis	1146	36	38	0.95 (0.64–1.26)	3238	125	120	1.04 (0.86–1.22)	15938	385	373	1.03 (0.93–1.14)	55428	650	598	1.09 (1.00–1.17)
Pelvis	4465	265	233	1.14 (1.00–1.27)	9562	538	420	1.28 (1.17–1.39)	29685	905	798	1.13 (1.06–1.21)	89706	1574	1283	1.23 (1.17–1.29)
Breast	3010	191	167	1.14 (0.98–1.31)	5185	311	285	1.09 (0.97–1.21)	12866	550	529	1.04 (0.95–1.13)	34097	855	711	1.20 (1.12–1.28)
Lymphoma	356	12	13	0.92 (0.40–1.45)	801	34	21	1.62 (1.07–2.16)	3054	74	64	1.16 (0.89–1.42)	10302	154	111	1.39 (1.17–1.61)
Leukemia	45	1	2	0.50 (0.00–1.48)	301	6	8	0.75 (0.15–1.35)	3054	55	45	1.22 (0.90–1.55)	11095	127	106	1.20 (0.99–1.41)
Others	1068	72	52	1.38 (1.06–1.70)	3175	128	128	1.00 (0.83–1.17)	11008	380	300	1.27 (1.14–1.39)	36207	622	472	1.32 (1.21–1.42)
Total	11245	618	551	1.12 (1.03–1.21)	24861	1237	1072	1.15 (1.09–1.22)	86530	2498	2289	1.09 (1.05–1.13)	281173	4210	3548	1.19 (1.15–1.22)

[a] Observed number of prosthesis for the cancer patients.
[b] Expected number of prosthesis in the general population.

Table 4
Cox regression models, stratified by the period of cancer diagnosis.

	Period 1: earlier than 1970			Period 2: 1970–1979			Period 3: 1980–1989			Period 4: 1990 and later		
	IRR[a]	95% CI	*p*	IRR[a]	95% CI	*p*	IRR[a]	95% CI	*p*	IRR[a]	95% CI	*p*
Gender												
Male	1 ref			1 ref			1 ref			1 ref		
Female	0.8	0.5–1.1	0.16	0.8	0.6–1.0	0.003	0.8	0.7–0.9	<0.001	0.8	0.7–0.9	<0.001
Age when diagnosed cancer												
16–49	0.1	0.0–0.6	<0.001	0.2	0.0–0.4	<0.001	0.4	0.3–0.5	<0.001	0.9	0.7–1.1	0.35
50–59	0.3	0.0–0.8	<0.001	0.3	0.1–0.5	<0.001	0.6	0.5–0.7	<0.001	0.8	0.7–0.9	<0.001
60–69	1 ref			1 ref			1 ref			1 ref		
70–79	4.3	2.8–5.8	0.054	2.7	2.4–3.0	<0.001	2.6	2.5–2.7	<0.001	1.6	1.5–1.7	<0.001
80–89	No est			2.1	0.1–4.1	0.46	5.9	5.6–6.2	<0.001	3.0	2.9–3.1	<0.001
Cancer location												
Above the shoulders	1 ref			1 ref			1 ref			1 ref		
Shoulders to diaphragm. without breast	0.3	0.0–2.3	0.24	0.7	0.1–1.3	0.38	1.3	0.9–1.7	0.27	1.4	1.1–1.7	0.014
Diaphragm to pelvis	1.0	0.5–1.5	0.84	0.9	0.6–1.2	0.52	1.1	0.9–1.3	0.28	1.3	1.1–1.5	0.009
Pelvis	1.2	0.9–1.5	0.21	1.1	0.9–1.3	0.30	1.3	1.1–1.5	0.009	1.6	1.4–1.8	<0.001
Breast	1.4	1.0–1.8	0.052	1.0	0.7–1.3	0.96	1.2	1.0–1.4	0.072	1.5	1.3–1.7	<0.001
Lymphoma	0.9	0.3–1.5	0.86	1.7	1.3–2.1	0.014	1.6	1.3–1.9	<0.001	1.7	1.5–1.9	<0.001
Leukemia	0.9	0.0–2.9	0.89	1.0	0.2–1.8	0.96	2.4	2.1–2.7	<0.001	1.6	1.3–1.9	<0.001
Others	1.4	1.0–1.8	0.12	0.9	0.6–1.2	0.38	1.3	1.1–1.5	0.006	1.3	1.1–1.5	0.013

[a] Adjusted for age, gender and cancer location.

To examine the causes that were registered as reasons for the total hip arthroplasty we reviewed the diagnoses given in the NAR. For these sub-analyses we only included patients that had their cancer diagnosis after 1990. This was to ensure that none had an arthroplasty between the cancer diagnosis and the start of the NAR (Table 5).

3. Statistics

We calculated standardized incidence ratios (SIRs) [13]. For given time periods this SIRs are defined as the number of observed hip prostheses in different groups of cancer patients, divided by the expected number of hip prosthesis for a corresponding subset of the Norwegian population with respect to gender, age, and calendar year. These expected numbers are calculated based on incidence rates of hip prosthesis in the general Norwegian population. The incidence was calculated as the number of hip prostheses reported to NAR, divided by the Norwegian population, taking into account the age, gender and period of calendar years as in Andersen and Vaeth [14].

Since the data from the CRN had a much longer follow-up period than the NAR data, we had left-censored observation times. We therefore used Cox regression models for left censored data [15], including an offset for the population risk for prostheses. However, the stratified analyses for the last time period (after 1990) are identical to standard Cox regression. The observation times ranged from the date of the first cancer diagnosis to the date of the first hip arthroplasty. The patient's date of death or emigration, or the cut-off date of the study (December 31st 2006) were considered censored observations. The results from the Cox regression models were presented as Incidence Rate Ratios (IRR) and could be interpreted as the rate between incidences for the different categories for each variable. The analyses for the cause specific endpoints (reasons for receiving hip prostheses) were performed using ordinary Cox-regression analyses and reported as rate ratios (RR).

As different treatment regimens of possible relevance to the risk of having a subsequent prosthesis have been employed after the start of CRN, a variable called "Period" was introduced in the analyses. This variable grouped the years of cancer diagnosis in 4 different categories. Category 1: Cancer diagnosis prior to 1970; Category 2: Cancer diagnosis between 1970 and 1979 inclusively; Category 3: Cancer diagnosis between 1980 and 1989, inclusively; Category 4: Cancer diagnosis 1990 or later (Tables 2–4).

For all analyses, we used the statistical packages S-Plus (S-Plus 7.0 for Windows; MathSoft Inc., Seattle, Washington) and SPSS (SPSS 15.0 for Windows; SPSS Inc., Chicago, Illinois). All *p*-values were two-sided and *p*-values less than 5% were considered statistically significant.

4. Results

The mean age was 66 years at the time of the patients first cancer diagnosis. Mean age for females was 64 years and mean age for males was 67 years at cancer diagnosis. There was 52% males.

Compared to the general population the SIR of having a subsequent prosthesis was statistically significantly higher, with SIR of 1.15 (95% CI: 1.12–1.17) for all cancer patients (Table 2).

4.1. Stratified analysis

The SIR for males was 1.14 (95% CI: 1.09–1.18), while females displayed SIR of 1.15 (95% CI: 1.12–1.18). SIR increased with age of cancer patients at diagnosis and was 1.09 (95% CI: 1.04–1.14) for patients aged 50–59 years old compared to 1.26 (95% CI: 1.15–1.38) for those aged 80–89 years. Only the youngest patients (16–49 years) deviated from this pattern, where the SIR was 1.15 (95% CI: 1.09–1.22).

Stratified by the anatomical site we found that patients with tumours in the area between the shoulders and diaphragm excluding breast cancer, had the lowest SIR with 0.69 (95% CI: 0.57–0.81) of receiving a hip prosthesis. Patients with tumours above the shoulders had an SIR not statistically significant below 1, whereas SIRs were higher than 1 for the remaining locations. The highest SIR was found for malignant lymphomas 1.30 (95% CI: 1.15–1.46) (Table 2).

4.2. Period of calendar years

SIRs for women were significantly higher than 1 for all 4 periods (Table 3), consistent with the results for the whole period. The SIRs for men were not statistically significantly higher than 1 for the first 3 periods. Only for the last period SIR was significantly higher than 1 for men, the SIR for the whole period thus became

Table 5
Cox regression analyses for patients with diagnosed cancer in 1990 or later with reasons for receiving a primary total hip replacement related to the cancer location as endpoint.

Location (number)	Osteoarthritis		Rheumatoid arthritis		Fracture of femoral neck		Congenital dysplasia		Caputnecrosis[a]		Cancer[a]		Other[a]	
	No	RR[b] (95% CI)	No	RR[b] (95% CI)	No	RR[b] (95% CI)	No	RR[b] (95% CI)	No	RR[b] (95% CI)	No	RR[b] (95% CI)	No	RR[b] (95% CI)
Above the shoulders (14667)	94	1 ref	6	1 ref	28	1 ref	10	1 ref	4	1 ref	2	1 ref	4	1 ref
Shoulders to diaphragm. without breasts (29671)	47	0.7 (0.5–1.0) $p = 0.083$	6	1.5 (0.5–4.8) $p = 0.46$	17	0.9 (0.5–1.6) $p = 0.71$	1	0.2 (0.0–1.4) $p = 0.10$	2	1.1 (0.2–5.9) $p = 0.94$	8	5.3 (1.1–25.3) $p = 0.036$	2	0.8 (0.1–4.4) $p = 0.80$
Diaphragm to pelvis (55428)	472	1.3 (1.0–1.6) $p = 0.027$	19	0.8 (0.3–2.0) $p = 0.65$	108	0.9 (0.6–1.3) $p = 0.49$	22	0.8 (0.4–1.7) $p = 0.61$	10	0.9 (0.3–2.8) $p = 0.80$	9	2.2 (0.5–10.5) $p = 0.30$	23	1.8 (0.6–5.4) $p = 0.26$
Pelvis (89706)	1160	1.4 (1.2–1.8) $p = 0.001$	70	1.4 (0.6–3.3) $p = 0.40$	217	0.9 (0.6–1.4) $p = 0.75$	83	1.3 (0.7–2.5) $p = 0.42$	26	0.9 (0.3–2.7) $p = 0.87$	23	2.1 (0.5–9.1) $p = 0.31$	49	1.7 (0.6–4.8) $p = 0.30$
Breast (34097)	600	1.4 (1.1–1.8) $p = 0.003$	34	1.1 (0.5–2.7) $p = 0.77$	130	0.9 (0.6–1.3) $p = 0.53$	53	1.2 (0.6–2.4) $p = 0.60$	9	0.6 (0.2–1.9) $p = 0.38$	20	5.2 (1.2–23.3) $p = 0.030$	31	1.9 (0.7–5.4) $p = 0.24$
Lymphoma (10302)	98	1.5 (1.1–1.9) $p = 0.009$	7	1.6 (0.5–4.7) $p = 0.41$	18	0.9 (0.5–1.5) $p = 0.60$	10	1.4 (0.6–3.3) $p = 0.46$	7	2.5 (0.7–8.5) $p = 0.14$	4	2.8 (0.5–15.0) $p = 0.24$	12	4.2 (1.4–13.0) $p = 0.013$
Leukemia (11095)	69	1.1 (0.8–1.5) $p = 0.57$	6	1.5 (0.5–4.6) $p = 0.50$	21	1.0 (0.6–1.8) $p = 0.92$	6	1.1 (0.4–3.1) $p = 0.81$	4	1.9 (0.5–7.7) $p = 0.37$	18	18.5 (4.3–79.7) $p = 0.001$	6	2.6 (0.7–9.1) $p = 0.15$
Others (36207)	438	1.5 (1.2–1.8) $p = 0.001$	41	2.1 (0.9–5.0) $p = 0.090$	68	0.7 (0.4–1.0) $p = 0.077$	34	1.3 (0.6–2.6) $p = 0.52$	11	0.9 (0.3–3.0) $p = 0.91$	16	3.7 (0.9–16.3) $p = 0.078$	29	2.5 (0.9–7.1) $p = 0.086$

[a] The most common reasons for operation have check boxes, all other reasons the orthopaedic surgeon has to define as "other reasons".
[b] Adjusted for gender and age.

significantly elevated also for males. The youngest patients (16–49 years of age) had an increased risk for prosthesis in the last period (SIR = 1.64, 95% CI: 1.42–1.86). Cancer located above the shoulders resulted in no statistically significant differences for any periods, while the SIR for cancer in the pelvic area was significantly increased for all periods. For breast cancer only the last period had a significantly increased SIR (Tables 2 and 3).

4.3. Regression analysis

The Cox regression analyses showed that women with cancer had a significantly lower relative incidence for prosthesis than men with cancer in the last 3 periods (Table 4). We found that, for all periods, patients younger than 60–69 years (at the time of their cancer diagnosis) had a reduced risk for prosthesis, while patients older than 60–69 years had an increased risk. However, not all risk estimates were statistically significant (Table 4). Cancer above the shoulders was set as the reference group when comparing cancer location. No statistically significant differences were found in the first period. In period 2 the only significant difference was observed for malignant lymphomas IRR 1.7 (95% CI: 1.3–2.1). In period 3 cancer between the shoulders and diaphragm (without breast cancer), cancer between diaphragm and pelvis, and breast cancer showed no differences in the risk of receiving a prosthesis compared to cancer above the shoulders. All other groups displayed statistically significant differences. In the last period, all locations showed a significantly increased risk for prosthesis compared to the reference location.

As to cancer diagnosed in 1990 or later and compared to cancer located above the shoulders, all other locations except for cancer located between the shoulders and diaphragm (without breast cancer) displayed an increased risk for total hip replacement due to osteoarthritis (Table 5). Only for leukemia this increase was not statistically significant compared to cancer located above the shoulders. The risk of receiving a total hip replacement due to cancer was increased for all cancer locations, but only statistically significant for cancer located between the shoulders and the diaphragm (without breast cancer) RR 5.3 (95% CI: 1.1–25.3), breast cancer RR 5.2 (95% CI: 1.2–23.3), and for leukemia RR 18.5 (95% CI: 4.3–79.7).

5. Discussion

In this study we have found a small though statistically significant increase in the risk for receiving a total hip prosthesis for cancer patients, compared to the incidences of prostheses in the Norwegian population. This tendency was consistent, also stratified by the different anatomical sites of the cancers. Surprisingly, the increase was not highest for cancers located to the pelvic area, even though we hypothesized that cancers in this area, which may have been treated with radiation, could have an even further increased risk for prosthesis due to a dysfunction of the bone healing.

We found an increased risk in need for total hip arthroplasty due to osteoarthritis and due to cancer in our data. The relation between the other cancer diagnoses and the indications for THA was however vague.

It is a weakness of this study that we only have available a register of total hip arthroplasties as endpoint. Patients with malignancies may often be treated with hemi arthroplasties as this is considered to be a less complicated procedure in patients with comorbidities and limited life expectancy. These procedures are not found in the register of total hip arthroplasties. Since 2005 the Norwegian Hip Fracture Register [16] have registered hip fractures in Norway, including hemi arthroplasty, but at present, data from

this register is not sufficiently complete to be considered in this study due to the short follow up.

This observational study is based on two well documented national registers with high compliance. However, an analytic difficulty of the study is that the cancer register was started 34 years prior to the start of the hip register. Thus, there may be a large proportion of cancer patients that may have received hip replacements before the hip register started, this was to some extent accounted for in the analyses. Furthermore, the most advanced cancer cases may have an increased risk for hip prosthesis, but they also have the higher mortality rates. Concerning these malignancies, physicians may be reluctant to refer cancer patients to arthroplasty for some period of time due to their high risk of postoperative complications or expected early death. Thus, we suspect that the risk of joint damage to the hip joint might be higher than the observed risk for hip replacement. As survival and the prevalence of cancer patients increase [10] there will probably be an increased need for hip prostheses among these individuals in years to come.

We hypothesized findings of an increased risk for prosthesis in patients with cancer in the pelvic area, but we did not find these results as strong as expected. This may depend on our categorization of the cancers. Our data did not include information on radiation therapy. The group of pelvic cancer patients includes diagnoses with other treatments than radiation therapy. In early years, surgical treatment alone has been used in many gynaecological cancers and cancer in rectum or urinary bladder.

We did not find any register based studies examining the risk of hip prostheses after a cancer diagnosis, we only found case studies examining pelvic irradiation and total hip arthroplasty [17,18]. These studies focused on treatment of the cancer in patients who had received total hip arthroplasty. There are also some studies on the risk for hip fracture after cancer diagnosis and pelvic irradiation [19,20]. These studies reported an increased risk for pelvic fracture after pelvic irradiation. In this paper we could not study this question due to insufficient information about radiation techniques and doses, and the fact that pelvic fractures seldom need hip arthroplasty.

A Danish study on the fracture risk in men after prostate cancer concluded with an increased risk for fracture at all ages, but most strikingly in men aged 50–65 [19]. They attribute this to androgen deprivation therapy. Another study from the US concluded with an increased risk for pelvic or hip fractures in older women following pelvic irradiation [20]. However, population-based studies investigating the risk of skeletal long-term effects after cancer treatment are lacking.

The increase in the risk for receiving total hip replacement in cancer patients, which we found in this study, could be linked to the treatment following the cancer diagnosis. However, it may also be common causes explaining both the risk for receiving cancer and later receiving a total hip prosthesis. For instance there may be life style factors related to the risk for cancer that also increase the risk for a ruined hip joint, with a subsequent need for a hip replacement. Such common causes or factors may be obesity [21], smoking, alcohol abuse, occupation or genetic factors.

The increased SIR for breast cancer may indicate that the treatment for breast cancer may elevate the risk for total hip prosthesis, but there may also be underlying common causes increasing both the risk for breast cancer and a hip prosthesis, as age at which menopause occurs. Menopause may further more be related to the risk for breast cancer [22] and menopause may also be related to bone mineral density (BMD) and fractures [23]. Fracture of the femoral neck as an indication for hip arthroplasty is significantly increased after breast cancer [24]. Many of these patients are younger than 49 years and may have had a total hip prosthesis as preferred treatment, especially after 1990.

Some of the breast cancer patients may have developed premature menopause as a consequence of their treatment, followed by premature osteoporosis despite the use of osteoporosis protection. Tamoxifen (antagonist of the estrogen receptor in breast tissue) was introduced in Norway in the mid-eighties. Breast cancer patients may furthermore not have the same hormone replacement therapy (HRT) as their peers, which could lead to a difference between cancers and non-cancer patients in the risk for osteoporosis.

Included in the youngest age group are also patients with primary bone cancers that receive total hip prostheses as part of their initial treatment.

Survivors after malignant lymphoma, and leukemia had the highest risk of arthroplasty. Particularly long follow-up of these cancer survivors may be one explanation for this observation. Further, the two former groups are treated with high doses of cortiocosteroids, in case of leukemia during long periods often during childhood. It is well known that corticosteroids decrease osteoblast activity and thus bone structure modeling, consistent with our observation of increased risk of caput necrosis. The same, though at a lower degree, is true for survivors after malignant lymphoma, many of them also receiving radiotherapy which may include the pelvic area and/or the hip.

Extending our study to include both total hip arthroplasty and hip fractures treated with hemi arthroplasty as end points would be interesting in the future, when the follow up time are longer than today for the Hip Fracture Register.

To conclude, we found a small increase in the risk for a total hip replacement in cancer patients. To increase the strength and relevance of our findings, information on the type and dose of the radiation therapy and other treatments would be desirable.

Disclaimer

Some of the data in this article are from the Cancer Registry of Norway. The Cancer Registry of Norway is not responsible for the analysis or interpretation of the data presented.

Conflict of interests

None declared.

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