

# Lower birth rate in patients with total hip replacement

## A nationwide population-based study in Finland

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**Background and purpose** — There have been few studies on the effect of THR on pregnancy or delivery, and they have mainly been based on small and regional data. We evaluated the birth rate nationwide in patients of fertile age with THR.

**Patients and methods** — This nationwide population-based cohort study was based on registry data on 5,863 Finnish THR patients who had undergone a THR between 1985 and 2006, and who were aged 15–45 years (females) or 15–50 years (males) at the time of THR. The matched reference cohort consisted of 17,575 sex- and age-matched individuals (3 for each patient) who were alive and resident in Finland at the time of the patient's THR. Birth rate and Cox hazard ratios (HRs) with 95% CI for live births were calculated.

**Results** — The birth rate after THR was approximately 20–60% lower in the male and female patient groups than in the reference individuals. The probability of having a live birth after THR was lower in female patients than in reference individuals, in all but the oldest age group (40–45 years). The same phenomenon was seen in male patients in all but the youngest age group (15–19 years). Adjustment for potential confounders increased the probability of THR patients having a live birth compared to reference individuals, but the birth rate was still clearly reduced (in men, adjusted HR = 0.80, 95% CI: 0.69–0.92; in women, adjusted HR = 0.56, 95% CI: 0.46–0.68).

**Interpretation** — THR has a substantial effect on the birth rate of offspring, in both women and men. THR patients had a lower birth rate and probability of having a child after surgery, even after taking possible confounders into account.

Approximately 25% of all total hip replacement (THR) procedures are carried out on younger people, and slightly more than 50% on women (Lucht 2000, Furnes et al. 2001, Puolakka et al. 2001, Malchau et al. 2002).

There have been few studies on the effects of THR on pregnancy or delivery and vice versa. In addition, such studies have been mainly based on small material and regional data (Monaghan et al. 1987, Ostensen 1993, McDowell and Lachiewicz 2001, Boot et al. 2003, Meldrum et al. 2003, Yazici et al. 2003, Ginsel and Pijnenborg 2005, Sierra et al. 2005, Stea et al. 2007). Previous studies have not found any correlation between THR and complications during pregnancy or delivery (McDowell and Lachiewicz 2001, Meldrum et al. 2003, Sierra et al. 2005). Furthermore, neither pregnancy nor delivery has been shown to reduce the survival of the THR (McDowell and Lachiewicz 2001, Meldrum et al. 2003, Sierra et al. 2005, Stea et al. 2007). Previous studies have also suggested that THR is not a contraindication for normal vaginal birth (Monaghan et al. 1987, Ostensen 1993, Meldrum et al. 2003, Yazici et al. 2003, Sierra et al. 2005, Stea et al. 2007). Women of fertile age who have undergone a THR procedure are often concerned about the effect of their hip replacement on pregnancy and delivery (Smith et al. 2008). In addition, sex life can also be limited after THR, at least in patients with rheumatoid arthritis (RA) (Balderson and Brattström 1979). Previous studies have focused on pregnancy and delivery in women with THR. To the best of our knowledge, there have been no studies that have analyzed birth rate after THR.

We analyzed the effect of THR on birth rate using nationwide population-based registry data. We also assessed whether diabetes mellitus (DM) and RA affect the fertility of patients who have undergone THR. Our hypothesis of a lower birth rate was more sociologically-based than biologically-based. Women with THR may be more concerned about the course of pregnancy, and people with THR may have reduced sexual activity. Furthermore, the effects of the use of bone cement, or metal-on-metal articulation, on semen quality and fertility in men are still unclear.

## Patients and methods

The study was based on information recorded in 4 national registries in Finland. Information on THRs was obtained from the Finnish Arthroplasty Register, which is part of the mandatory Implant Register maintained by the Finnish National Institute of Health and Welfare. The Arthroplasty Register has information on all primary arthroplasty procedures carried out in Finland (Puolakka et al. 2001) The coverage of the Register is good, and most of the content corresponds well with hospital record data. Currently, over 97% of all implantations are recorded (Finnish Arthroplasty Register 2015).

We included patients who underwent a THR between 1985 and 2006 and who were aged from 15 to 45 years (females) or 15 to 50 years (males) at the time of the THR. Although men are usually fertile long after 50 years of age, we did not include men over 50 years of age at the time of the THR, to avoid having senior THR patients during the follow-up (0–31 years). Information on the reference group without THR was obtained from the mandatory Population Register, which is maintained by the Finnish Population Register Center. For each patient, 3 reference individuals without THRs, who were alive and resident in Finland at the time of the patient's THR, were selected with matching for sex, age, place of residence, and mother tongue. Information on previous live-born children before THR (0 vs.  $\geq 1$ ), marital status (never married vs. ever married), emigration, and death for the whole study population was gathered from the Population Register. Information on diabetes mellitus (DM) and rheumatoid arthritis (RA) was obtained from the Social Insurance Institution of Finland, which maintains the register of medical reimbursements due to chronic diseases and includes information on DM and RA. The prerequisite for reimbursement is a medical certificate showing that the diagnosis was based on clinical examination, that it fulfilled international criteria, and that a board-certified medical doctor carried out the examination. If information on the person was not present in the register, he/she was classified as not having these diseases.

We were able to link all the information from these 4 national registers using the unique personal identification number assigned to all residents of Finland.

## Statistics

The Cox multiple regression model with hazard ratios (HRs) and 95% confidence intervals was used to evaluate the risk for the first live-born child in patients after THR, in relation to reference individuals without THR. The start of the follow-up was the date of the patient's THR. The date of the THR of the patient was also the start of the follow-up for the corresponding reference individuals. The endpoint of the follow-up was the date of birth of a first live-born child after the start of the follow-up, date of emigration of the patient, date of death of the patient, or the common closing date (January 26, 2011), whichever occurred first.

Stratified analyses were conducted according to age at the start of follow-up (< 20, 20–34, 35–39 and  $\geq 40$  years), number of live births before THR, marital status, DM, and RA. Separate adjusted multivariable analyses were conducted, which included age at the time of THR, marital status, number of previous live-born children before THR, and DM or RA diagnosis as potential confounding factors. The age at the start of the follow-up was used as a continuous variable in these adjusted analyses. All the analyses were conducted separately for men and women. PASW Statistics for Windows, SPSS version 18.0, and STATA 8.2 were used for the statistical analyses. The subjects registered in the registries were not contacted, so according to Finnish regulations, informed consent was not required.

## Results

The THR patient group comprised 3,434 men and 2,429 women, and the reference group comprised 10,299 men and 7,276 women. The mean follow-up time was 11 (0–31) years for male patients and 11 (0–31) years for male reference individuals, and for women the mean follow-up time was 14 (0–31) years for patients and 14 (0–31) years for reference individuals. The mean age at the start of follow-up was 43 (15–50) years in men and 38 (15–46) years in women. During the follow-up, the number of first live-born children after THR was 435 for patients and 2,213 for reference individuals (Table 1).

Birth rate varied according to age at the start of follow-up, according to the number of previous live-born children before THR, and according to marital status (Table 2). However, birth rate was lower in all the patient groups than in reference individuals, in both sexes, and regardless of number of previous children. Male THR patients with DM had a higher birth rate than reference individuals without THR but with DM. The same was seen in male THR patients with RA. In women, the birth rate was lower in THR patients with either DM or RA than in reference individuals. Birth rate was lower in all age groups of the patient population than in reference individuals. These differences were especially obvious in female patients in the 2 youngest age groups and in male patients aged 20–35 years.

The reduced probability of a live-born child when comparing patients with reference individuals could also be seen in Cox regression models (Table 3). Overall, the probability of having a live-born child after THR was lower in male THR patients (HR = 0.69, CI: 0.60–0.79) and female THR patients (HR = 0.47, CI: 0.40–0.55) than in reference individuals, and also in adjusted analyses (for men, adjusted HR (aHR) = 0.80, 95% CI: 0.69–0.92; for women, aHR = 0.56, CI: 0.46–0.68) (Table 3). Female THR patients had a lower probability of having a live-born child than reference individuals, in all but the oldest age group (40–45 years). The same phenomenon was seen in male patients, in all but the youngest age group

**Table 1.** Numbers of subjects and live births in patients with total hip arthroplasty (THA) and reference individuals without THA according to age at the start of follow-up, number of previous live-born children before THA, marital status, diabetes mellitus diagnosis, and rheumatoid arthritis diagnosis in Finland, 1985–2006

	Men				Women			
	No. of subjects		No. of live births		No. of subjects		No. of live births	
	Patient	Ref.	Patient	Ref.	Patient	Ref.	Patient	Ref.
Age in years at the start of follow-up								
15–19	28	84	6	29	50	150	15	90
20–34	414	1,240	127	571	621	1,847	140	824
35–39	509	1,528	64	257	571	1,722	22	167
40–45	1,151	3,465	36	193	1,187	3,557	4	28
46–50 for men	1,332	3,982	20	54	N/A	N/A	N/A	N/A
No. of previous live-born children before THA								
0	1,101	2,984	95	435	831	1,871	100	552
≥ 1	2,333	7,315	159	669	1,598	5,405	81	557
Marital status								
Never married	887	2,466	32	183	628	1,370	34	190
Ever married	2,547	7,833	222	921	1,801	5,906	147	919
Diabetes mellitus								
Yes	87	174	4	6	35	48	2	4
No	3,347	10,125	250	1,098	2,394	7,228	179	1,105
Rheumatoid arthritis								
Yes	505	86	44	4	811	68	70	6
No	2,929	10,213	210	1,100	1,618	7,208	111	1,103
Total	3,434	10,299	254	1,104	2,429	7,276	181	1,109

N/A: not applicable.

**Table 2.** Birth rate (per 10,000 person-years) with 95% CI in patients with total hip replacement (THR) and reference individuals without THR according to age at the start of follow-up, number of previous live-born children before THR, marital status, diabetes mellitus diagnosis, and rheumatoid arthritis diagnosis in Finland, 1985–2006

	Men		Women	
	Patient Rate (95% CI)	Reference Rate (95% CI)	Patient Rate (95% CI)	Reference Rate (95% CI)
Age in years at the start of follow-up				
15–19	216 (97–480)	377 (262–542)	216 (130–358)	570 (463–700)
20–34	300 (252–357)	515 (474–559)	165 (140–195)	400 (374–429)
35–39	114 (89–145)	149 (132–169)	25 (16–38)	63 (54–74)
40–45	27 (20–38)	47 (41–54)	2.4 (0.9–6.4)	5.4 (3.7–7.8)
46–50 for men	13 (8.7–21)	12 (8.9–15)	N/A	N/A
Number of previous live-born children				
0	82 (67–100)	145 (132–159)	86 (70–104)	247 (227–268)
≥ 1	60 (51–70)	77 (72–83)	35 (28–44)	71 (65–77)
Marital status				
Never married	36 (25–50)	78 (67–90)	39 (28–55)	116 (101–134)
Ever married	76 (67–87)	99 (93–106)	57 (48–66)	109 (102–116)
Diabetes mellitus				
Yes	52 (19–138)	38 (17–84)	46 (12–185)	70 (26–186)
No	67 (59–76)	95 (90–101)	52 (45–61)	110 (108–117)
Rheumatoid arthritis				
Yes	64 (47–86)	40 (15–108)	53 (42–67.5)	73 (33–163)
No	67 (59–77)	95 (90–101)	52 (43–62)	110 (104–117)
Total	67 (59–75)	95 (89–100)	52 (45–60)	110 (104–116)

(15–19 years). Adjustment for potential confounding factors (age at the start of follow-up, number of live-born children before THR, marital status, DM, and RA) reduced the probability of having a live-born child in THR patients compared

to reference individuals. In THR patients with DM or RA, however, HRs were similar.

## Discussion

The main result of this population-based study was that THR had a substantial effect on birth rate when comparing THR patients and reference individuals, and in both women and men. THR patients had a lower birth rate and a lower probability of having a child after surgery. Even after taking possible confounding factors into account, THR patients still had a lower probability of having a child, and in women this difference was especially evident (for men, aHR = 0.80; for women, aHR = 0.56). Our study is the first of its kind and gives baseline information about the birth rate of offspring in both women and men who have undergone THR.

The study had some limitations. The identification of patients with DM or RA may have been incomplete. The diagnosis of DM was based on special medication reimbursements due to chronic diseases. Everyone with at least one reimbursement period due to the disease during their lifetime is included in the register. The reimbursement is based on the diagnosis of DM or RA, and therefore DM or RA medications prescribed for other indications are not included in the reimbursements due to these chronic diseases. Furthermore, it is possible that some of the subjects with recently diagnosed DM or RA were not yet included in the register. Also, some DM patients such as diabetes type-II patients are not reimbursed for medication and therefore do not use drugs for their treatment. Such patients were not included in the register. Information

on patients who did not want reimbursement for DM or RA medication was not available. In addition, if the diagnosis of DM or RA was made for a permanently institutionalized patient, information on reimbursement would not necessar-

**Table 3. Hazard ratio (HR) with 95% CI for a live-born child after total hip replacement (THR) in patients in relation to reference individuals without THR according to various demographic factors, diabetes mellitus diagnosis, and rheumatoid arthritis diagnosis in Finland, 1985–2006**

	Men HR (95% CI)	Women HR (95% CI)
Crude	0.69 (0.60–0.79)	0.47 (0.40–0.55)
Adjusted <sup>a</sup>	0.80 (0.69–0.92)	0.56 (0.46–0.68)
Age in years at the start of follow-up		
15–19	0.57 (0.24–1.4)	0.34 (0.20–0.60)
20–34	0.61 (0.50–0.74)	0.43 (0.36–0.51)
35–39	0.74 (0.56–0.97)	0.38 (0.25–0.60)
40–45	0.57 (0.40–0.81)	0.43 (0.15–1.2)
46–50 for men	1.12 (0.67–1.9)	N/A
Number of previous live births before THR		
0	0.58 (0.46–0.72)	0.36 (0.29–0.44)
≥ 1	0.75 (0.63–0.89)	0.48 (0.38–0.61)
Marital status		
Never married	0.48 (0.33–0.70)	0.36 (0.25–0.51)
Ever married	0.74 (0.64–0.86)	0.51 (0.43–0.61)
Diabetes mellitus		
Yes	1.32 (0.37–4.7)	0.64 (0.12–3.5)
No	0.69 (0.60–0.79)	0.47 (0.40–0.55)
Rheumatoid arthritis		
Yes	1.81 (0.65–5.1)	0.84 (0.37–1.9)
No	0.67 (0.58–0.78)	0.44 (0.36–0.54)

HR: hazard ratio. Reference (HR = 1.0) are individuals without THR.

<sup>a</sup> Hazard ratio adjusted for age at the start of follow-up, number of previous live births before THR, marital status, diabetes mellitus, and rheumatoid arthritis.

ily be included in the database. Those patients were probably under-represented in our study. However, the cost of medications for DM and RA is high in Finland, so very few people with DM or RA decline reimbursement for these medications.

Marital status did not confound the effect of THR on birth rate in our study, but it slightly modified the association. As exact information on marital status at the time of THR was not available, information on the first marriage was used. Information on DM and RA diagnosis was obtained at the time of THR. Due to missing information on possible changes in marital status, DM or RA, these factors were not included in the analyses as time-dependent covariates, and residual confounding due to these factors is possible.

We did not have information on possible gynecological or urological procedures, or any other factors that might reduce fertility or cause infertility. Also, no information on spontaneous or induced abortions was available. Exclusion of these factors may have affected residual confounding, so our results should be interpreted with caution.

We restricted age of the study cohort to women aged from 15 to 45 and to men aged from 15 to 50 at the time of THR. Aging affects a woman's reproductive potential through menopause, but the effects of aging on the fertility of a man remain poorly defined (Johnson et al. 2015). However, men over 51 years are still of fertile age. Exclusion of the offspring of men over 50 at the THA may have biased our results, if the birth rate differed

substantially between THA patients and reference individuals in this age group.

According to earlier studies, pregnancy and delivery can occur safely after THR (Sierra et al. 2005, Stea et al. 2007). Pregnancy and delivery are not associated with lower function of the prosthesis and the radiographic appearance of the prosthesis is not adversely affected by pregnancy (Ostensen 1993). Pregnancy does not increase the number of early revisions of hip prostheses (Smith et al. 2008), and pregnancy and delivery are not associated with lower survival of hip prostheses. Furthermore, there is no increase in pregnancy-related complications in pregnancy after THR (McDowell and Lachiewicz 2001, Smith et al. 2008). In all these earlier studies, the study groups have been small. In addition, no previous studies have been carried out on the birth rate of offspring of men in partnerships after THR.

One explanation for the lower birth rate in all THR patients might be a lower quality of life in THR patients than in people with no THR (Räsänen et al. 2007). It has been reported that THR patients fared worse in many areas of perceived health (Räsänen et al. 2007). Another study showed that quality of life is similar in THR patients and in people without THR, in most dimensions (Stea et al. 2007). In contrast, it has also been found that people who have a condition that may require THR suffer from a lower quality of life (Sierra et al. 2005, Stea et al. 2007). It has also been reported that THR reduces hip-related problems in the sexual life of RA patients (Baldursson and Brattström 1979). Overall, THR improves quality of life compared to the pre-operational situation in many dimensions, and may therefore increase birth rate as the patient's quality of life improves after surgery.

Having had live-born children before THR affected the birth rate after THR in both men and women. Compared to those who already had children, both patients and reference individuals with no children before surgery had a higher birth rate after surgery. While the birth rate was consistently higher in the reference population, the difference in birth rates between THR patients and their designated references was less pronounced in those who had previously had live-born children. This change in birth rates can also be seen as a change in hazard ratios for a live-born child when comparing THR patients with reference individuals. This could be due to a tendency of the reference group to have reached their planned family size at a younger age because of their higher quality of life.

In summary, patients with THR have a lower birth rate after surgery than people without THR. The most probable reason for this is the underlying hip disease causing a lower quality of life.

MA, ES, HH, ML, and AE had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. MA, ES, and AE contributed to the conception and design of the study. ML drafted the manuscript. AE supervised the study. HH was responsible for the statistical analyses. All authors participated in the interpretation of data and in critical revision of the manuscript.

No competing interests declared.

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