Low adherence to cervical cancer screening after subtotal hysterectomy

Lea Laird Andersen[1-3], Lars Mikael Alling Møller[4] & Helga Margrethe Gimbel[1, 2]

ABSTRACT

INTRODUCTION: A reason for not recommending subtotal hysterectomy is the risk of cervical pathology. We aimed to evaluate cervical cancer screening and to describe cervical pathology after subtotal and total hysterectomy for benign indications.

METHODS: Data regarding adherence to screening and pathology results from the national Danish registry (Patobank) were obtained on women from a randomised clinical trial and an observational study of subtotal versus total abdominal hysterectomy from the time of surgery until 2014.

RESULTS: We included 501 women (259 subtotal hysterectomies and 242 total hysterectomies). The mean follow-up time was 14.1 years, and the mean age at follow-up was 62.1 years. After subtotal hysterectomy, 9.7% were not invited for screening. Adherence to screening was 61.4%; 8.5% were not screened. After total hysterectomy, 14.5% were not invited, 6.6% adhered to screening and 65.7% were not screened. We found a minimum of one abnormal test in 28 (10.8%) after subtotal hysterectomy and one after total hysterectomy. No cervical cancers were found.

CONCLUSIONS: Adherence to cervical cancer screening after subtotal hysterectomy in a Danish population is suboptimal and some patients have unnecessary tests performed after total hysterectomy. Clarification of the use of cervical/vaginal smears after hysterectomy is needed to identify women at risk of cervical dysplasia or cancer.

FUNDING: Research Foundation of Region Zealand, University of Southern Denmark, Nykøbing Falster Hospital, Rigshospitalet and Roskilde Hospital, Denmark.

TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT01880710.

Removing the cervix as part of the hysterectomy procedure for benign indications remains controversial. The medical principle of doing as little as is necessary, in this case subtotal hysterectomy, is opposed to the fear of leaving a seemingly unnecessary cervix that could develop a cancer. The choice of procedure has varied between total and subtotal hysterectomy throughout the past century for different reasons [1]. In 10% of abdominal and 20% of laparoscopic hysterectomies performed in Denmark in 2011, the cervix was preserved (subtotal hysterectomy) [2]. At some units, subtotal hysterectomy is the standard treatment [3] as it is quicker, simpler and may yield fewer perioperative complications [1]. However, for this to be warranted, it is essential that women have regular cervical smears performed after subtotal hysterectomy and that the risk of cervical cancer is low.

Smears of the vaginal vault are of no proven value after total hysterectomy for benign indications [4]. On the contrary, they may lead to anxiety and discomfort for the patient and generate unnecessary costs [5, 6]. The recommendations differ around the world: The US Preventive Services Task Force recommends avoiding screening after total hysterectomy for benign indications [4]. Inversely, in the UK there is a specific guideline regarding smears after total hysterectomy [7].

In Denmark, the national screening programme invites women aged 23-50 years of age to attend a cervical cancer screening every three years and women aged 50-64 years to attend cancer screening every five year [8]. A guideline on screening after hysterectomy is not available.

Based on a randomised clinical trial (RCT) and an observational study (OS) of subtotal (SAH) versus total (TAH) abdominal hysterectomy, we evaluated cervical cancer screening after hysterectomy in Denmark.

METHODS

An RCT was performed in 1996-2000 to evaluate SAH and TAH regarding uro-genital outcomes [9]. An OS in women who declined participation in the RCT was performed concurrently; these women chose the surgical method themselves [10]. All participants had normal cervical smears prior to surgery and no history of abnormal smears [9, 10]. The women were informed when entering the studies that they should continue cervical cancer screening if they had an SAH.

The cohorts were followed by postal questionnaires for up to 14 years post-operatively. Details of inclusion, exclusion, surgical procedures and power calculations, as well as the questionnaire results from the RCT and OS have been published previously [9-13]. To evaluate the screening programme, we received data on all women in the cohorts from a national pathology registry (Patobank) that covers cervical/vaginal vault smears and any other cervical/vaginal pathology tests taken in Denmark from the time of hysterectomy until February 2014. We

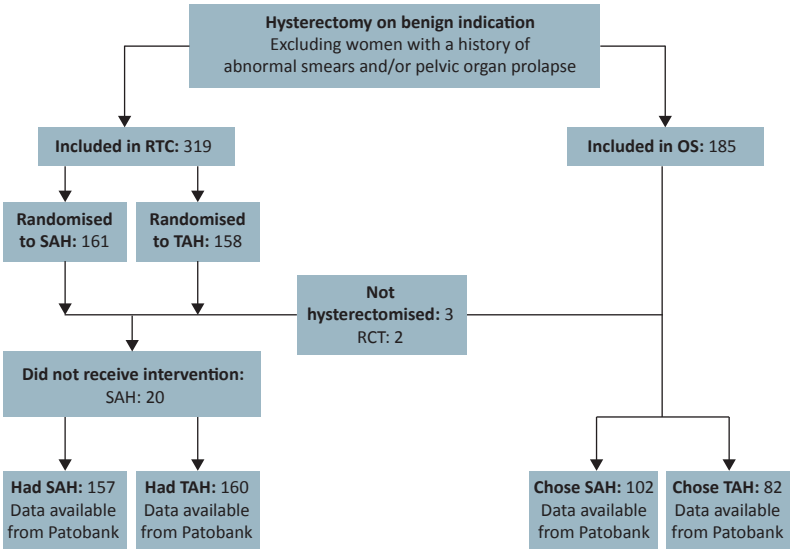
ORIGINAL ARTICLE

1) Department of Obstetrics and Gynaecology, Nykøbing Falster Hospital
2) University of Southern Denmark
3) Women and Children's Health Research Unit, Juliane Marie Centre, Rigshospitalet
4) Department of Obstetrics and Gynaecology, Roskilde Hospital, Denmark

Dan Med J 2015;62(12):A5165

FIGURE 1

Flow chart of participants in the randomized clinical trial and observational study.



OS = observational study; RCT = randomized clinical trial; SAH = subtotal abdominal hysterectomy; TAH = total abdominal hysterectomy.

received data regarding invitations to screening, cervical/vaginal smears taken and all cervical pathology results from time of hysterectomy until February 2014. The individual follow-up time for participants was from the date of hysterectomy until the first of the following events: death, emigration, 65th birthday or 1 February 2014. The 65th birthday was included to focus on smears taken within period of the national screening programme. Adherence to screening was defined as a minimum of one smear per five years of follow-up as this is the normal screening frequency in this age group in Denmark. Abnormal smears were categorised as inflammatory, abnormal cytology (including dysplasia or cancer) or unspecific. All data were analysed according to type of hysterectomy.

The data were analysed using SASjmp version 10, SAS institute, Cary, North Carolina, USA. The Danish Data Protection Agency and the Regional Ethics Committee in Region Zealand approved the study (J. No.: sj-268). Separate consent from the participants was not required for this study; all participants gave informed consent upon inclusion into the RCT and OS. Tests of statistical significance were carried out by chi-squared tests for categorical data and t-test for continuous data. Analyses were done both separately for the two cohorts and on data pooled from the two cohorts. The results described are the pooled results from the RCT and the OS.

Trial registration: ClinicalTrials.gov Identifier: NCT01880710.

RESULTS

We retrieved data from 501 women from Patobank (RCT n = 317 (SAH: 157, TAH 160), OS n = 184 (SAH: 102, TAH 82)) (**Figure 1**). Seven women from the SAH group and three women from the TAH group had a follow-up time of less than three years.

The participants in the RCT and the OS did not differ with regard to baseline characteristics (**Table 1**) except for mean follow-up time, which was longer for the RCT; however, the difference is not clinically relevant. More women in the TAH group than in the SAH group were smokers at the time of surgery. No other significant differences were found with regard to participant characteristics. The results from the RCT and the OS were comparable; these separate results are shown in the tables. In the text below, we present the results based on pooled data from the RCT and the OS.

Table 2 summarises invitations to screening as well as active withdrawals from screening. We found no difference between surgical groups in the number of women who had received at least one invitation since hysterectomy. In the SAH group, 9.7% of the women were never invited. The women's stated reasons for withdrawal are given in Table 2. Approximately half of the women from the SAH group who withdrew from screening gave hysterectomy as the reason (23/49 women). **Table 3** shows adherence to the screening programme in the two surgical groups. A total of 34.3% of the TAH group had one or more vaginal vault smears taken after hysterectomy.

A total of 29 women had at least one abnormal smear. Women with an abnormal smear were primarily found in the SAH group (n = 28, 10.8%). Only one abnormal smear was found in the TAH group; it showed atypical cytology with negative high-risk HPV and was classified as reactive changes. Re-test after one year showed normal cells. No invasive cervical cancers were found in any of the groups. Of the 29 women with abnormal tests, nine tests were classified as inflammatory, ten as abnormal cytology/pathology and ten as unspecific. All abnormal tests led to repeat smears, biopsies or conization. None of the smears taken by the investigator of this study were abnormal.

A total of 16 women (in all from the RCT and OS) had their cervix removed after the subtotal hysterectomy. The reasons for this varied and included vaginal bleeding (n = 5), pelvic organ prolapse (n = 4), inflammation (n = 1), dysplasia (n = 1), pain (n = 1), leiomyosarcoma of the uterus (n = 1) and cancer of the bladder (n = 1). For 2 participants, the reason for removal of the cervix could not be established.

DISCUSSION

We found that approximately six of ten women adhered to cervical cancer screening after SAH; however, almost one in ten of the SAH group was not invited to cervical screening after hysterectomy. In the TAH group, 34.3% of the women had at least one vaginal vault smear taken after hysterectomy.

In the SAH group, 10.8% had a minimum of one abnormal cervical smear. No cervical cancers were found in the follow-up period.

One in ten women from the SAH group were never invited to participate in the national screening programme for cervical cancer. As far as we know, this has not been described previously. These women have been excluded from the programme; nevertheless, they still have a cervix and therefore an indication for screening. The women in the SAH group who did not have a smear taken in the follow-up period are at increased risk of having a late diagnosis of cervical pre-cancer or even cancer. In Denmark, the overall cervical screening compliance rate is about 66.6% [14]. We found that 61.7% were fully adherent to the screening programme, and about 90% had at least one smear done. So, the participation rate after SAH in our trial is comparable to that observed in the overall population.

More than 90% of the women in the SAH group have at least one smear taken in the follow-up period. This indicates that they are aware that they should continue screening and are motivated to do so. Nonetheless, almost 20% actively withdrew from the screening programme, half of them giving hysterectomy as the reason for their withdrawal. This could indicate that the importance of continued screening after SAH is not clear to everyone. All of the women in the SAH group were informed at entry into the trial to continue screening after hysterectomy. However, it remains unknown whether the discontinuation is due to incorrect advice from a doctor later on or a misunderstanding on the part of the participants.

About one third of the TAH group had at least one smear taken despite not having a cervix. It has been shown that cervical screening programmes effectively reduce the number of invasive cervical cancers [15]; however, it is costly, induces anxiety among the women and should be used appropriately. A British NHS national guideline recommends the following programme regarding vaginal vault smears after total hysterectomy [7]: No indication for further tests if the woman had regular cervical smears for ten years prior to hysterectomy and no abnormal smears. If the woman had regular smears without abnormal findings for less than ten years prior to hysterectomy, one vaginal vault smear should be taken after six months. If any smears taken prior to hysterectomy were abnormal, further smears are recommended. In the US, regular vaginal smears after hysterectomy have not been recommended since 2003;

TABLE 1

Characteristics of participants in the randomized clinical trial and the observational study according to surgical group.

	RCT (N = 317)		OS (N = 184)		p-value	
	SAH (n = 157)	TAH (n = 160)	SAH (n = 102)	TAH (n = 82)	RCT vs OS	SAH vs TAH
Age[a], yrs, mean (range)	62.2 (45.8-82.2)	61.6 (42-83.2)	63.04 (48.1-78.8)	62.3 (51.5-79.0)	0.15	0.11
Follow-up time[b], yrs, mean (range)	14.3 (0-17.8)	14.3(0-17.7)	13.2 (0.8-16.8)	14.0 (0.6-16.3)	0.011*	0.26
Parity, mean (range)	1.75 (0-5)	1.82 (0-4)	1.8 (0-6)	1.5 (0-3)	0.23	0.72
Smoking > 5 cigarettes/day[d], n (%)	42 (26.8)	60 (37.5)	27 (27.8)	28 (35.9)	0.86	0.02*
Alcohol > 14 units/week[d], n (%)	15 (9.6)	13 (8.1)	17 (17.5)	6 (7.7)	0.13	0.093
BMI, kg/m^2, mean (range)						
Preoperatively	26 (17.8-42.6)	25.2 (17.1-47.3)	25.4 (17.2-38.3)	25.6 (19-35.9)	0.75	0.32
14 yrs[c]	27.2 (17.7-42.6)	26.4 (16.7-50.1)	25.8 (17.2-37.2)	25.7 (18.4-43.3)	0.08	0.39
Indication for hysterectomy, n (%)						
Fibroids	93 (59.3)	92 (57.5)	65 (63.7)	35 (42.7)	0.38	0.054
Abnormal uterine bleeding	50 (31.9)	54 (33.8)	29 (28.43)	34 (41.5)	0.74	0.16
Dysmenorrhoea	6 (3.8)	6 (3.8)	2 (1.96)	3 (3.7)	0.72	0.69
Pelvic pain	8 (5.1)	5 (3.1)	4 (3.9)	6 (7.3)	0.49	0.97
Endometriosis	0	0	1 (0.98)	2 (2.4)	0.023*	0.52
Other	0	3 (1.9)	1 (0.98)	2 (2.4)	0.50	0.08

BMI = body mass index; OS = observational study; RCT = randomized clinical trial; SAH = subtotal abdominal hysterectomy; TAH = total abdominal hysterectomy.

*) Statistically significant.

a) At time of follow-up (1 Feb 2014).

b) Calculated from date of surgery until the 1st of the following: Death, left Denmark, turned 65 yrs of age (end of screening) or Feb 2014.

c) At follow-up available for 189 women from the RCT (SAH: n = 98, TAH: n = 92) and 118 from the OS (SAH: n = 63, TAH: n = 53).

d) At time of surgery.

TABLE 2

Invitations, reminders and withdrawals from the cervical cancer screening programme.

	RCT (N = 317)		OS (N = 184)		p-value[a]	
	SAH (n = 157)	TAH (n = 160)	SAH (n = 102)	TAH (n = 82)	RCT vs OS	SAH vs TAH
Invitations, n, median (min.-max.)	3 (0-7)	2 (0-6)	3 (0-5)	2 (0-4)	0.08	< 0.0001*
Women receiving min. 1 invitation, n (%)	148 (94.3)	132 (82.5)	86 (84.3)	75 (91.5)	0.78	0.1
Reminders, n, median (min.-max.)	1 (0-9)	1 (0-10)	1 (0-10)	1 (0-8)	0.21	0.36
Reasons for active withdrawal from screening, n (%)						
"I had a hysterectomy"	13 (8.3)	110 (68.8)	10 (9.8)	45 (54.9)	0.045*	< 0.0001*
"I do not wish to participate"	5 (3.2)	4 (2.5)	2 (1.96)	4 (4.9)	0.79	0.69
Other reasons	9 (5.7)	11 (6.9)	10 (9.8)	17 (20.7)	0.002*	0.10
Withdrawn from screening in total	27 (17.2)	125 (78.1)	22(21.6)	66 (80.5)	0.98	< 0.0001*

OS = observational study; RCT = randomized clinical trial; SAH = subtotal abdominal hysterectomy; TAH = total abdominal hysterectomy.
*) Statistically significant
a) t-test for continuous data, testing if means are different, χ^2-test for categorical data.

TABLE 3

Adherence to the cervical cancer screening program defined as minimum one smear pr. five years of follow-up. The values are n (%).

	RCT (N = 317)		OS (N = 184)	
	SAH (n = 157)	TAH (n = 160)	SAH (n = 102)	TAH (n = 82)
No screening	10 (6.3)	105 (65.6)	12 (11.8)	54 (65.9)
Screening less frequently than every 5 yrs	49 (31.2)	44 (27.5)	29 (28.4)	23 (28.0)
Adherent to screening	98 (62.4)	11 (6.9)	61 (59.8)	5 (6.1)

OS = observational study; RCT = randomized clinical trial; SAH = subtotal abdominal hysterectomy; TAH = total abdominal hysterectomy.

however, a study from 2010 showed that about 60% of these women still had vaginal smears done [16].

The benign hysterectomy rate in Denmark is around 180/100,000 woman years [17] resulting in approximately 4,500 benign hysterectomies performed annually in Denmark. In almost 90% of these cases, the cervix is removed [18]. We found that 34.3% of the women who had a total hysterectomy had at least one smear taken since their hysterectomy. If this is the case for all women who undergo total hysterectomy in Denmark, about 1,450 women who undergo total hysterectomy each year have at least one vaginal vault smear taken after hysterectomy. The price of one test is approximately 17.4 Euros; so if 1,450 tests are performed unnecessarily, the annual cost of the Danish cervical screening programme could be reduced by about 25,230 Euros. A cost-effectiveness analysis performed in the US [5] concluded that regular smears after total hysterectomy without indication are not cost-effective and should not be recommended.

The inclusion criterion for participation in the RCT and OS was no previous abnormal pap-smear [9]. Furthermore, all women in our trial had a normal pap-smear at their entry into the trial. According to the NHS criteria, there should be no reason for continued follow-up [7].

Because of the lack of a guideline in Denmark, the women as well as the general practitioners may be uncertain as to whether the smear is indicated or not — especially when the women continue to receive invitations as established in the present study. A study from the UK [19] showed that greater knowledge among general practitioners and practice nurses was associated with fewer vaginal vault smears taken. This may also be the case in Denmark. The lack of a guideline may lead to excessive testing under the "better safe than sorry" mantra.

We found no cervical cancers in our follow-up. A Swedish registry-based study found that mean time from hysterectomy to diagnosis of cervical stump cancer was 17.6 years [20]. Our follow-up may be too short to fully elucidate this, especially in a cohort of the size of ours. Cervical stump cancers have been reported to be seen in 1-3% of women who have undergone subtotal hysterectomy [20]. Thus, if our follow-up time is long enough, we would expect to find 2.5-7.7 cases in our material. Nevertheless, our participants may be less likely to develop cervical stump cancer because they were excluded from participation if they had prior abnormal smears or abnormal smear at their entry into the trial.

A strength of the present study is that we can compare women who have undergone SAH with comparable women who have undergone TAH. The women who have had a total hysterectomy are often excluded from trials involving the screening programme. Therefore, the trials do not investigate unnecessary smears taken in this group of women. A second strength is that we have information on all women included in the trials because of the unique personal identification number used in Denmark and the national registry, Patobank.

Weaknesses of the study are that our follow-up

time is 14 years, which might be too short to fully evaluate the risk of cervical stump cancer. In addition, our study population might be too small to evaluate cervical stump cancer as it occurs only rarely. Also, we are not able to distinguish between smears taken as part of the screening programme and smears taken for other reasons. Furthermore, we have not validated the data from the Patobank against medical charts or other national registries; so the completeness of the register could be questioned.

CONCLUSIONS

In conclusion, the question is whether the extra smears, removal of the cervix and potential cancers outweigh the short-term benefits of shorter surgical time and maybe fewer complications [1] associated with subtotal compared with total hysterectomy. None of the clinical outcomes previously reported from randomised clinical trials of subtotal versus total abdominal hysterectomy [9, 11, 12] suggest a long-term benefit of leaving the cervix. Women facing the choice of subtotal or total hysterectomy should be thoroughly informed about the pros and cons, and the importance of continued cervical cancer screening after subtotal hysterectomy must be emphasised. Furthermore, it is essential for a screening programme that it targets the correct people and no one else. Better evidence regarding who should have additional smears after total hysterectomy and evidence-based guidelines on this matter in order to avoid unnecessary tests after total hysterectomy would be of great importance.

Finally, to get a full picture of the cervical pathology following subtotal hysterectomy, a nationwide registry based study is recommended.

CORRESPONDENCE: *Lea Laird Andersen.* E-mail: lland@regionsjaelland.dk/lealairdandersen@gmail.com

ACCEPTED: 2 October 2015

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE

1. Sutton C. Past, present, and future of hysterectomy. J Minim Invasive Gynecol 2010;17:421-35.
2. Dansk hysterektomi database. Danish hysterectomy database yearly report 2011. Dansk hysterektomi database. 1-10-0012.
3. Wallwiener M, Taran FA, Rothmund R et al. Laparoscopic supracervical hysterectomy (LSH) versus total laparoscopic hysterectomy (TLH): an implementation study in 1,952 patients with an analysis of risk factors for conversion to laparotomy and complications, and of procedure-specific re-operations. Arch Gynecol Obstet 2013;288:1329-39.
4. Sirovich BE, Welch HG. Cervical cancer screening among women without a cervix. JAMA 2004;291:2990-3.
5. Fetters MD, Lieberman RW, Abrahamse PH, Sanghvi RV, Sonnad SS. Cost-effectiveness of pap smear screening for vaginal cancer after total hysterectomy for benign disease. J Low Genit Tract Dis 2003;7:194-202.
6. Morioka-Douglas N, Hillard PJ. No Papanicolaou tests in women younger than 21 years or after hysterectomy for benign disease. JAMA Intern Med 2013;173:855-6.
7. Stokes-Lampard H, Wilson S, Waddell C, Bentley L. Vaginal vault cytology tests: analysis of a decade of data from a UK tertiary centre. Cytopathology 2011;22:121-9.
8. Danish Health and Medicines Authority. Danish health and medicines authority recommendation for cervical cancer screening. Copenhagen: Danish Health and Medicines Authority, 2012.
9. Gimbel H, Zobbe V, Andersen BM et al. Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. BJOG 2003;110:1088-98.
10. Gimbel H, Zobbe V, Andersen BM et al. Total versus subtotal hysterectomy: an observational study with one-year follow-up. Aust N Z J Obstet Gynaecol 2005;45:64-67.
11. Andersen L, Zobbe V, Ottesen B et al. Five-year follow up of a randomised controlled trial comparing subtotal with total abdominal hysterectomy. BJOG 2015;122:851-7.
12. Andersen LL, Ottesen B, Alling Moller LM et al. Subtotal versus total abdominal hysterectomy: randomized clinical trial with 14-year questionnaire follow-up. Am J Obstet Gynecol 2015;212:758.e1-758.e54.
13. Gimbel H, Zobbe V, Andersen BJ et al. Lower urinary tract symptoms after total and subtotal hysterectomy: results of a randomized controlled trial. Int Urogynecol J Pelvic Floor Dysfunct 2005;16:257-262.
14. DKLS. Dansk kvalitetsdatabase for livmoderhalskræftscreening, DKLS. Årsrapport 2013 [Yearly report of the Danish Quality database for cervical cancer screening]. DKLS, 2013.
15. Pettersson BF, Hellman K, Vaziri R, Andersson S, Hellstrom AC. Cervical cancer in the screening era: who fell victim in spite of successful screening programs? J Gynecol Oncol 2011;22:76-82.
16. Cervical cancer screening among women by hysterectomy status and among women aged ≥65 years – United States, 2000-2010. MMWR Morb Mortal Wkly Rep 2013;61:1043-7.
17. Lykke R, Blaakaer J, Ottesen B et al. Hysterectomy in Denmark 1977-2011: changes in rate, indications, and hospitalization. Eur J Obstet Gynecol Reprod Biol 2013;171:333-8.
18. DHHD. Danish hysterectomy and hysteroscopy database, national yearly report 2012. 2013.
19. Stokes-Lampard H, Wilson S, Allan T, Waddell C, Kehoe S. Vaginal vault smears – 'know more – do less': a questionnaire survey of primary health care practitioners. Cytopathology 2005;16:244-51.
20. Hellstrom AC, Hellman K, Pettersson BF, Andersson S. Carcinoma of the cervical stump: fifty years of experience. Oncol Rep 2011;25:1651-4.