Published in final edited form as:

Fertil Steril. 2007 July ; 88(1): 156–162.

Influence of Hysterectomy on Long-Term Fracture Risk

L. Joseph Melton III, M.D.^a, Sara J. Achenbach, M.S.^b, John B. Gebhart, M.D.^c, Ebenezer O. Babalola, M.D.^c, Elizabeth J. Atkinson, M.S.^b, and Adil E. Bharucha, M.D.^d

^a*Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN.*

^b*Division of Biostatistics, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN.*

^c*Department of Obstetrics and Gynecology, Mayo Clinic College of Medicine, Rochester, MN.*

^d*Division of Gastroenterology, Department of Internal Medicine, Mayo Clinic College of Medicine, Rochester, MN.*

Abstract

Objective—To assess long-term fracture risk following hysterectomy, with or without oophorectomy.

Design—Population-based cohort study.

Setting—Olmsted County, Minnesota.

Patients—9258 Olmsted County women who underwent hysterectomy in 1965–2002 compared to an equal number of age- and sex-matched community controls.

Interventions—Observational study of the effect of hysterectomy for various indications on subsequent fractures.

Main outcome measures—Fractures of any type, and at osteoporotic sites (e.g., hip, spine, and wrist) alone, as assessed by electronic review of inpatient and outpatient diagnoses in the community.

Results—Compared to controls, there was a significant increase (hazard ratio [HR], 1.21; 95% CI, 1.13–1.29) in overall fracture risk among the women with hysterectomy, but osteoporotic fracture risk was not elevated (HR, 1.09; 95% CI, 0.98–1.22). Most hysterectomy indications were associated with fractures generally, albeit often not statistically significantly, but only operations for uterine prolapse were associated with osteoporotic fractures (HR, 1.33; 95% CI, 1.01–1.74). Oophorectomy was not an independent predictor of fracture risk (HR, 1.0; 95% CI, 0.98–1.15).

Conclusions—Hysterectomy does not appear to pose much long-term risk for fractures, but the association of fractures with surgery for uterine prolapse deserves further attention.

Keywords

hysterectomy; fracture; cohort study; oophorectomy; pelvic prolapse

Send correspondence and reprint requests to Dr. L. J. Melton III, Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, 200 First Street S.W., Rochester, MN 55905. Telephone: (507)284-5550; Fax: (507)284-1516; e-mail: melton.j@mayo.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interest: The authors have no conflicts of interest with respect to this work.

INTRODUCTION

We previously showed that osteoporotic fracture risk was elevated 1.5-fold among 340 women who underwent bilateral oophorectomy following a natural menopause (1). To the extent that the ovaries contribute to postmenopausal estrogen production via extragonadal conversion of ovarian androgens to estrogen (2), oophorectomy might have exacerbated bone loss in these women and increased their risk of fracture. However, this association could not be confirmed in a subsequent analysis carried out among elderly women in the Study of Osteoporotic Fractures cohort, even though serum testosterone levels were reduced among the women who had a bilateral oophorectomy after menopause compared to unoperated women (3).

One possible explanation for the apparent discrepancy is that subjects in our study were more than 6 years older on average at the time of their oophorectomy. Upon closer inspection, there was a 20% reduction in age-adjusted fracture risk among the subset of these postmenopausal women who had an elective oophorectomy in the course of hysterectomy for endometrial cancer or vaginal bleeding. By contrast there was a 1.4-fold increase in osteoporotic fracture risk in the subset whose bilateral oophorectomy was elective in the course of a hysterectomy for uterine prolapse (L. J. Melton, unpublished data), which is more frequently an indication for surgery among older women (4). Since almost all bilateral oophorectomies are performed in conjunction with hysterectomy (5,6), the possibility therefore arises that the observed association between postmenopausal oophorectomy and fractures was not actually related to age at surgery, but rather was due to (i.e., confounded by) the indication for the underlying hysterectomy.

To address this possibility more directly, we assessed long-term fracture risk in the large cohort of Olmsted County, MN, women who had a hysterectomy in 1965-02, including pre- and postmenopausal women, those with and without oophorectomy and those with vaginal as well as abdominal hysterectomies.

MATERIALS AND METHODS

Population-based epidemiologic research can be conducted in Olmsted County because medical care is virtually self-contained within the community, and complete (inpatient and outpatient) medical records on County residents are available for review (7). Following approval by Mayo's Institutional Review Board, we used this unique database (the Rochester Epidemiology Project) to identify all Olmsted County women who underwent a hysterectomy between January 1, 1965 and December 31, 2002. As reported previously (8), 9893 hysterectomies were performed in this population. However, 615 patients from the hysterectomy file (6%) who refused to authorize use of their medical records for research (9) were excluded from the original study, and an additional 20 women declined to participate in this follow-up analysis.

After further approval from the Institutional Review Board, the remaining 9258 women with hysterectomy were individually matched by age (98% within ± 1 year of birth year) to Olmsted County women without a history of hysterectomy. The hysterectomy cases and their age-matched controls were then followed forward in time through their linked medical records in the community (retrospective cohort study). Each subject's complete inpatient and outpatient medical record at each local provider of medical care was searched electronically for the occurrence of any fracture through the comprehensive diagnostic and surgical indices that are part of the Rochester Epidemiology Project (7). Follow-up continued until death or the most recent clinical contact.

Fractures were classified by anatomical site, but information on the degree of trauma involved in each fracture event was not available. Thus, 'osteoporotic' fractures were taken to be those

of the proximal femur, lumbar/thoracic vertebrae or distal forearm, the skeletal sites traditionally linked to osteoporosis (10). By convention, these are further defined as fractures due to moderate trauma, but nothing about osteoporosis protects bones from severe trauma, and this convention is now being questioned (11).

Among the cases, the type and indications for hysterectomy were identified electronically using specific procedure and diagnostic codes as described elsewhere (8). For the purpose of this study, hysterectomies were broadly categorized as abdominal or vaginal.

Where there were multiple diagnoses, the principal indication for surgery was assigned using the hierarchical system established by the Centers for Disease Control and Prevention (4). If cancer of the reproductive tract was one of the listed diagnoses, it was deemed the primary indication. Next, if debulking of cancer of the urinary or intestinal tract were listed, that was assigned as the indication. In the absence of a cancer diagnosis, a precancerous condition (e.g., endometrial hyperplasia) was designated if present. The diagnoses were then scanned for uterine leiomyoma, endometriosis or uterine prolapse, and the first of these diagnoses listed was assigned as the primary indication. The same approach was used for menstrual disorders (e.g., menorrhagia), menopausal disorders (e.g., postmenopausal bleeding), and inflammatory diseases of the pelvis. The remaining records were placed in the “other” category.

The influence of hysterectomy on subsequent fracture risk was evaluated using three basic methods of analysis, all carried out using the Statistical Analysis System (SAS Institute, Inc., Cary, NC). In the primary analysis, the risk of fractures in the cases was compared directly with that in their matched controls utilizing a stratified proportional hazards model with the case/control pairs forming the strata (12). In such analyses, the follow-up of both members of a pair is censored at the earliest event (i.e., fracture) or follow-up date of either member. Hazard ratios (HR) compared the rate of occurrence of fractures in cases versus controls.

In the second method of analysis, the cumulative incidence of a new fracture (1 minus the probability of survival-free-of-fracture) was projected for up to 30 years following the index date (date of hysterectomy for each case and her matched control) using product-limit methods (13). In comparing cases to controls, follow-up was censored at the earlier of the two last dates of follow-up for each case-control pair. A log-rank test was used to compare cumulative fracture incidence (14).

In the final approach, Cox proportional hazards models (12) were used to assess the impact of various covariates (e.g., age, calendar year of surgery, type of hysterectomy, indication, oophorectomy) on the subsequent risk of fractures among the cases alone. Univariate relationships between the risk of specific fractures and each clinical characteristic under consideration were first assessed. Stepwise methods with forward selection and backward elimination were then used to choose independent variables for the final models. The dependent variable was time until fracture, and the independent variables were the clinical characteristics at baseline, with oophorectomy and pelvic floor repair (which could have occurred before or after the hysterectomy) handled as time-dependent covariates. For the final multivariable models, as well as for the univariate models, the assumption of proportional hazards was examined and was not violated for the variables considered.

RESULTS

During the 38-year study period, 9893 hysterectomies were performed in this population, but 635 women did not authorize use of their medical records for research purposes. Thus, 9258 hysterectomies were included in this analysis. Of these, 6353 (69%) were performed as a single procedure, while 2905 (31%) hysterectomies were combined with a pelvic floor repair procedure; an additional 215 pelvic floor repairs were done before or after the hysterectomy.

Altogether, 5141 (56%) hysterectomies were performed vaginally, and 4117 (44%) were abdominal operations. Fifty (1%) of the vaginal hysterectomies were laparoscopically assisted, while subtotal (i.e., supracervical, $n = 57$) and radical hysterectomies ($n = 78$) comprised negligible proportions of the abdominal hysterectomies.

The indications for the hysterectomies are delineated in Table 1. As would be expected, surgery for uterine fibroids was the most common indication for hysterectomy. Otherwise, cancer indications dominated the abdominal hysterectomies, while prolapse and menstrual disorders were more often indications for vaginal hysterectomy.

The median age at hysterectomy was 44 years (mean $\pm$ SD, 46.2 ± 12.5 years), and the operated women were subsequently followed for 139,831 person-years (median, 13.6 years per subject). During this period of observation, 2639 subjects experienced at least one fracture, for a crude fracture incidence rate of 18.9 per 1000 person-years. Women in the control group were of comparable age (45.7 ± 12.5 years) due to the matching and were followed for a total of 144,321 person-years (median, 14.0 years per subject). When censored so as to be identical for each member of a case-control pair, follow-up totaled 112,825 person-years (median, 9.5 years; range, 0 to 40 years) in each group. During this more restricted period of observation, the number of women who experienced a fracture was not much greater among cases (2135, 23%) than controls (1879, 20%), but the cumulative incidence of any subsequent fracture differed significantly ($p < 0.001$) between the two groups given the large sample size (Figure 1).

Compared to controls, the overall risk of fracture was elevated 1.21-fold (95% CI, 1.13-1.29) among the women with hysterectomy. There were statistically significant increases in the hazard ratio for fractures of the hands and feet and also of the vertebrae (Table 2). However, no increase was seen in fractures of the distal forearm or proximal femur, and the risk of a fracture at any of the traditional osteoporotic fracture sites (i.e., hip, spine, or distal forearm) was not significantly elevated (HR, 1.09; 95% CI, 0.98-1.22).

The relative risk of any fracture, and of osteoporotic fractures alone, by indication for the hysterectomy is shown in Table 3. Statistically significant increases in overall fracture risk were seen for women operated for cancer debulking, endometriosis, uterine prolapse, and menstrual disorders. However, only prolapse was associated with a statistically significant increase in osteoporotic fracture risk.

In a multivariate analysis, (Table 4), the independent predictors of any fracture among the women with hysterectomy included increasing age (HR per 10-year increase, 1.30; 95% CI, 1.26-1.34), more recent surgery (HR per 10 years, 1.14; 95% CI, 1.09-1.19) and a hysterectomy indication of uterine/vaginal prolapse (HR 1.16; 95% CI, 1.04-1.29). The latter association was independent of age despite the fact that prolapse was a more frequent indication for surgery among older than younger women (i.e., 27% of hysterectomies at age ≥ 70 years compared to 17% at ages 50-69 years and only 10% at ages < 50 years). By contrast, pelvic floor repair was not a significant predictor of fracture risk after adjusting for the prolapse indication. There was no overall increase in fracture risk associated with vaginal versus abdominal hysterectomy (HR, 1.00; 95% CI, 0.93-1.08) nor with oophorectomy in 6093 women (66%) as a time-dependent variable (HR, 1.06; 95% CI, 0.98-1.15), although 94% of them occurred within one year of the hysterectomy.

DISCUSSION

Given equivocal results from the Women's Health Initiative (15), estrogen treatment, when used at all (16), may increasingly be restricted to women at high risk of fracture (17). Of particular interest is the risk of fracture among the 633,000 women who undergo hysterectomy annually (18). Hysterectomy was shown by others to be equivalent to postmenopausal status

in doubling fracture risk over a 2-year period in perimenopausal women (19), but it is necessary to quantify fracture risk long-term, not just in the perimenopausal period where short-term estrogen use may be indicated for relief of menopausal symptoms. In the present study, spanning all ages and with follow-up extending to 40 years, overall fracture risk was elevated by 21% among the women who had undergone hysterectomy. This raises two general possibilities: First, that the hysterectomy was causally related to the increase in risk and, second, that it was just an indicator of an underlying predisposition (confounding).

Hysterectomy per se could have an adverse effect on the skeleton by compromising the ovarian blood supply, thus causing premature ovarian failure (20,21); and serum bioavailable testosterone levels but not bioavailable estradiol levels are reduced among women with hysterectomy and ovarian conservation (22). With a few exceptions (23-25), however, most studies have found no excessive bone loss following hysterectomy alone (26-34). Moreover, if premature sex steroid deficiency were the predominant mechanism, one would expect fracture risk to increase with younger age at surgery (35). The opposite was true in this analysis, and the association of fractures with increasing age, as documented here, is well known (10). In addition, we found no difference in subsequent fracture risk between the two surgical approaches to hysterectomy.

On the other hand, most indications for hysterectomy were associated with some increase in overall fracture risk, although the increases were statistically significant in only 4 of 10 indications despite the large numbers of women involved. Even where significant, the effect sizes were modest ($HR < 1.8$), and there was little increase in fracture risk among women operated for leiomyomata or premalignant conditions, which together accounted for over half of all hysterectomies. The indication most closely associated with overall fracture risk, and the only one significantly associated with osteoporotic fractures, was uterine prolapse. This condition may be a marker for estrogen deficiency (36,37), although oral contraceptive use and hormone replacement therapy appear not to be protective (38,39). If so, the association with fractures previously seen with postmenopausal oophorectomy (1), which was also most evident in the subset of women with prolapse, is likely an indirect one due to confounding by the indication for the concomitant hysterectomy.

Indeed, the present results are consistent with data from the Study of Osteoporotic Fractures (3) in concluding that oophorectomy is not independently associated with osteoporotic fracture risk among women with hysterectomy. In this analysis, we lacked any information about the use of estrogen treatment, which could have masked an adverse effect of oophorectomy on fracture risk in these women. However, in a separate study, we showed that estrogen replacement had only a modest effect among premenopausal women with bilateral oophorectomy since few of them were treated beyond the usual age of natural menopause (6). Likewise, in an observational study, there was little influence of estrogen on subsequent fractures among women who were already postmenopausal at the time of oophorectomy (1), whereas significant reductions in hip, spine and wrist fractures were seen in a randomized controlled trial of estrogen treatment among older women (15).

One of the strengths of our study was the use of a large population-based inception cohort that includes almost all of the women in the community who underwent a hysterectomy. In addition, the controls were selected from an enumeration of the Olmsted County population, and therefore should have been representative of community residents generally (7). Furthermore, the patients were followed forward from the date of their operation for up to 40 years (median, 13.6 years), and fractures were ascertained using the resources of the Rochester Epidemiology Project (7), which allowed access to all outpatient and inpatient data so that outcomes could be assessed comparably in cases and controls.

There are also corresponding limitations of a study based on electronic medical record review. In particular, we were unable to specify the actual mechanisms that might influence fracture risk as there was no routine evaluation of bone loss, bone turnover or other measures of bone quality nor any assessment of sex steroid levels. Such studies are needed, particularly among women with uterine prolapse. Nonetheless, our overall results indicate that osteoporotic fractures do not represent a substantial problem for most women undergoing hysterectomy, whether or not an oophorectomy is performed, and this is consistent with most previous studies showing little excessive bone loss following hysterectomy. These observations may be germane to the controversy concerning “prophylactic” oophorectomy in these women (40).

Acknowledgments

The authors would like to thank Mrs. Mary Roberts for preparing the manuscript.

Role of the funding source: This work was supported by research grants AG04875, HD41129 and AR30582 from the National Institutes of Health, U.S. Public Health Service. The National Institutes of Health played no direct role in the conduct of this study or in the preparation of this report.

This project was supported in part by research grants AG04875, HD41129 and AR30582 from the National Institutes of Health, U.S. Public Health Service. None of the authors has a financial conflict of interest with respect to this work.

REFERENCES

1. Melton LJ III, Khosla S, Malkasian GD, Achenbach SJ, Oberg AL, Riggs BL. Fracture risk after bilateral oophorectomy in elderly women. *J Bone Miner Res* 2003;18:900–5. [PubMed: 12733730]
2. Riggs BL, Khosla S, Melton LJ III. Sex steroids and the construction and conservation of the adult skeleton. *Endocrine Rev* 2002;23:279–302. [PubMed: 12050121]
3. Antoniucci DM, Sellmeyer DE, Cauley JA, Ensrud K, Schneider JL, Vesco KK, et al. Postmenopausal bilateral oophorectomy is not associated with increased fracture risk in older women. The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res* 2005;20:741–7. [PubMed: 15824846]
4. Lepine LA, Hillis SD, Marchbanks PA, Koonin LM, Morrow B, Kieke BA, et al. Hysterectomy surveillance—United States, 1980–1993. *Mor Mortal Wkly Rep CDC Surveill Summ* 1997;46:1–15.
5. Brett KM, Pokras R, Madans JH, Peterson HB. National trends in bilateral oophorectomy, 1965–1990. *J Women’s Health* 1994;3:337–45.
6. Melton LJ III, Crowson CS, Malkasian GD, O’Fallon WM. Fracture risk following bilateral oophorectomy. *J Clin Epidemiol* 1996;49:1111–5. [PubMed: 8826990]
7. Melton LJ III. History of the Rochester Epidemiology Project. *Mayo Clin Proc* 1996;71:266–74. [PubMed: 8594285]
8. Babalola E, O’Bharucha A, E. Schleck C, D. Gebhart J, B. Zinsmeister A, R. Melton L J III. Decreasing utilization of hysterectomy: A population-based study in Olmsted County, Minnesota, 1965–2002. *Am J Obstet Gynecol* (in press)
9. Melton LJ III. The threat to medical-records research. *N Engl J Med* 1997;337:1466–70. [PubMed: 9380105]
10. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet* 2002;359:1761–7. [PubMed: 12049882]
11. Sanders KM, Pasco JA, Ugoni AM, Nicholson GC, Seeman E, Martin TJ, et al. The exclusion of high trauma fractures may underestimate the prevalence of bone fragility fractures in the community: The Geelong Osteoporosis Study. *J Bone Miner Res* 1998;13:1337–42. [PubMed: 9718203]
12. Cox DR. Regression models and life-tables (with discussion). *J Royal Stat Soc* 1972 (Series B) 34:187–220
13. Kaplan EL, Meier P. Non-parametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457–81.
14. Kalbfleisch, JD.; Prentice, RL. The statistical analysis of failure time data. J Wiley & Sons; New York: 1980.

15. Jackson RD, Wactawski-Wende J, LaCroix AZ, Pettinger M, Yood RA, Watts NB, et al. Effects of conjugated equine estrogen on risk of fractures and BMD in postmenopausal women with hysterectomy: Results from the Women's Health Initiative Randomized Trial. *J Bone Miner Res* 2006;21:817–28. [PubMed: 16753012]
16. U.S. Preventive Services Task Force. Hormone replacement therapy for primary prevention of chronic conditions: recommendations and rationale. October 2002. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/clinic/3rduspstf/hrt/hrtrr.htm>
17. Nguyen TV, Center JR, Eisman JA. Association between breast cancer and bone mineral density: The Dubbo Osteoporosis Epidemiology Study. *Maturitas* 2000;36:27–34. [PubMed: 10989239]
18. Kozak LJ, Hall MJ, Owings MF. National Hospital Discharge Survey: 2000 annual summary with detailed diagnosis and procedure data. National Center for Health Statistics. *Vital Health Stat* 2002;13(153):1–194.
19. Torgerson DJ, Campbell MK, Thomas RE, Reid DM. Prediction of perimenopausal fractures by bone mineral density and other risk factors. *J Bone Miner Res* 1996;11:293–7. [PubMed: 8822354]
20. Siddle N, Sarrel P, Whitehead M. The effect of hysterectomy on the age at ovarian failure: identification of a subgroup of women with premature loss of ovarian function and literature review. *Fertil Steril* 1987;47:94–100. [PubMed: 3539646]
21. Dean S. Hysterectomy and bone mineral density. *Br J Hosp Med* 1997;57:207–9. [PubMed: 9176599]
22. Laughlin GA, Barrett-Connor E, Kritz-Silverstein D, von Mühlen D. Hysterectomy, oophorectomy, and endogenous sex hormone levels in older women: the Rancho Bernardo Study. *J Clin Endocrinol Metab* 2000;85:645–51. [PubMed: 10690870]
23. Hreshchysyn MM, Hopkins A, Zylstra S, Anbar M. Effects of natural menopause, hysterectomy, and oophorectomy on lumbar spine and femoral neck bone densities. *Obstet Gynecol* 1988;72:631–8. [PubMed: 3419740]
24. Watson NR, Studd JW, Garnett T, Savvas M, Milligan P. Bone loss after hysterectomy with ovarian conservation. *Obstet Gynecol* 1995;86:72–7. [PubMed: 7784026]
25. Duraes Simões R, Chada Baracat E, Szjenfeld VL, de Lima GR, Jose Goncalves W, Bortoletto C. Effects of simple hysterectomy on bone loss. *Revista Paulista de Medicina* 1995;113:1012–5. [PubMed: 8731286]
26. Johansson C, Mellström D, Milsom I. Reproductive factors as predictors of bone density and fractures in women at the age of 70. *Maturitas* 1993;17:39–50. [PubMed: 8412842]
27. Ravn P, Lind C, Nilas L. Lack of influence of simple premenopausal hysterectomy on bone mass and bone metabolism. *Am J Obstet Gynecol* 1995;172:891–5. [PubMed: 7892881]
28. Tuppurainen M, Kröger H, Saarikoski S, Honkanen R, Alhava E. The effect of gynecological risk factors on lumbar and femoral bone mineral density in peri- and postmenopausal women. *Maturitas* 1995;21:137–45. [PubMed: 7752951]
29. Carranza-Lira S, Murillo-Urbe A, Martinez Trejo N, Santos-González J. Changes in symptomatology, hormones, lipids, and bone density after hysterectomy. *Int J Fertil Womens Med* 1997;42:43–7. [PubMed: 9113835]
30. Larcos G. Hysterectomy with ovarian conservation: effect on bone mineral density. *Aust NZ J Obstet Gynaecol* 1998;38:452–4.
31. Grainge MJ, Coupland CA, Cliffe SJ, Chilvers CE, Hosking DJ. Reproductive, menstrual and menopausal factors: which are associated with bone mineral density in early postmenopausal women? *Osteoporos Int* 2001;12:777–87. [PubMed: 11605745]
32. Forsmo S, Schei B, Langhammer A, Forsén L. How do reproductive and lifestyle factors influence bone density in distal and ultradistal radius of early postmenopausal women? The Nord-Trøndelag Health Survey, Norway. *Osteoporos Int* 2001;12:222–9. [PubMed: 11315241]
33. Cheng S, Sievänen H, Heinonen A, Uusi-Rasi K, Carbone L, Tylavsky F, et al. Does hysterectomy with ovarian conservation affect bone metabolism and density? *J Bone Miner Metab* 2003;21:12–6. [PubMed: 12491088]
34. Kritz-Silverstein D, von Mühlen DG, Barrett-Connor E. Hysterectomy and oophorectomy are unrelated to bone loss in older women. *Maturitas* 2004;47:61–9. [PubMed: 14706767]
35. van Der Voort DJ, van Der Weijer PH, Barentsen R. Early menopause: increased fracture risk at older age. *Osteoporos Int* 2003;14:525–30. [PubMed: 12730751]

36. Smith P, Heimer G, Norgren A, Ulmsten U. Localization of steroid hormone receptors in the pelvic muscles. *Eur J Obstet Gynecol Reproduct Biol* 1993;50:83–5.
37. Lang JH, Zhu L, Sun ZJ, Chen J. Estrogen levels and estrogen receptors in patients with stress urinary incontinence and pelvic organ prolapse. *Int J Gynaecol Obstetr* 2003;80:35–9.
38. Mant J, Painter R, Vessey M. Epidemiology of genital prolapse: observations from the Oxford Family Planning Association Study. *Br J Obstet Gynaecol* 1997;104:579–85. [PubMed: 9166201]
39. Nygaard I, Bradley C, Brandt D. Pelvic organ prolapse in older women: prevalence and risk factors. The Women's Health Initiative (WHI). *Obstet Gynecol* 2004;104:489–97. [PubMed: 15339758]
40. Parker WH, Broder MS, Liu Z, Shoupe D, Farquhar C, Berek J. Ovarian conservation at the time of hysterectomy for benign disease. *Obstet Gynecol* 2005;106:219–26. [PubMed: 16055568]

Figure 1.

Cumulative incidence of any fracture among 9258 Rochester, Minnesota women following a hysterectomy in 1965-02 and 9258 age-matched controls. Follow-up began at the time of hysterectomy (or comparable date in controls) and was censored at the earlier time of fracture or last follow-up for each member of a case-control pair.

TABLE 1

Indication for hysterectomy, by type, among Olmsted County, Minnesota, women, 1965-2002.

Indication	Abdominal n (%)	Vaginal n (%)	Total n (%)
Cancer of reproductive tract	637 (15.5)	312 (6.1)	949 (10.3)
Debulking of urinary/GI cancer	104 (2.5)	22 (0.4)	126 (1.4)
Pre-cancerous conditions	971 (23.6)	1202 (23.4)	2173 (23.5)
Uterine leiomyomata	1262 (30.7)	1345 (26.2)	2607 (28.2)
Endometriosis	437 (10.6)	268 (5.2)	705 (7.6)
Uterine/vaginal prolapse	45 (1.1)	1094 (21.3)	1139 (12.3)
Menstrual disorders	347 (8.4)	770 (15.0)	1117 (12.1)
Menopausal disorders	42 (1.0)	37 (0.7)	79 (0.9)
Inflammatory diseases of pelvis	202 (4.9)	68 (1.3)	270 (2.9)
Other indications	70 (1.7)	23 (0.4)	93 (1.0)
All indications	4117 (100)	5141 (100)	9258

n = number of procedures.

% = percentage per column.

TABLE 2

Number of fractures observed by skeletal site among 9258 Olmsted County, Minnesota, women following a hysterectomy in 1965-02 (cases) compared directly to 9258 age-matched community controls, with the count of each group affected (n) and the hazard ratio (HR) from a stratified hazards model. Follow-up of both members of a case-control pair was censored at the earliest follow-up date.^a

Site	Cases n	Controls n	HR (95% CI)
Skull/face	98	106	0.91 (0.69-1.21)
Hands/fingers	405	330	1.25 (1.08-1.45)
Distal forearm	350	327	1.09 (0.93-1.27)
Other arm	397	380	1.04 (0.90-1.20)
Clavicle/scapula/sternum	82	71	1.21 (0.88-1.67)
Ribs	253	225	1.11 (0.93-1.34)
Vertebrae	251	198	1.28 (1.06-1.55)
Pelvis	25	22	1.14 (0.64-2.02)
Proximal femur	192	198	1.00 (0.82-1.22)
Other leg	524	492	1.09 (0.96-1.24)
Feet/toes	588	467	1.32 (1.16-1.50)
Any site	2135	1879	1.21 (1.13-1.29)

^a Subjects were censored by death, emigration from the community or the occurrence of the indicated fracture.

TABLE 3

Fracture risk following hysterectomy in 1965-2002 among 9258 Olmsted County, Minnesota, women compared to 9258 age-matched community controls, by indication for surgery.

Indication (n)	Any fracture HR (95% CI) ^a	Osteoporotic fracture HR (95% CI) ^a
Cancer of reproductive tract (949)	1.21 (0.97-1.51)	1.03 (0.74-1.44)
Debulking of urinary or GI cancer (126)	1.82 (1.01-3.29)	2.00 (0.86-4.67)
Pre-cancerous conditions (2173)	1.10 (0.96-1.26)	0.97 (0.77-1.21)
Uterine leiomyomata (2607)	1.12 (0.98-1.27)	0.99 (0.81-1.22)
Endometriosis (705)	1.46 (1.11-1.92)	1.38 (0.81-2.33)
Uterine/vaginal prolapse (1139)	1.28 (1.07-1.54)	1.33 (1.01-1.74)
Menstrual disorders (1117)	1.50 (1.21-1.87)	1.23 (0.79-1.92)
Menopausal disorders (79)	0.93 (0.44-1.98)	0.57 (0.17-1.95)
Inflammatory diseases of pelvis (270)	1.18 (0.79-1.77)	1.44 (0.76-2.72)
Other indications (93)	1.29 (0.48-3.45)	1.50 (0.25-8.98)

^aHazard ratio from a stratified hazards model.

TABLE 4

Univariate and multivariate hazard ratios (HR)^a for the development of any new fracture among 9258 Olmsted County, Minnesota, women following a hysterectomy in 1965-02.

Risk factor^b	Univariate HR (95% CI)	Multivariate HR (95% CI)
Age at surgery (per 10-year increase)	1.32 (1.28-1.36)	1.30 (1.26-1.34)
Calendar year (per 10-year increase)	1.16 (1.11-1.21)	1.14 (1.09-1.19)
Uterine prolapse indication (yes versus no)	1.25 (1.13-1.39)	1.16 (1.04-1.29)
Pelvic floor repair (yes vs no)	1.13 (1.05-1.22)	-

^aProportional hazards models where the event is a fracture and the dependent variable survival time (days) free of fracture.

^bOnly risk factors that were significant in the univariate and/or multivariate analyses are included in the table.