Food and Drug Administration

Quantitative Assessment of the Prevalence of Unsuspected Uterine Sarcoma in Women Undergoing Treatment of Uterine Fibroids

Summary and Key Findings
April 17, 2014

The FDA conducted a review of published and unpublished scientific literature, including patients operated on from 1980 to 2011 to estimate the prevalence of unsuspected uterine sarcoma and uterine leiomyosarcoma in patients undergoing hysterectomy or myomectomy for presumed benign fibroids (leiomyoma). The review included cohort and cross-sectional studies with a numerator (cases of uterine sarcoma or leiomyosarcoma (LMS)) and denominator (total patient population assessed), regardless of sample size. FDA's primary analysis included 9 of the 18 identified studies.[1]

Estimated prevalence of unsuspected sarcoma

The 18 identified studies are listed in the TABLE.[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18] Five of the nine studies in the primary analysis were conducted in the United States. Hysterectomy was the sole surgical procedure in six of the studies, hysterectomy or myomectomy in one study and myomectomy alone in two studies. Sample sizes ranged from 104 to 1429 (mean=1018; median=1115). The number of patients with unsuspected uterine sarcoma in each study ranged from 0 to 7, as it did for LMS (mean=2.1; median=1.0).

During hysterectomy or myomectomy for presumed benign leiomyoma, the prevalence of unsuspected uterine sarcoma and LMS, was 2.8 (95% CI: 1.8-4.5) per 1,000 persons and 2.0 (95% CI: 1.1-3.8) per 1,000 persons, respectively.[2] These translate to an unsuspected uterine sarcoma in 1 in 352 women and an unsuspected LMS in 1 in 498 women undergoing hysterectomy or myomectomy for presumed benign leiomyoma. There were insufficient data to stratify by age.

Conclusion

This analysis indicates that the prevalence of unsuspected uterine sarcoma in patients undergoing hysterectomy or myomectomy for presumed benign leiomyoma is 1 in 352 and the prevalence of unsuspected uterine leiomyosarcoma is 1 in 498.

---

[1] The 9 studies comprising the primary analysis consisted of 8 full publications and 1 abstract. Nine studies were excluded from the primary analysis because they either included patients undergoing hysterectomy for non-leiomyoma-related conditions (n=7), contained insufficient detail (n=1) or were published in a non-English language (n=1).

[2] Prevalence estimates were calculated using a random effects model using a generalized linear mixed model in SAS 9.3 (PROC GLIMMIX). Proportions and 95% confidence intervals (calculated using the exact binomial method) were converted to rates per 1000 persons. Additional analyses using a simple pooled approach and a random-effects model based on the DerSimonian-Laird method produced similar prevalence estimates.

Quantitative Assessment of the Prevalence of Unsuspeted Uterine Sarcoma in Women Undergoing Treatment of Uterine Fibroids

If laparoscopic power morcellation is performed in women with unsuspected uterine sarcoma, there is a risk that the procedure will spread the cancerous tissue within the abdomen and pelvis, significantly worsening the patient's likelihood of long-term survival. For this reason, and because there is no reliable method for predicting whether a woman with fibroids may have a uterine sarcoma, the FDA discourages the use of laparoscopic power morcellation during hysterectomy or myomectomy for uterine fibroids.

The FDA is convening an outside panel of experts in obstetrics and gynecology to discuss information related to laparoscopic power morcellation at a public meeting. The FDA plans to discuss a comprehensive analysis of scientific literature in greater detail at that time.

See FDA's April 17, 2014, Safety Communication "Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy: FDA Safety Communication" for additional recommendations for Patients and Health Care Providers.

Quantitative Assessment of the Prevalence of Unsuspeted Uterine Sarcoma in Women Undergoing Treatment of Uterine Fibroids

TABLE. Studies reporting unsuspected uterine sarcomas and leiomyosarcomas, 1980-2014

Author	Year Published	Study Years	Procedure(s)	Indication(s)	Country	Total Patients	Number of Uterine Sarcomas	Rate of Uterine Sarcoma (95%CI)	Number of Leiomyosarcomas	Rate of Leiomyosarcoma (95% CI)
Primary Analysis										
Leibsohn, et al.[1]	1990	1983-1988	Hysterectomy	Leiomyoma(s)	U.S.	1429	7	4.9 (2.0-10.1)	7	4.9 (2.0-10.1)
Reiter, et al.[2]	1992	1986-1989	Hysterectomy	Leiomyoma(s)	U.S.	104	0	0.0 (0.0-34.9)	0	0.0 (0.0-34.9)
Parker, et al.[3]	1994	1988-1992	Hysterectomy or Myomectomy	Leiomyoma(s)	U.S.	1332	3	2.3 (0.5-6.6)	1	0.8 (0.0-4.2)
Takamizawa, et al.[4]	1999	1983-1997	Hysterectomy	Leiomyoma(s)	Japan	923	2	2.2 (0.3-7.8)	1	1.1 (0.0-6.0)
Sinha, et al.[5]	2008	1998-2005	Myomectomy	Leiomyoma(s)	India	505	2	4.0 (0.5-14.2)	2	4.0 (0.5-14.2)
Kamikabeya, et al.[6]	2010	1987-2008	Hysterectomy	Leiomyoma(s)	Brazil	1364	2	1.5 (0.2-5.3)	1	0.7 (0.0-4.1)
Rowland, et al.[7]	2011	2006-2011	Hysterectomy	Leiomyoma(s)	U.S.	1115	5	4.5 (1.5-10.4)	3	2.7 (0.6-7.8)
Leung, et al.[8]	2012	1999-2005	Hysterectomy	Leiomyoma(s)	France	1297	3	2.3 (0.5-6.8)	3	2.3 (0.5-6.8)
Seidman, et al.[9]	2012	2005-2010	Myomectomy*	Leiomyoma(s)	U.S.	1091	2	1.8 (0.2-6.6)	1	0.9 (0.0-5.1)
Not Included in Primary Analysis										
Frick, et al.[10]	2010	2005-2008	Hysterectomy	Pelvic Organ Prolapse	U.S.	644	0	0.0 (0.0-5.7)	0	0.0 (0.0-5.7)
Hageman, et al.[11]	2011	2006-2010	Hysterectomy	Multiple	U.S.	101	0	0.0 (0.0-35.9)	0	0.0 (0.0-35.9)
Mahajan, et al.[12]	2011	2007-2008	Hysterectomy	Pelvic Organ Prolapse	India	253	0	0.0 (0.0-14.5)	0	0.0 (0.0-14.5)
Ramm, et al.[13]	2012	2004-2009	Hysterectomy	Pelvic Organ Prolapse	U.S.	708	1	1.4 (0.0-7.8)	1	1.4 (0.0-7.8)
Wan, et al.[14]	2013	2003-2011	Hysterectomy	Pelvic Organ Prolapse	China	640	1	1.6 (0.0-8.7)	1	1.6 (0.0-8.7)
Theben, et al.[15]	2013	2005-2010	Hysterectomy	Multiple	Germany	1584	2	1.3 (0.2-4.6)	2	1.3 (0.2-4.6)
Ouldamer, et al.[16]	2014	2000-2011	Hysterectomy	Multiple	France	2179	2	0.9 (0.1-3.3)	0	0.0 (0.0-1.7)
Durand-Réville, et al.[17]€	1996	1989-1994	Hysterectomy	Leiomyoma(s)	France	660	6	9.1 (3.3-19.7)	6	9.1 (3.3-19.7)
Park, et al.[18]¥	2012	n/a	Not specified	Leiomyoma(s)	South Korea	22825	49	2.2 (1.6-2.8)	49	2.2 (1.6-2.8)

* Myomectomy was included in search terms. Cases of hysterectomy may have been included, but were not specified in search terms in the Methods section of the article.
€ Article in French. Primary analysis included only English language articles
¥ This was a reply to a reply of an article. Insufficient information was provided in the reply to include in the primary analysis.

REFERENCES

[1] Leibsohn S, d'Ablaing G, Mishell DR, Schlaerth JB. Leiomyosarcoma in a series of hysterectomies performed for presumed uterine leiomyomas. Am J Obstet Gynecol. 1990;162(4):968-974.

[2] Reiter RC, Wagner PL, Gambone JC. Routine hysterectomy for larger asymptomatic uterine leiomyomata – a reappraisal. Obstet Gynecol. 1992;79(4):481-4.

[3] Parker WH, Fu YS, Berek JS. Uterine sarcoma in patients operated on for presumed leiomyoma and rapidly growing leiomyoma. Obstet Gynecol. 1994;83(3):414-8.

[4] Takamizawa S, Minakami H, Usui R, Noguchi S, Ohwada M, Suzuki M, et al. Risk of complications and uterine malignancies in women undergoing hysterectomy for presumed benign leiomyomas. Gynecol Obstet Invest. 1999;48(3):193-6.

[5] Sinha R. Hegde A, Mahajan C, Dubey N, Sundaram M. Laparoscopic myomectomy: do size, number, and location of the myomas form limiting factors for laparoscopic myomectomy? J Minim Invasive Gynecol. 2008;15(3):292-300.

[6] Kamikabeya TS, Etchebehere RM, Nomelini RS, Murta EF. Gynecological malignant neoplasias diagnosed after hysterectomy performed for leiomyoma in a university hospital. European journal of gynaecological oncology. 2010;31(6):651-3.

[7] Rowland M, Lesnock J, Edwards R, Richard S, Zorn K, Sukumvanich P, et al. Occult uterine cancer in patients undergoing laparoscopic hysterectomy with morcellation. Gynecol Oncol. 2012;127(1):S29.

[8] Leung F, Terzibackian JJ. Re "The impact of tumor morcellation during surgery on the prognosis of patients with apparently early uterine leiomyosarcoma". Gynecol Oncol. 2012;124(1):172-173

[9] Seidman MA, Oduyebo T, Muto MG, Crum CP, Nucci MR, Quade BJ. Peritoneal dissemination complicating morcellation of uterine mesenchymal neoplasms. PLoS One. 2012;7(11):e50058.

[10] Frick AC, Walters MD, Larkin KS, Barber MD. Risk of unanticipated abnormal gynecologic pathology at the time of hysterectomy for uterovaginal prolapse. American journal of obstetrics and gynecology. 2010;202(5):507.e1-4.

[11] Hagemann IS, Hagemann AR, Livolsi VA, Montone KT, Chu CS. Risk of occult malignancy in morcellated hysterectomy: A case series. Int J Gynecol Pathol. 2011;30(5):476-83.

[12] Mahajan G, Kotru M, Batra M, Gupta A, Sharma S. Usefulness of histopathological examination in uterine prolapse specimens. The Australian & New Zealand journal of obstetrics & gynaecology. 2011;51(5):403-5.

[13] Ramm O, Gleason JL, Segal S, Antosh DD, Kenton KS. Utility of preoperative endometrial assessment in asymptomatic women undergoing hysterectomy for pelvic floor dysfunction. International urogynecology journal. 2012;23(7):913-7.

[14] Wan OY, Cheung RY, Chan SS, Chung TK. Risk of malignancy in women who underwent hysterectomy for uterine prolapse. The Australian & New Zealand journal of obstetrics & gynaecology. 2013;53(2):190-6.

[15] Theben JU, Schellong AR, Altgassen C, Kelling K, Schneider S, Grosse-Drieling D. Unexpected malignancies after laparoscopic-assisted supracervical hysterectomies (LASH): an analysis of 1,584 LASH cases. Archives of gynecology and obstetrics. 2013;287(3):455-62.

[16] Ouldamer L, Rossard L, Arbion F, Marret H, Body G. Risk of Incidental Finding of Endometrial Cancer at the Time of Hysterectomy for Benign Condition. Journal of minimally invasive gynecology. 2014;21(1):131-5.

[17] Durand-Reville M, Dufour P, Vinatier D, Martin de Lassalle E, Lucot JP, Monnier JC, et al. [Uterine leiomyosarcomas: a surprising pathology. Review of the literature. Six case reports]. Journal de gynecologie, obstetrique et biologie de la reproduction. 1996;25(7):710-5

[18] Park JY. Re "The impact of tumor morcellation during surgery on the prognosis of patients with apparently early uterine leiomyosarcoma". Gynecol Oncol. 2012;124(1):173.