Global Journal of Medical research: E
Gynecology and Obstetrics
Volume 14 Issue 4 Version 1.0 Year 2014
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals Inc. (USA)
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

The Accuracy of Surgical Assessment of Gross Myometrial Invasion as a Predictor of Lymphatic Metastases in Women with Endometrial Carcinoma

By Andrew P.Soisson, Jessica Pittman, Mark K. Dodson, Tom Belnap, Braydon Rowley & William Sause

Saint Vincent College, United States

Abstract- Objective: The objective of this study was to determine if the surgeon can accurately predict the depth of myometrial tumor invasion in women with endometrial cancer, and if tumor invasion will correlate with node metastases.

Methods: We identified 1,943 women with endometrial carcinoma who underwent hysterectomy. Of these, 295 underwent comprehensive surgical staging including lymph node analysis. All subjects also underwent gross examination of the uterine specimen by their surgeon where the depth of myometrial invasion was recorded. Patients with grade III tumors or papillary serous and clear cell histology were excluded. The presence or absence of myometrial invasion was then correlated with the incidence of nodal involvement to determine if this system can be used to predict tumor spread at the time of hysterectomy.

Keywords: endometrial, cancer, depth of invasion.

GJMR-E Classification : NLMC Code: WP 390, WJ 190

Strictly as per the compliance and regulations of:

The Accuracy of Surgical Assessment of Gross Myometrial Invasion as a Predictor of Lymphatic Metastases in Women with Endometrial Carcinoma

Andrew P.Soisson [α], Jessica Pittman [σ], Mark K. Dodson [ρ], Tom Belnap [ω], Braydon Rowley [¥] & William Sause [§]

Synopsis: In this study, low-grade tumors with less than 50% invasion by surgeon prediction were associated with a 3% incidence of nodal metastases.

Abstract- Objective: The objective of this study was to determine if the surgeon can accurately predict the depth of myometrial tumor invasion in women with endometrial cancer, and if tumor invasion will correlate with node metastases.

Methods: We identified 1,943 women with endometrial carcinoma who underwent hysterectomy. Of these, 295 underwent comprehensive surgical staging including lymph node analysis. All subjects also underwent gross examination of the uterine specimen by their surgeon where the depth of myometrial invasion was recorded. Patients with grade III tumors or papillary serous and clear cell histology were excluded. The presence or absence of myometrial invasion was then correlated with the incidence of nodal involvement to determine if this system can be used to predict tumor spread at the time of hysterectomy.

Results: The ability of the surgeon to accurately predict the depth of myometrial invasion was 82%, sensitivity was 57%, specificity 89%, positive predictive value 62% and the negative predictive value was 88%. If this system was used as the indication for nodal evaluation the authors would have missed 3% of women with nodal metastases who had less than 50% myometrial invasion.

Conclusions: Gross evaluation of the hysterectomy specimen can accurately predict depth of myometrial invasion. However, in our analysis 3% of women with less than 50% invasion had node involvement. If the surgeon had used the absence of myometrial invasion to omit nodal assessment, these lesions would have been missed. Therefore, we feel that nodal assessment should be considered in the majority of cases.

Keywords: endometrial, cancer, depth of invasion.

I. Introduction

Endometrial carcinoma is the 4th most common cancer in females and the most common gynecologic malignancy with approximately 43,470 cases and 7,950 deaths per year diagnosed in the United States[1]. New diagnoses are rare before the age of 40 and increase ten-fold from ages 40-49. The vast majority of women with endometrial cancer are postmenopausal and the median age is 55[2,3]. Most women with endometrial carcinoma develop postmen opausal vaginal bleeding that prompts them to seek medical attention. Diagnosis of the malignancy is usually made by endometrial biopsy or dilation and curettage of the uterine cavity. Therefore, over 80% of women with endometrial adenocarcinoma are diagnosed with early stage disease that ultimately equates to a high overall cure rate[4]. Treatment options for women with stage I or II endometrial carcinoma include anti-estrogen therapy, primary radiation, and most commonly hysterectomy. Anti-estrogen therapy (progesterone) is associated with low response rates in postmenopausal women, and radiation as a primary treatment is technically difficult in many cases and is used infrequently. Therefore, surgical treatment is the most common treatment modality and is associated with high cure and good local control rates.

Surgery usually includes complete hyste rectomy, bilateral salpingo-oophorectomy,cytologic analysis of pelvic fluid for malignant cells, and retroperitoneal lymph node assessment for the presence or absence of lymphatic metastases. Despite the fact that lymph node assessment has not been shown to offer a therapeutic benefit[5,6], many believe it allows practitioners the opportunity to recommend more appropriate post-surgical adjunctive therapies, and the Society of Gynecologic Oncologists (SGO) recommends that it be performed in most cases[7]. However, not all surgeons have been trained to perform retroperitoneal lymph node assessment and the procedure is associated with some surgical morbidity and even mortality[8]. Thus, many surgeons utilize tumor grade and depth of myometrial invasion as clinical variables to predict the incidence of lymphatic metastases and therefore, an indication for lymph node assessment at the time of surgery. Myometrial invasion is a critical prognostic factor in women with low-risk factors such as

Author α σ ρ: University of Utah/Department of Obstetrics and Gynecology and The Huntsman Cancer Institute.
Author ω ¥ §: Clinical Oncology Services/Intermountain Health Corporation.

grade I an II tumors and endometriod histology. Multiple reports have shown that the surgeon's ability to measure and predict the depth of symmetrical invasion is fairly accurate[9-13], and is as good as pathologic examination by frozen section[14-16]. However, this surgical strategy has not been as extensively studied as a model to predict the true presence or absence of lymphatic metastases in a large cohort of women with endometrial cancer who have undergone complete surgical staging and who have had the uterus examined by the surgeon at the time of hysterectomy to measure the depth of myometrial invasion. The purpose of this study was to evaluate the accuracy of surgical prediction of myometrial invasion by endometrial tumor and to determine the accuracy of this method as a model for predicting lymph node involvement by tumor.

II. Materials and Methods

The state tumor registry was used to identify all women with endometrial cancer who underwent hysterectomy as their initial and primary treatment during the time period of the study. The authors created a surgical registry and abstracted the medical records, including surgical operative reports, anesthesia records, pathology reports and in-patient record of hospital stay. The collection of data and recruitment of patients for this study was approved by the institutional review board at our institution. From 1993 to 2010, 1,943 women were diagnosed with endometrial cancer and underwent hysterectomy as their primary treatment at one of 11 institutions in our geographical area. These included community and tertiary medical centers. Of these, 295 had examination under anesthesia, surgical evaluation of the pelvis and upper abdomen, oophorectomy, analysis of pelvic washings, pelvic retroperitoneal lymph node sampling, and evaluation of the uterine specimen for gross myometrial invasion by the surgeon. All cases were performed by one of three gynecologic oncologists at one of three tertiary medical centers who used the exact same methodology to evaluate the uterus and to predict the depth of tumor invasion. Only patients with endometriod histology and grade I or II tumors were included in the analysis as most gynecologic oncologists would routinely perform lymph node analysis in grade III or clear cell and papillary serous tumors.

Myometrial invasion was recorded as equal to or less than 50%, or greater than 50% invasion of the thickness of the myometrium at the maximal depth of penetration of the tumor. In each case after completing the surgical procedure, the surgeon would make a lateral incision at the 3' and 6" position of the uterine cervix and extend it to the fundus to expose the entire endometrial surface for gross examination. Lateral perpendicular full thickness incisions were then made through the endometrium and myometrium in at least two areas of the anterior and posterior surface of the uterus to assess the depth of symmetrical invasion. Depth of invasion was recorded by the surgeon in the operative report and later abstracted into a surgical database.

III. Results

The mean weight of the 295 study patients was 194 pounds and the mean body mass index was 32.3. One hundred and seven (36%) women in the study group had hypertension, 53 (18%) had adult onset diabetes mellitus (AODM), and 21 (7%) were cigarette smokers. One hundred fifty five women (52%) had grade I tumors and 140 (48%) were grade II. Women with poorly differentiated tumors (grade III) or unusual histology such as clear cell or papillary serous tumors were eliminated from the analysis. Two hundred sixty nine women (91%) had their ovaries removed at the time of surgery. All 295 women underwent hysterectomy, analysis of pelvic washings and pelvic lymph node sampling. The mean estimated blood loss was 316 ml. and 29 women underwent transfusion (10%) in the immediate postoperative period.

At the completion of the hysterectomy the primary surgeon examined the uterus and estimated the maximal depth of symmetrical invasion of the tumor. In 242 cases the surgeon accurately estimated the depth of invasion compared to histologic examination on permanent sections for an overall accuracy rate of 82%. There were 53 cases where the surgeon did not predict the true depth of symmetrical invasion. The sensitivity was calculated as 57%, specificity 89%, positive predictive value was 62%, and the negative predictive value was 88%.

The overall incidence of retroperitoneal lymph node metastases was 4% (n=12). In 62 cases the surgeon estimated that the depth of invasion was greater than 50% and of these 6 (10%) had nodal metastases and 56 (90%) had no evidence of nodal involvement by tumor. In 233 cases the surgeon estimated less than or equal to 50% symmetrical invasion and of these 6 (3%) had lymph node metastases and 227 (97%) were not involved with tumor.

IV. Discussion

Extrauterine spread of tumor cells is the most significant poor prognostic factor associated with decreased survival in women with endometrial cancer. The most common anatomic site of metastatic disease is to the pelvic and para-aortic retroperitoneal lymph nodes. Approximately 7-10% of women with endometrial adenocarcinoma will have retroperitoneal lymph node metastases, and the presence or absence of nodal metastases will impact postoperative adjuvant therapy and subsequent cure rates[4]. The relatively high likelihood of nodal spread, the impact on recommending postoperative therapies, and the relatively low morbidity associated with node sampling has prompted

the Society of Gynecologic Oncologists to recommend that retroperitoneal node sampling be performed in most women with endometrial cancer[7]. Unfortunately, not all women with endometrial cancer undergo complete surgical staging or care by gynecologic oncologists in the United States. Gynecologists and surgeons in non-tertiary centers often employ preoperative and intra-operative strategies to assess the likelihood of nodal spread, which is used to determine if nodal sampling is performed at the time of hysterectomy[17,18].

Preoperative radiographic imaging modalities evaluating retroperitoneal metastases are limited, have not been sufficiently studied in large groups of women, and are largely inaccurate[19,20]. Preoperative radiographic evaluation of myometrial invasion using ultrasonography (US), magnetic resonance imaging (MRI), and positron emission tomography (PET) are fairly comparable in their ability to accurately predict the depth of myometrial invasion. Multiple studies have demonstrated that US has an accuracy rate of approximately 65-75% and sensitivity and specificity of 70% for predicting depth of invasion compared to final histology[21-23]. Transvaginal ultrasound employing saline infusion will increase the accuracy of myometrial invasion detection slightly[24]. Magnetic resonance imaging is comparable with an accuracy, sensitivity, and specificity of 62-95%, 79-92%, and 72-100% respectively[25-29]. Finally, PET imaging appears to offer no increased accuracy compared to other radiographic modalities[30-32].

Estimation of myometrial invasion grossly by the surgeon at the time of hysterectomy has also been evaluated in multiple studies incorporating large numbers of women; these indicate that the accuracy rates, sensitivity, and specificity are comparable to or somewhat better than radiographic assessment. Reported rates for accuracy are 82-91%, sensitivity 65-84%, and specificity 83-96%[9-11,33]. Estimation of depth of invasion at the time of the hysterectomy by frozen section is comparable in accuracy to gross inspection by the surgeon. Studies using frozen section only as a predictor of myometrial invasion have accuracy rates of 70-90%[14,34-36]. Studies comparing frozen section to gross invasion in the same surgical setting show equivalent accuracy rates for the two methods[37,38]. In our study we confirm the results of prior investigations and show that surgeon assessment of myometrial invasion of less than or greater than 50% of the thickness of the myometrium is fairly accurate. Our results of 82% accuracy compare favorably to other reports.

Surgical algorithms incorporating depth of myometrial invasion as a method to assess the likelihood of retroperitoneal lymph node metastases has been less well studied. Tumor size has been shown to be a predictor of metastatic disease since 1987[39] and was used as an intraoperative factor along with depth of myometrial invasion by frozen section by Kumar and colleagues at the Mayo Clinic[40]. We chose not to use tumor size as a factor since frozen section evaluation is not rapidly available at our institution. Multiple authors have shown that depth of invasion determined at the time of surgery by the surgeon or pathologist does not accurately predict the presence or absence of retroperitoneal lymph node involvement. These reports indicate that many patients undergo lymph node resection unnecessarily and, more importantly, some do not have node assessment when they should have. Traen[41] reported on 72 women with grade I tumors who underwent complete surgical staging. In their analysis, 4% had lymph node assessment unnecessarily and 7% did not have nodal analysis when they should have. Papadia[42] reviewed data from Gynecologic Oncology Group (GOG) protocol 33 and analyzed 174 women with early stage endometrial cancer that were surgically staged. They concluded that a substantial number of cases had suboptimal management when gross inspection of the uterus and frozen section to determine the depth of myometrial invasion was used as a methodology for assessing lymph node status. In our analysis, we attempt to retrospectively evaluate a surgical system where depth of invasion is used at the time of hysterectomy to indicate whether node sampling should be performed in women with endometriod histology and grade I or II tumors. In this system, the surgeon could accurate predict depth of invasion but 3% of the subjects would not have had node assessment performed when metastases to the retroperitoneum were present. Therefore, we recommend that lymph node assessment be performed in the majority of women undergoing hysterectomy for endometrial carcinoma as we believe the incidence of significant morbidity such as vascular injury[43] associated with lymph node sampling is far less significant than not detecting lymph node metastases.

V. Conflict of Interest Statement

The authors declare there are no conflicts of interest.

References Références Referencias

1. Jemal A, Siegel R, Xu J, Ward E. Cancer Statistics, 2010. CA Cancer J Clin. 2010;60:277-300.
2. Hunn J, Dodson MK, Webb J, Soisson AP. Endometrial cancer – current state of the art therapies and unmet clinical needs: The role of surgery and preoperative radiographic assessment. Adv Drug Deliv Rev 2009; 61:890-5.
3. Erkanli S, Ayhan A. Fertility-sparing therapy in young women with endometrial cancer. I J Gynecol Care. 2010;20:1170-1187.
4. Creasman WT, Morrow CP, Bundy BN, et al. Surgical pathologic spread patterns of endometrial

cancer. A gynecologic group study. Cancer. 1987;60:2035-2041.
5. Kitchener H, Swart AMC, Qian W, Amos C, Parmar MKB. Efficacy of systematic pelvic lymphadenec tomy in endometrial cancer (MRC ASTEC trial): a randomized study. Lancet. 2009;373:125-36.
6. Benedetti P, Basile S, Maneschi F, Lissoni A, Signorelli M, Scambia G, et al. Systematic pelvic lymphadenectomy vs no lymphadenectomy in early-stage endometrial carcinoma: Randomized clinical trial. J Natl Cancer Inst. 2008;100:1707-1716.
7. Management of endometrial cancer. ACOG Practice Bulletin No. 65. American College of Obstetricians and Gynecologists. Obstet Gynecol 2005;106:413–25.
8. Lachance JA, Everett EN, Greer B, Mandel L, Swisher E, Tamimi H, Goff B. The effect of age on clinical/pathologic features, surgical morbidity, and outcome in patients with endometrial cancer. Gynecol Oncol. 2006;101:470-5.
9. Mao Y, Wan X, Lv W, Xie X. Evaluation of the accuracy of intra-operative gross examination for the surgical management of endometrial cancer. European J Obstet Gynecol and Reproductive Biology. 2008;141:179-82.
10. Franchi M, Ghezzi F, Melpingano M, Cherchi PL, Scarabelli C, Apolloni C, Zanaboni F. Clinical value of intraoperative gross examination in endometrial cancer. Gynecol Oncol. 2000;76:357-61.
11. Vorgias G, Hintipas E, Katsoulis M, Kalinogolou N, Dertimas B, Akrivos T. Intraoperative gross exami nation of myometrial invasion and cervical infiltration in patients with endometrial cancer: Decision-making accuracy. Gynecol Oncol. 2002; 85:483-86.
12. Yahata T, Aoki Y, Tanaka K. Prediction of myometrial invasion in patients with endometrial carcinoma: comparison of magnetic resonance imaging, transvaginal sonography, and gross visual inspection. Eur J Gynaecol Oncol. 2007;28:193-5.
13. Doering DL, Barnhill DR, Weiser EB, Burke TW, Woodward JE, Park RC. Intraoperative evaluation of depth of myometrial invasion in stage I endometrial adenocarcinoma. Obstet Gynecol. 1989;74:930-3.
14. Maneschi F, Sarno M, Mancione AM, Perugini A, Partenzi A. Endometrial carcinoma: intraoperative evaluation of myometrial invasion. A prospective study. Minerva Ginecol. 2008;60:267-72.
15. Altintas A, Vardar MA, Demir C, Tuncer I. Intraoperative assessment of depth of myometrial invasion in endometrial carcinoma. Eur J Gynaecol Oncol. 1999;20:329-31.
16. Frumovitz M, Slomovitz BM, Singh DK, Broaddus RR, Abrams J, Sun CC, Bevers M, Bodurka DC. Frozen section analysis as predictors of lymphatic spread in patients with early-stage uterine cancer. J Am Coll Sur. 2004;199:388-93.
17. Roland PY, Kelly FJ, Kulwicki CY, Bitzer D, Curcio M, Orr JW. The benefits of a gynecologic oncologist: a pattern of care study for endometrial cancer treatment. Gynecol Oncol. 2004;93:125-30.
18. Pearl ML, Villella JA, Valea FA, DiSilvestro PA, Chalas E. Outcomes of endometrial cancer patients undergoing surgery with gynecology oncology involvement. Obstet Gynecol. 2002;100:724-9.
19. Loubeyre P, Undurraga M, Petignat P. Non-invasive modalities for predicting lymph node spread in early stage endometrial cancer. Surg Oncol. 2011;20: 102-8.
20. Sorosky JI. Endometrial cancer. Obstet Gynecol. 2008;111:436-47.
21. Ruangvutilert P, Sutantawibul A, Sunsaneevithayakul P, Boriboonhirunsarn D, Chuenchom T. Accuracy of transvaginal ultrasound for the evaluation of myometrial invasion in endometrial carcinoma. J Med Assoc Thai. 2004;87:47-52.
22. Yahata T, Aoki Y, Tanaka K. Prediction of myometrial invasion in patients with endometrial carcinoma: comparison of magnetic resonance imaging, transvaginal ultrasonography, and gross visual inspection. Eur J Gynaecol Oncol. 2007;28:193-5.
23. Merisio BR, Piantelli G, Rolla M, Melpignano M, Nardelli GB. Preoperative transvaginal ultrasonogra phy and intraoperative gross examination for assessing myometrial invasion by endometrial cancer. J Ultrasound Med. 2008;27:349-55.
24. Takac I. Transvaginal ultrasonography with and without saline infusion in assessment of myometrial invasion of endometrial cancer. J ultrasound Med. 2007;26:949-7.
25. Nasi F, Fiocchi F, Pecchi A, Rivasi F, Torricelli P. MRI evaluation of myometrial invasion by endometrial carcinoma. Comparison between fast-spin-echo T2w and coronal-FMPSPGR gadolinium-dota-enhanced sequences. Radiol Med (Torino). 2005;110:199-210.
26. Nakao Y, Yokoyama M, Hara K, Koyamatsu Y, Yasunaga M, Araki Y, Watanabe Y, Iwasaka T. MR imaging in endometrial carcinoma as a diagnostic tool for the absence of myometrial invasion. Gynecol Oncol. 2006;102:343-7.
27. Torricelli P, Ferraresi S, Fiocchi F, Ligabue G, Jasonni VM, Di Monte I, Rivasi F. 3-T MRI in the preoperative evaluation of depth of myometrial infiltration in endometrial cancer. AJR Am J Roentgenol. 2008;190:489-95.
28. Cabrita S, Rodrigues H, Abreu R, Martins M, Teixeira L, Marques C, Mota F, de Oliveira CF. Magnetic resonance imaging in the preoperative staging of endometrial carcinoma. Eur J Gynaecol Oncol. 2008;29:135-7.
29. Vasconcelos C, Felix A, Cunha TM. Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: comparison of

magnetic resonance imaging and histopathologic evaluation. J Obstet Gynaecol. 2007;27:65-70.
30. Suzuki R, Miyagi E, Takahashi N, Sukegawa A, Suzuki A, Koike I, Sugiura K, Okamoto N, Inoue T, Hirahara F. Validity of positron emission tomography using fluro-2-deoxyglucose for the preoperative evaluation of endometrial cancer. Int J Gynecol Cancer.2007;17:890-6.
31. Horowitz NS, Dehdashti F, Herzog TJ, Rader JS, Powell MA, Gibb RK, Grigsby PW, Siegel BA, Mutch DG. Preoperative evaluation of FDG-PET for detecting pelvic and para-aortic lymph node metastasis in uterine corpus cancer. Gynecol Oncol. 2004;95:546-51.
32. Kitajima K, Murakami K, Yammasaki E, Fukasawa I, Inaba N, Kaji Y, Sugimura K. Acuracy of 18F-FDG PET/CT in detecting pelvic and paraaortic lymph node metastasis in patients with endometrial cancer. Am J Roentgenol. 2008;190:1652-8.
33. Doering DL, Barnhill DR, Weiser EB, Burke TW, Woodward JE, Park RC. Intraoperative evaluation of depth of myometrial invasion in stage I endometrial adenocarcinoma. Obstet Gynecol. 1989;74:930-33.
34. Kucera E, Kainz C, Reinthaller A, Sliutz G, Leodolter S, Kucera H, Breitenecker G. Accuracy of intraoperative frozen-section diagnosis in stage I endometrial adenocarcinoma. Gynecol Obstet Invest. 2000;49:62-6.
35. Furukawa N, Takekuma M, Takahashi N, Hirashima Y. Intraoperative evaluation of myometrial invasion and histologic type and grade in endometrial cancer: diagnostic value of frozen section. Arch Gynecol Obstet. 2010;28:913-7.
36. Case AS, Rocconi RP, Straughn JM, Conner M, Novak L, Wang W, Huh WK. A prospective blinded evaluation of the accuracy of frozen section for the surgical management of endometrial cancer. Obstet Gynecol. 2006;108:1375-9.
37. Altintas A, Cosar E, Vardar MA, Demir C, Tuncer I. Intraoperative assessment of depth of myometrial invasion in endometrial carcinoma. Eur J Gynaecol Oncol. 1999;20:329-31.
38. Ghaemmaghami F, Aminimoghaddam S, Modares-Gilani M, et al. Assessment of gross examination and frozen section of uterine specimen in endometrial cancer patients. Arch Gynecol Obstet. 2010;282:685-89.
39. Schink JC, Lurain JR, Wallemark CB, Chmiel JS. Tumor size in endometrial cancer: a prognostic factor for lymph node metastasis. Obstet Gynecol. 1987;70:215-9.
40. Kumar S, Medeiros F, Dowdy SC, et al. A prospective assessment of the reliability of frozen section to direct intraoperative decision making in endometrial cancer. Gynecol Oncol. 2012;127:525-31.
41. Traen K, Holund B, Mogensen O. Accuracy of preoperative tumor grade and intraoperative gross examination of myometrial invasion in patients with endometrial cancer. Acta Obstet Gynecol Scand. 2007;86:739-41.
42. Papadia A, Azioni G, Brusaca B, Fulcheri E, Nishida K, Menoni S, Simpkins F, Lucci JA. Frozen section underestimates the need for surgical staging in endometrial cancer patients. Int J Gynecol Cancer. 2009;19:1570-3.
43. Nunns D, Williamson K, Swaney L, Davy M. The morbidity of surgery and adjuvant radiotherapy in the management of endometrial carcinoma. Int J Gynecol Cancer. 2000;10:233-38.

This page is intentionally left blank