Iran J Cancer Prev. 2017 February; 10(2):e5285. doi: 10.5812/ijcp.5285.

Published online 2017 February 18. **Research Article**

Positive Peritoneal Cytology as a Predictor of Prognosis in Early Stage of Endometrioid Adenocarcinoma

Setare Akhavan,[1] Zohre Kazemi,[1] Abbas Alibakhshi,[2] Mitra Modaresgilani,[1] Azamsadat Mousavi,[1] Azar Ahmadzadeh,[1] and Khadije Rezaie Kahkhayi[1]

[1]Department of Gynecologic Oncology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, IR Iran
[2]Department of General Surgery, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

*Coresponding author: Zohre Kazemi, Imam Khomeini Hospital, Keshavarz Blv, Tehran, IR Iran. Tel: +98-9153414404, E-mail: zohrekazemi@sbmu.ac.ir

Received 2016 January 04; **Revised** 2016 January 22; **Accepted** 2017 February 11.

Abstract

Background: Peritoneal cytology has been reported to be an independent risk factor for poor survival, but it is not included in the current international federation of gynecology and obstetrics (FIGO) staging system for risk stratification.
Objectives: We aimed to investigate the prognostic significance of positive peritoneal cytology (PPC) in patients with early stage endometrioid adenocarcinoma.
Methods: Medical profiles of patients with uterine carcinoma referring to Imam Khomeini hospital and Mirza Koochak Khan hospital between September, 2005 and December, 2011 have been reviewed. Patients had a complete staging procedure and peritoneal cytology evaluation.
Results: Among 220 patients with mean age of 56.3 $\pm$ 9.1 years, 204 were Negative for peritoneal cytology (NPC) and 16 showed PPC. In the group of patients with endometrioid adenocarcinoma, 125 were in stage I and 32 were in stage II. Univariate analysis on patients with endometrioid adenocacinoma revealed that stage II (OR = 7.12, 95% CI = 2.95-22.10, P value < 0.001), stage III (OR = 8.04, 95% CI = 2.14 - 30.09, P value < 0.001), stage IV (OR = 58.09, 95% CI = 13.74 - 245.66, P value < 0.001), recurrence of either intra (OR = 32.65, 95% CI = 12.2 - 86.7, P value < 0.001) or extra pelvic (OR = 14.54, 95% CI = 4.4 - 47.7, P value < 0.001), and the number of lymph nodes involvement (OR = 5.59, 95% CI = 2.5 - 12.51, P value < 0.001) were significantly associated with survival. Also, patients with PPC had significantly poorer survival compared to those with negative peritoneal cytology; 38% Vs 88% were alive after 5 years (P value < 0.0001). Mean 5-year survival in PPC and NPC patients were 3.31 years and 4.74 years, respectively.
Conclusions: Our study demonstrated that positive peritoneal cytology is an independent prognostic factor in patients with early stage endometrioid adenocarcinoma. We propound that peritoneal cytology adds back into the future FIGO staging criteria revision. Until then, peritoneal washings should still be considered as an important part for accurate risk-stratification.

Keywords: Early Stage, Endometrioid Adenocarcinoma, Peritoneal Cytology, Survival

1. Background

Endometrial carcinoma is the most common gynecologic malignancy and every gynecologist will encounter it during his/her practice. The exact incidence of endometrial carcinoma in the Middle East countries is unclear, but it is estimated to show a growing trend as do developed countries. In the United States endometrial cancer was diagnosed in an estimated 52,630 women in 2014, with 8590 surrendering to their disease (1). The most common histo-pathological subtype of endometrial carcinoma is endometrioid adenocarcinoma (2).

Patients' symptoms may be different from abnormal uterine bleeding and vaginal discharge to abdominal or pelvic pain, abdominal distension, early satiety, or change in bowel or bladder function in patients with advanced stages, resembling the ovarian carcinoma symptoms (3, 4).

As in most cases, postmenopausal bleeding is the initial symptom. Approximately 75% of patients are restricted to the early stages at the time of diagnosis and these patients would experience five-year survival rates of about 95%. But as the disease spreads extra uterine tissues, survival decreases to 67% and 23%, for those with regional or distant disease, respectively (5). Unopposed estrogen exposure, late menopause, obesity, nulli-parity, diabetes, estrogen secreting ovarian tumors, polycystic ovarian syndrome, anovulation, and tamoxifen administration have been proposed as risk factors (6-14).

The endometrial carcinoma would spread through different pathways, including direct expansion, free transtubal implantation, blood and lymphatic invasion. Lymphatic spread occurs three times more than the blood dissemination. In this manner, malignant cells reach the parametrium, vagina, ovaries and retroperitoneal, pelvic and para-aortic lymph nodes (15). Several authors tried to

describe recurrence risk factors of endometrial carcinoma. These factors can be divided into uterine and extra-uterine (15). Uterine factors include histological type, grade (16), depth of myometrial invasion (17), cervical involvement (15, 18), vascular invasion (4, 19, 20), presence of atypical endometrial hyperplasia (21), hormone receptor status and DNA ploidy (22). Extra-uterine factors embrace adnexal involvement, intra-peritoneal metastasis, positive peritoneal cytology (23, 24) and pelvic and para-aortic lymph node metastasis (16, 25).

The incidence of positive peritoneal cytology in patients with early stage endometrial cancer has been reported to range from 5% - 10% (26, 27). Based on 1988 international federation of gynecology and obstetrics (FIGO) staging system for endometrial cancer, peritoneal cytology was used as a stage defining variable. According to this staging algorithm, patients with stage I or stage II endometrial cancer who developed positive peritoneal cytology were upstaged to stage IIIA , even in the absence of any other evidence of extra-uterine disease spread (28-30).

Researchers reported that if positive cytology existed as the only manifestation of extra-uterine disease, patients would experience better prognosis than those with adnexal or serosal involvement, which is equivalent to stage III disease (28, 31). In fact these findings suggested that positive cytology cannot predict survival outcomes independently and other clinic-pathological features should be considered as well. However, other investigators have shown that positive cytology is an independent risk factor in both groups of patients with early and advanced stage disease (30, 32-34). Given this uncertainty, 2009 FIGO staging system states that "positive cytology has to be reported separately without affecting the stage" (35).

In this regard, we aimed to investigate the effect of positive peritoneal cytology on prognosis of patients with endometrial cancer. Considering the fact that most studies on this topic were conducted in developed countries, we assume this study would be the first one to conduct on patients in developing countries.

2. Methods

This study was held retrospectively on patients with primary diagnosis of uterine carcinoma referring to Imam Khomeini hospital and Mirza Koochak Khan hospital, Tehran University of Medical Sciences, Tehran, Iran from September, 2005 to December, 2011.

The institutional review board and ethic committee of Imam Khomeini hospital and Mirza Koochak Khan hospital approved the study protocol. All patients gave informed consent. Patients with diagnosis of endometrioid adenocarcinoma and examination of peritoneal cytology at the time of definitive surgery were enrolled in the study. Patients with prior pelvic irradiation or chemotherapy were excluded. All patients were staged according to the 2009 FIGO staging criteria, after a complete staging procedure (total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and/or para-aortic lymphadenectomy) and pathological review. Patients were divided into three groups based on their age at initial admission; age $<$ 50 years, 50 to 65 years, and $>$ 65 years. The grade was described as follows: grade I = well differentiated, grade II = moderately differentiated and grade III = poorly differentiated. Lymph node involvement was assessed in patients who experienced recurrence and was coded as positive or negative. Use of adjuvant radiation therapy was collected. Each patient's specific cause of death was recorded. Survival was calculated as the number of years from cancer diagnosis to the date of death due to the disease.

Patients were followed by means of history and physical examination every 3 month for the first 2 years after surgery, then every 6 month for the subsequent 3 years. Papanicolaou smear and imaging of the chest, abdomen, and pelvis were performed twice a year for 2 years, then annually for the subsequent 3 years. All recurrences were biopsy-proven.

Properly powered sample size was calculated to be 200. The chi-square test was used to compare the distribution of demographic and clinical characteristics between patients with positive peritoneal cytology and those with negative peritoneal cytology. Survival was estimated using the Kaplan-Meier method and differences between groups were compared using the Enter Method. Cox proportional hazards regression models were developed to examine the effect of positive peritoneal cytology on disease specific survival while controlling for other clinical and demographic characteristics. Statistical analyses were performed using IBM SPSS software version 20 (Chicago, IL, USA). P values $\leq$ 0.05 were considered significant.

3. Results

A total number of 220 patients with mean age of 56.3 $\pm$ 9.1 years (range: 31 - 81 years) enrolled in the study and 204 were negative for peritoneal cytology (NPC) and 16 showed positive peritoneal cytology (PPC). Demographic and clinical features of the entire patients were as shown in Table 1. When comparing patients with and without positive peritoneal cytology, there were no significant differences in patients' age at diagnosis (P = 0.737). Patients with NPC were more frequently diagnosed with grade I (91% vs. 9%, P value $<$ 0.05), stage I (98% vs. 2%, P value $<$ 0.001) and stage II (92% vs. 8%, P $<$ 0.0001), and favorable histologic types such as

adenocarcinoma (94% vs. 6%, P = 0.028). Also, patients with PPC had more frequently lymph node involvement in recurrence episode (68% Vs 32%, P value < 0.001). Additionally, recurrence was more common in PPC patients (38% Vs 12%, P = 0.031).

In 125 patients with endometrioid adenocarcinoma of stage I disease, the myometrical invasion of < 50% was seen in 70 patients and 55 were diagnosed with > 50 % myometrical invasion. Interestingly, there were 2 patients with PPC in the first group, but it was not statistically significant (P > 0.05). There were 32 patients with stage II endometrioid adenocarcinoma.

Univariate analysis on patients with endometrioid adenocacinoma revealed that the following variables were significantly associated with survival: stage II (OR = 7.12, 95% CI = 2.95 - 22.10, P value < 0.001), stage III (OR = 8.04, 95% CI = 2.14 - 30.09, P value < 0.001), stage IV (OR=58.09, 95% CI = 13.74 - 245.66, P value < 0.001), recurrence of either intra (OR = 32.65, 95% CI = 12.2-86.7, P value < 0.001) or extra pelvic (OR = 14.54, 95% CI = 4.4 - 47.7, P-value < 0.001), and the number of lymph nodes involvement (OR = 5.59, 95% CI = 2.5 - 12.51, P value < 0.001).

Also, patients with positive peritoneal cytology had a significantly poorer survival compared to those with negative peritoneal cytology: 38% vs. 88% were alive after 5 years, respectively (P value < 0.0001). Mean 5-year survival in PPC and NPC patients were 3.31 years and 4.74 years, respectively (Figure 1).

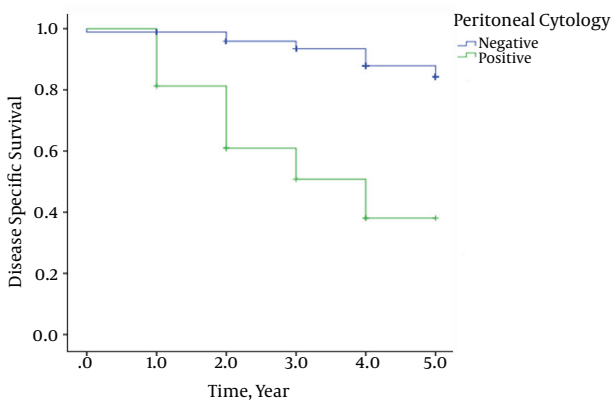

Figure 1. Kaplan-Meier Disease Specific Survival of Patients with Endometrioid Adenocarcinoma of Early Stages by Cytology Status (Time: Year)

There were 8 intra-pelvic and 10 extra-pelvic recurrences in patients with endometrioid adenocarcinoma (Table 2).

4. Discussion

Peritoneal washings would be considered positive if malignant cells appeared as the result of trans-tubal dissemination of primary tumor, tumor extension via myometrium/serosal lymphatics, or exfoliation of cells from disease at other extra-uterine sites (30).

Previous investigators reported that malignant peritoneal cytology was associated with an adverse effect on survival, only when other extra-uterine sites of malignancy were present and not if endometrial cancer was still confined to the uterus (30, 32). Others believed that malignant peritoneal cytology is an indicator of aggressive tumor behavior rather than disease spread through peritoneal space (33, 36). On the other hand, the majority of studies have shown the association between malignant cytology and other adverse prognostic features such as high grade disease, non-endometrioid histology, and deep myometrial invasion (30, 37-39).

Our results indicate that positive peritoneal cytology is an independent predictor of survival among patients with 2009 FIGO stage I and stage II endometrioid adenocarcinoma. The survival was found to be significantly worse in patients with PPC compared to those with NPC. However, this finding can be questioned by the fact that most patients in the PPC group might have deep myometrial invasion and this is the reason for poor survival in PPC patients. But the fact that their survival was worse compared to the corresponding patients with NPC provides indirect evidence that positive cytology is indeed an independent prognostic factor in these patients (40). A Special finding in the results which drew our attention was presence of two patients with PPC in group of patients with myometrical invasion < 50%. We do not know the exact pathogenesis of disease spread in these cases, but we assume that blood or lymphatic dissemination could cause disease spread in the peritoneum.

Although a few studies have failed to prove the prognostic significance of positive peritoneal cytology in patients with early stage endometrioid adenocarcinoma (41, 42), most studies especially those with large number of patients have confirmed its significance as an independent predictor of survival (43). In addition, several studies have shown that if peritoneal washing becomes positive for malignant cells, outcomes would be the same in women with endometrial cancer otherwise confined to the uterus, as those women with serosal or adnexal metastasis (37, 44-46). These findings support the idea that patients with stage I/II endometrial cancer who had positive peritoneal cytology should be placed in higher stage groups rather than what has been proposed by current FIGO staging criteria for accurate risk-stratification.

Table 1. Comparison of Clinical and Demographic Variables of Patients with Positive and Negative Peritoneal Cytology[a]

	Levels	Cytology			P Value
		Overall	Negative	Positive	
Age	< 50	95 (43.2)	88 (43.1)	7 (43.8)	0.737
	50 - 65	108 (49.1)	101 (49.5)	7 (43.8)	
	> 65	17 (7.7)	15 (7.4)	2 (12.4)	
Grade	I	83 (37.7)	76 (37.3)	4 (25.0)	< 0.05
	II	95 (43.2)	90 (44.1)	5 (31.3)	
	III	42 (19.1)	38 (18.6)	7 (43.8)	
Pathological Subtypes	Endometrioid Adenocarcinoma	177 (80.5)	168 (82.4)	9 (56.3)	0.028
	Papillary	15 (6.8)	12 (5.9)	3 ()	
	Clear cell/serous	11 (5.0)	10 (4.9)	1 (6.3)	
	Carcinosarcoma	17 (7.7)	14 (6.9)	3 (18.7)	
Lymph Node Involvement in Recurrence	Negative	195 (88.6)	190 (93.1)	5 (31.3)	< 0.001
	Positive	25 (11.4)	14 (6.9)	11 (68.7)	
Stage	I	139 (63.2)	136 (66.7)	3 (18.8)	< 0.001
	II	51 (23.2)	47 (23.0)	4 (25.0)	
	III	24 (10.9)	19 (9.3)	5 (31.3)	
	IV	6 (2.7)	2 (1.0)	4 (25.0)	
Recurrence	No	190 (86.4)	180 (88.2)	10 (62.5)	0.031
	Pelvic	12 (5.5)	11 (5)	1 (0.5)	
	Extra pelvic	18 (8.2)	13 (5.9)	5 (2.3)	
	> 50	55 (44)	55 (100)	-	

[a]Values are expressed as No. (%).

Table 2. Associated Factors with Mean 5-Year Survival of Patients with Endometrioid Adenocarcinoma

	5-Year Survival					
	Levels	B	SE	EXP(B)(OR)	95% CI for OR	P Value
Lymph Node Involvement in Recurrence	Positive	1.72	0.41	5.59	2.50, 12.51	< 0.001
Stage	II	1.96	0.57	7.12	2.95, 22.10	< 0.001
	III	2.08	0.67	8.04	2.14, 30.09	
	IV	4.06	0.73	58.09	13.74, 245.66	
Recurrence	Intra-pelvic	3.84	0.49	32.65	12.2, 86.7	< 0.001
	Extra-pelvic	2.67	0.60	14.54	4.4, 47.7	
Cytology	Positive	2.24	0.43	9.43	3.3, 15.2	< 0.001

Postoperative adjuvant therapy is another contributing factor in patients' survival but we are not able to make comment on whether or not the presence of PPC should influence postoperative adjuvant therapy recommendations. Considering the fact that PPC patients were more prone to high-risk or high-intermediate risk features such as non-endometrioid histology, deep myometrial invasion and high grade disease than NPC patients, it would be expected to have this treatment. Future studies could be dedicated to investigation of the exact impact of chemotherapy administration on prognosis of patients with PPC.

Our study has several limitations that must be consid-

ered. The major defect of this study was the small number of patients in PPC group.

Similarly, we were not able to determine the factors that separate patients who needed to receive chemotherapy in both PPC and NPC groups, because current guidelines do not indicate chemotherapy in patients with early stages of endometrioid adenocarcinoma.

In conclusion, our study shows that positive peritoneal cytology is an independent prognostic factor in patients with early stage endometrioid adenocarcinoma. Although peritoneal cytology has not been used since FIGO staging criteria 2009, it is still requested by the FIGO to be reported separately. We propound that peritoneal cytology adds back into the surgical staging for endometrial cancer in future FIGO staging criteria revision. Until then, peritoneal washings should stay still as an important part for accurate risk-stratification of patients with early stage endometrial cancer.

Acknowledgments

The authors declare no conflict of interests.

Footnotes

Authors Contribution: Non declared.

Conflict of Interest: Non declared.

Fondding/Support: Non declared.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* 2013;**63**(1):11–30. doi: 10.3322/caac.21166. [PubMed: 23335087].
2. Albertini AF, Devouassoux-Shisheboran M, Genestie C. Pathology of endometrioid carcinoma. *Bull Cancer.* 2012;**99**(1):7–12. doi: 10.1684/bdc.2011.1526. [PubMed: 22231875].
3. S. G. O. Clinical Practice Endometrial Cancer Working Group , Burke WM, Orr J, Leitao M, Salom E, Gehrig P, et al. Endometrial cancer: a review and current management strategies: part I. *Gynecol Oncol.* 2014;**134**(2):385–92. doi: 10.1016/j.ygyno.2014.05.018. [PubMed: 24905773].
4. Ranjbar R, Nejatollahi F, Nedaei Ahmadi AS, Hafezi H, Safaie A. Expression of Vascular Endothelial Growth Factor (VEGF) and Epidermal Growth Factor Receptor (EGFR) in Patients With Serous Ovarian Carcinoma and Their Clinical Significance. *Iran J Cancer Prev.* 2015;**8**(4):e3428. doi: 10.17795/ijcp-3428. [PubMed: 26478789].
5. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al. Cancer statistics, 2008. *CA Cancer J Clin.* 2008;**58**(2):71–96. doi: 10.3322/CA.2007.0010. [PubMed: 18287387].
6. Pike MC, Peters RK, Cozen W, Probst-Hensch NM, Felix JC, Wan PC, et al. Estrogen-progestin replacement therapy and endometrial cancer. *J Natl Cancer Inst.* 1997;**89**(15):1110–6. [PubMed: 9262248].
7. Soliman PT, Wu D, Tortolero-Luna G, Schmeler KM, Slomovitz BM, Bray MS, et al. Association between adiponectin, insulin resistance, and endometrial cancer. *Cancer.* 2006;**106**(11):2376–81. doi: 10.1002/cncr.21866. [PubMed: 16639730].
8. Fisher B, Costantino JP, Redmond CK, Fisher ER, Wickerham DL, Cronin WM. Endometrial cancer in tamoxifen-treated breast cancer patients: findings from the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14. *J Natl Cancer Inst.* 1994;**86**(7):527–37. [PubMed: 8133536].
9. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet.* 2008;**371**(9612):569–78. doi: 10.1016/S0140-6736(08)60269-X. [PubMed: 18280327].
10. Soler M, Chatenoud L, Negri E, Parazzini F, Franceschi S, la Vecchia C. Hypertension and hormone-related neoplasms in women. *Hypertension.* 1999;**34**(2):320–5. [PubMed: 10454461].
11. Gallup DG, Stock RJ. Adenocarcinoma of the endometrium in women 40 years of age or younger. *Obstet Gynecol.* 1984;**64**(3):417–20. [PubMed: 6462572].
12. Soliman PT, Oh JC, Schmeler KM, Sun CC, Slomovitz BM, Gershenson DM, et al. Risk factors for young premenopausal women with endometrial cancer. *Obstet Gynecol.* 2005;**105**(3):575–80. doi: 10.1097/01.AOG.0000154151.14516.f7. [PubMed: 15738027].
13. McPherson CP, Sellers TA, Potter JD, Bostick RM, Folsom AR. Reproductive factors and risk of endometrial cancer. The Iowa Women's Health Study. *Am J Epidemiol.* 1996;**143**(12):1195–202. [PubMed: 8651218].
14. Zhou B, Yang L, Sun Q, Cong R, Gu H, Tang N, et al. Cigarette smoking and the risk of endometrial cancer: a meta-analysis. *Am J Med.* 2008;**121**(6):501–508 e3. doi: 10.1016/j.amjmed.2008.01.044. [PubMed: 18501231].
15. Patrelli TS, Berretta R, Rolla M, Vandi F, Capobianco G, Gramellini D, et al. Pelvic lymphadenectomy in endometrial cancer: our current experience. *Eur J Gynaecol Oncol.* 2009;**30**(5):536–8. [PubMed: 19899410].
16. Morrow CP, Bundy BN, Kurman RJ, Creasman WT, Heller P, Homesley HD, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. *Gynecol Oncol.* 1991;**40**(1):55–65. [PubMed: 1989916].
17. Berretta R, Merisio C, Piantelli G, Rolla M, Giordano G, Melpignano M, et al. Preoperative transvaginal ultrasonography and intraoperative gross examination for assessing myometrial invasion by endometrial cancer. *J Ultrasound Med.* 2008;**27**(3):349–55. [PubMed: 18314512].
18. Rakhsha A, Yousefi Kashi AS, Hoseini SM. Evaluation of Survival and Treatment Toxicity With High-Dose-Rate Brachytherapy With Cobalt 60 in Carcinoma of Cervix. *Iran J Cancer Prev.* 2015;**8**(4):e3573. doi: 10.17795/ijcp-3573. [PubMed: 26478798].
19. Al Kushi A, Lim P, Aquino-Parsons C, Gilks CB. Markers of proliferative activity are predictors of patient outcome for low-grade endometrioid adenocarcinoma but not papillary serous carcinoma of endometrium. *Mod Pathol.* 2002;**15**(4):365–71. doi: 10.1038/modpathol.3880531. [PubMed: 11950909].
20. Nofech-Mozes S, Ackerman I, Ghorab Z, Ismiil N, Thomas G, Covens A, et al. Lymphovascular invasion is a significant predictor for distant recurrence in patients with early-stage endometrial endometrioid adenocarcinoma. *Am J Clin Pathol.* 2008;**129**(6):912–7. doi: 10.1309/CP3HGX7H753QQU8T. [PubMed: 18480008].
21. Merisio C, Berretta R, De Ioris A, Pultrone DC, Rolla M, Giordano G, et al. Endometrial cancer in patients with preoperative diagnosis of atypical endometrial hyperplasia. *Eur J Obstet Gynecol Reprod Biol.* 2005;**122**(1):107–11. doi: 10.1016/j.ejogrb.2005.01.001. [PubMed: 16154046].
22. Berretta R, Patrelli TS, Migliavacca C, Rolla M, Franchi L, Monica M, et al. Assessment of tumor size as a useful marker for the surgical staging of endometrial cancer. *Oncol Rep.* 2014;**31**(5):2407–12. doi: 10.3892/or.2014.3108. [PubMed: 24676344].
23. Gu M, Shi W, Barakat RR, Thaler HT, Saigo PE. Peritoneal washings in endometrial carcinoma. A study of 298 patients with histopathologic correlation. *Acta Cytol.* 2000;**44**(5):783–9. [PubMed: 11015980].

24. Turner DA, Gershenson DM, Atkinson N, Sneige N, Wharton AT. The prognostic significance of peritoneal cytology for stage I endometrial cancer. *Obstet Gynecol.* 1989;**74**(5):775–80. [PubMed: 2812655].
25. Hanson MB, van Nagell JJ, Powell DE, Donaldson ES, Gallion H, Merhige M, et al. The prognostic significance of lymph-vascular space invasion in stage I endometrial cancer. *Cancer.* 1985;**55**(8):1753–7. [PubMed: 3978563].
26. Garg G, Gao F, Wright JD, Hagemann AR, Zighelboim I, Mutch DG, et al. The risk of lymph node metastasis with positive peritoneal cytology in endometrial cancer. *Int J Gynecol Cancer.* 2013;**23**(1):90–7. doi: 10.1097/IGC.0b013e318275afd2. [PubMed: 23196758].
27. Momayyezi M, Fallahzadeh H, Momayyezi M. Construction and Validation the Lifestyle Questionnaire Related to Cancer. *Iran J Cancer Prev.* 2015;**8**(5):e3965. doi: 10.17795/ijcp-3965. [PubMed: 26634112].
28. Fadare O, Mariappan MR, Hileeto D, Wang S, McAlpine JN, Rimm DL. Upstaging based solely on positive peritoneal washing does not affect outcome in endometrial cancer. *Mod Pathol.* 2005;**18**(5):673–80. doi: 10.1038/modpathol.3800342. [PubMed: 15578078].
29. Kasamatsu T, Onda T, Katsumata N, Sawada M, Yamada T, Tsunematsu R, et al. Prognostic significance of positive peritoneal cytology in endometrial carcinoma confined to the uterus. *Br J Cancer.* 2003;**88**(2):245–50. doi: 10.1038/sj.bjc.6600698. [PubMed: 12610496].
30. Garg G, Gao F, Wright JD, Hagemann AR, Mutch DG, Powell MA. Positive peritoneal cytology is an independent risk-factor in early stage endometrial cancer. *Gynecol Oncol.* 2013;**128**(1):77–82. doi: 10.1016/j.ygyno.2012.09.026. [PubMed: 23032094].
31. Milgrom SA, Kollmeier MA, Abu-Rustum NR, Makker V, Gardner GJ, Barakat RR, et al. Positive peritoneal cytology is highly predictive of prognosis and relapse patterns in stage III (FIGO 2009) endometrial cancer. *Gynecol Oncol.* 2013;**130**(1):49–53. doi: 10.1016/j.ygyno.2013.04.013. [PubMed: 23603151].
32. Kadar N, Homesley HD, Malfetano JH. Prognostic factors in surgical stage III and IV carcinoma of the endometrium. *Obstet Gynecol.* 1994;**84**(6):983–6. [PubMed: 7970482].
33. Takeshima N, Nishida H, Tabata T, Hirai Y, Hasumi K. Positive peritoneal cytology in endometrial cancer: enhancement of other prognostic indicators. *Gynecol Oncol.* 2001;**82**(3):470–3. doi: 10.1006/gyno.2001.6301. [PubMed: 11520142].
34. Garg G, Morris RT, Solomon L, Toy EP, Kruger M, Clary K, et al. Evaluating the significance of location of lymph node metastasis and extranodal disease in women with stage IIIC endometrial cancer. *Gynecol Oncol.* 2011;**123**(2):208–13. doi: 10.1016/j.ygyno.2011.07.025. [PubMed: 21821278].
35. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. *Int J Gynaecol Obstet.* 2009;**105**(2):103–4. [PubMed: 19367689].
36. Preyer O, Obermair A, Formann E, Schmid W, Perrin LC, Ward BG, et al. The impact of positive peritoneal washings and serosal and adnexal involvement on survival in patients with stage IIIA uterine cancer. *Gynecol Oncol.* 2002;**86**(3):269–73. [PubMed: 12217747].
37. Havrilesky LJ, Cragun JM, Calingaert B, Alvarez Secord A, Valea FA, Clarke-Pearson DL, et al. The prognostic significance of positive peritoneal cytology and adnexal/serosal metastasis in stage IIIA endometrial cancer. *Gynecol Oncol.* 2007;**104**(2):401–5. doi: 10.1016/j.ygyno.2006.08.027. [PubMed: 17014898].
38. Li M, Wang Z, Zhao L, Li X, Wang J, Zhang C, et al. [Predictors of recurrence and prognosis in patients with stage I and II endometrial carcinoma]. *Zhonghua Fu Chan Ke Za Zhi.* 2014;**49**(6):455–9. [PubMed: 25169640].
39. Kato R, Hasegawa K, Torii Y, Hirasawa Y, Udagawa Y, Fukasawa I. Cytological scoring and prognosis of poorly differentiated endometrioid adenocarcinoma. *Acta Cytol.* 2015;**59**(1):83–90. doi: 10.1159/000375113. [PubMed: 25765171].
40. McLellan R, Dillon MB, Currie JL, Rosenshein NB. Peritoneal cytology in endometrial cancer: a review. *Obstet Gynecol Surv.* 1989;**44**(10):711–9. [PubMed: 2677857].
41. Grimshaw RN, Tupper WC, Fraser RC, Tompkins MG, Jeffrey JF. Prognostic value of peritoneal cytology in endometrial carcinoma. *Gynecol Oncol.* 1990;**36**(1):97–100. [PubMed: 2295459].
42. Lurain JR, Rumsey NK, Schink JC, Wallemark CB, Chmiel JS. Prognostic significance of positive peritoneal cytology in clinical stage I adenocarcinoma of the endometrium. *Obstet Gynecol.* 1989;**74**(2):175–9. [PubMed: 2748053].
43. Saga Y, Imai M, Jobo T, Kuramoto H, Takahashi K, Konno R, et al. Is peritoneal cytology a prognostic factor of endometrial cancer confined to the uterus?. *Gynecol Oncol.* 2006;**103**(1):277–80. doi: 10.1016/j.ygyno.2006.03.003. [PubMed: 16678244].
44. Bansal S, Buck AM, Herzog TJ, Deutsch I, Burke WM, Wright JD. Stage IIIA endometrial carcinoma: outcome and predictors of survival. *Obstet Gynecol.* 2009;**114**(1):100–5. doi: 10.1097/AOG.0b013e3181a94568. [PubMed: 19546765].
45. Elshaikh MA, Al-Wahab Z, Mahdi H, Albuquerque K, Mahan M, Kehoe SM, et al. Recurrence patterns and survival endpoints in women with stage II uterine endometrioid carcinoma: a multi-institution study. *Gynecol Oncol.* 2015;**136**(2):235–9. doi: 10.1016/j.ygyno.2014.12.012. [PubMed: 25511158].
46. Binesh F, Akhavan A, Behniafard N, Zabihi S, Hosseinizadeh E. Prognostic value of peritoneal washing cytology in gynecologic malignancies: a controversial issue. *Asian Pac J Cancer Prev.* 2014;**15**(21):9405–10. [PubMed: 25422232].