Am J Transl Res 2021;13(6):7164-7171
www.ajtr.org /ISSN:1943-8141/AJTR0131749

Original Article

Application of CT and MRI combined with VEGF-C and EGFR in the identification of endometrial cancer stages

Changsong Li[1*], Jingsheng Yu[2*], Zhexiang Fu[1]

[1]Department of Radiology, Hanchuan People's Hospital/Wuhan University People's Hospital of Hanchuan Hospital, Hanchuan, Hubei Province, China; [2]Department of Neurology, Xianning Central Hospital, The First Affiliated Hospital of Hubei University of Science and Technology, Xianning, Hubei Province, China. [*]Equal contributors and co-first authors.

Received February 10, 2021; Accepted March 11, 2021; Epub June 15, 2021; Published June 30, 2021

Abstract: Objective: To explore the application of computed tomography (CT) and magnetic resonance imaging (MRI) in combination with vascular endothelial growth factor-C (VEGF-C) and epidermal growth factor receptor (EGFR) in the identification of endometrial cancer stages. Methods: Clinical data of 84 patients with endometrial cancer who underwent surgery in our hospital were retrospectively analyzed. Before surgery, they were received inspection by CT and MRI and examination by VEGF-C and EGFR measurement. The pathological results after surgery were used as the gold standard, which was applied to compare the diagnostic accuracy of endometrial cancer stages by CT, MRI, and CT+MRI and to analyze how VEGF-C and EGFR expression and CT+MRI diagnosis correlated with relevant pathological parameters. Results: Using pathological results as the gold standard, the diagnostic accuracy of endometrial cancer stages via CT+MRI combined with VEGF-C+EGFR immunostaining was significantly higher (96.43%) compared with CT+MRI, CT, and MRI (91.67%, 70.24%, and 77.38%, respectively) (P<0.05). The positive rates of VEGF-C and EGFR expression in patients with different endometrial cancer stages identified by CT+MRI were significantly different (P<0.05). Spearman's rank correlation coefficient showed that the positive rates of VEGF-C and EGFR expression were both positively correlated with CT+MRI identified stages (r>0, P<0.05). The accuracy of CT+MRI diagnosed lymph node metastasis, myometrial infiltration, and interstitial infiltration was 90.48%, 92.86%, and 84.52%, respectively. The positive rates of VEGF-C and EGFR expression were significantly higher by lymph node metastasis compared with non-metastasis; the positive rates of VEGF-C and EGFR expression were significantly higher by deep myometrial infiltration compared with superficial infiltration; the positive rates of VEGF-C and EGFR expression were significantly higher by interstitial infiltration compared with no interstitial infiltration (P<0.05). Conclusion: CT and MRI combined with VEGF-C and EGFR can effectively identify endometrial cancer stages.

Keywords: Endometrial cancer, stage, computed tomography, magnetic resonance imaging, vascular endothelial growth factor-C, epidermal growth factor receptor

Introduction

Endometrial cancer develops in the epithelium of the endometrium. The high-risk population of this disease includes menopausal and postmenopausal women, with a morbidity of 20% to 30% among all female genital tract malignancies and a 5-year survival rate of 80%-90% [1]. Clinical symptoms in patients mainly include irregular vaginal bleeding, lower abdominal pain, menstrual disorders, and increased vaginal discharge, which severely affect women's normal lives and quality of life (QOL) [2, 3]. Most endometrial cancers progress slowly, of which early-stage tumors only invade the uterine cavity or endometrium. With the tumor progressing over time, it can affect the pelvic peritoneum, cervical canal, and fallopian tubes, and even metastasize to distant organs and lymph nodes that compromise the prognosis [4, 5].

Currently, there are many clinical approaches for the treatment of this disease, such as hormone therapy, radiotherapy, chemotherapy, and surgery. Clear evidence of tumor histological type and cancer stage provides the prerequisite for the selection of optional treatment strategy and the guarantee of therapeutic effi-

cacy. Pathological diagnosis is is the gold standard for identifying the characteristics and stage of the disease. This approach, however, is invasive and may damage normal tissue structures. Therefore, it is necessary to explore safer diagnostic methods.

Preoperative imaging examination has the advantages of less trauma and convenient inspection. For example, CT, MRI, and other inspection methods are used to examine tumor invasion, location, size, and so forth and have irreplaceable advantages in the identification of disease stages, early screening, and pathological grading. Among them, CT can clearly show invasion to surrounding organs and effectively determine whether there are lymph node and distant metastasis, but the insight of assessment for myometrial invasion is limited [6]. MRI can perform omnidirectional imaging, which features by good contrast and resolution of soft tissue to accurately display the size, location, shape, and interaction of the lesion with surrounding tissues. However, MRI requires enhanced scanning to visualize tumor's invasion to surrounding organs and is time-consuming. Thus, patients with restlessness and coma cannot commit to obtain clear images [7]. CT and MRI have their advantages and disadvantages, which are complementary to each other. Therefore, this study applies CT and MRI together for the diagnosis to improve the accuracy of tumor stage identification. VEGF-C is a VEGF-related protein, whose high expression indicates increased vascular permeability and increased neovascularization and lymphangiogenesis [8]. On the one hand, it can induce neovascularization around cancer cells by dissociating endothelial cells; on the other hand, VEGF-C can promote the extravasation of fibrinogen, increase vascular permeability, and promote the formation of blood vessels around cancer cells, thereby enhancing their invasion ability [9, 10]. EGFR is a common transmembrane tyrosine kinase receptor, whose high expression often indicates increased vascularization in tumors and inhibition of cell apoptosis. In clinical practice, EGFR is often used in combination with other biomarkers to identify the stage, or prognosis, of endometrial cancer [11, 12]. At present, it has been reported that CT combined with MRI shows a promising diagnostic value in the identification of endometrial cancer stage [13]. However, studies are limited regarding the correlation between the identification of cancer stages by these two methods and molecular indicators. Therefore, this study aimed to investigate the application of CT and MRI in combination with VEGF-C and EGFR in the identification of endometrial cancer stages.

Materials and methods

General information

The clinical data of 84 endometrial cancer patients who underwent surgery from December 2018 to June 2020 in our hospital were retrospectively analyzed. Patients' ages ranged from 35 to 72 years, with an average of 53.6±6.2 years. The course of the disease was 6 months to 12 years, with an average of 5.2±2.3 years. Participants included 50 cases with menopause and 34 cases without menopause. Pathologic types included 55 cases of endometrioid adenocarcinoma, 19 cases of clear cell carcinoma, 8 cases of serous papillary adenocarcinoma, and 2 cases of adenosquamous carcinoma. This study was approved by the Ethics Committee of our hospital.

Selection criteria

Inclusion criteria: (1) In accordance with the diagnostic criteria listed by "Guidelines for the Diagnosis and Treatment of Endometrial Cancer (Fourth Edition)" [12]; (2) Normal coagulation function; (3) CT and MRI examinations within 2 weeks before surgery; complete preoperative imaging data and postoperative pathologic data and in line with quality control requirements.

Exclusion criteria: (1) Previous CT and MRI examination contraindications, history of estrogen therapy, and history of pelvic radiotherapy; (2) Combination with other malignancies and other severe gynecologic diseases; (3) Pregnancy and lactation; (4) With severe acute pelvic infection; (5) Participation in other projects.

CT

The instrument was a 64-slice spiral CT machine (model: GE Optima 660, manufacturer: General Electric, US) to check the anterior bladder filling, supine position, and horizontal scanning. Parameters were set as voltage 120

kV, current 250-300 mA, layer thickness 0.625-1.25 mm, pitch 1-1.5, matrix 512*512, and display field 350 mm. Enhanced CT scanning: intravenous injection of non-ionic iodine contrast agent iohexol (General Electric Pharmaceuticals Shanghai Co., Ltd., China) with a high-pressure syringe, an injection rate of 3 mL/s, and a dose of 300 mL. The scanning was performed 25 s and 60 s after injection.

MRI

MRI examination was performed 48 hours after CT examination. The instrument was a Philips 1.5 T magnetic resonance machine (model: Multiva 1.5 T, manufacturer: Philips Medical) to inspect the anterior bladder filling, supine position, and regular plain scanning. Scanning sequence followed as T2W1 fat suppression sequence and coronary plane, fast spin wave T2W1 of cross-section and sagittal plane, and T2W1 fat suppression sequence. After plain scanning, intravenous injection of contrast agent gadopentetate meglumine (Beijing Beilu Pharmaceutical Co., Ltd., China) was applied for multi-phase enhanced scanning. The dose was 0.1 mmol/kg with 2 collections of each signal.

VEGF-C and EGFR staining

Key reagents and instruments: SP kit (Nanjing Jiancheng Institute of Biology, China), EGFR and VEGF-C monoclonal antibodies (Shanghai Sig Biotech Co., Ltd., China), OlympusBXSOWI photomicrography (Olympus, Japan), OLYMPUS AU5400 automatic biochemical analyzer (Olympus, Japan), paraffin microtome (Leica, Germany).

Procedures: The surgical samples were fixed, embedded in paraffin, sectioned, and subjected to immunohistochemistry and hematoxylin and eosin (H&E) staining using the Max Vision two-step method. Replacement of primary antibody (1:100) with PBS was used as a negative control, while a known endometrial cancer positive section was applied as a positive control. EGFR and VEGF-C antibodies were ready-to-use. 3,3'-Diaminobenzidine (DAB) was used for immunostaining. H&E was applied for counterstaining, and semi-quantitation was done under a microscope with high magnification. The score of the proportion of positive cells: 0 point for negative cells, 1 point for positive cells ≤10%, 2 points for 11-50%, 3 points for 51%-75%, and 4 points for >75% positive cells. The score of staining intensity: 0 point for colorless, 1 point for light yellow, 2 points for brownish yellow, and 3 points for brown. The sum of points from the above 2 categories was 0-1 as negative, 2-3 as weak positive, 4-5 as moderate positive, and 6-7 as strong positive.

Outcome measurements

Primary measurements: (1) Stages of endometrial cancer. The postoperative pathological results were used as the gold standard to compare the diagnostic accuracy of CT, MRI, CT+MRI, and CT+MRI+VEGF-C+EGFR in the identification of endometrial cancer stages. A. Surgical pathology: Tumor invasion limited to the uterus was defined as stage I; invasion to the cervix but not beyond the uterus was stage II; invasion of the uterine appendages and serosa and metastasis to the vagina was stage III; invasion of the small intestine, bladder and/or metastasis to distant organs was stage IV. B. CT: Tumor invasion limited to the normal myometrial layer with intact contour of the outer edge of the myometrium was defined as stage I; the central low-density tumor invasion in the cervix was stage II; invasion to the lateral wall, para-uterine and appendages was stage III; invasion of bladder, para-aortic lymph nodes, and even metastases to distant organs such as the liver, lungs, and omentum was stage IV. C. MRI: if the surface of the endometrium or myometrial layer was irregular, the outer edge of the myometrium was complete, and the tumor was found in the myometrial layer, it was defined as stage I; the tumor found in the cervix was stage II; periuterine infiltration and the continuously interrupted outer myometrial layer was stage III; low signal or missing in rectal wall or bladder was stage IV. D. CT+MRI: CT was applied to the invasion of peripheral organs and peripheral lymph nodes, while MRI was conducted for the lesions that occurred in the endometrium and uterine cavity. (2) Comparison of the positive rates of VEGF-C and EGFR expression in patients with stage I, stage II, stage III, and stage IV identified by CT+MRI. Spearman's rank correlation coefficient was carried out to analyze the correlation between the positive rate of VEGF-C expression, positive rate of EGFR expression, and stages by CT+MRI inspection.

Table 1. Identification of clinical stage by CT (n)

CT	Pathologic results				Total
	Stage I	Stage II	Stage III	Stage IV	
Stage I	13	2	2	1	18
Stage II	2	20	3	4	29
Stage III	2	4	18	2	26
Stage IV	0	2	1	8	11
Total	17	28	24	15	84

Note: CT: computed tomography.

Table 2. Identification of clinical stage by MRI (n)

MRI	Pathologic results				Total
	Stage I	Stage II	Stage III	Stage IV	
Stage I	14	2	1	1	18
Stage II	1	22	2	3	28
Stage III	2	3	20	2	27
Stage IV	0	1	1	9	11
Total	17	28	24	15	84

Note: MRI: magnetic resonance imaging.

Table 3. Identification of clinical stage by CT+MRI (n)

CT+MRI	Pathologic results				Total
	Stage I	Stage II	Stage III	Stage IV	
Stage I	16	1	0	0	17
Stage II	0	25	1	1	27
Stage III	1	2	23	1	27
Stage IV	0	0	0	13	13
Total	17	28	24	15	84

Note: CT: computed tomography; MRI: magnetic resonance imaging.

Table 4. Identification of clinical stage by CT+MRI+VEGF-C+EGFR (n)

CT+MRI+VEGF-C+EGFR	Pathologic results				Total
	Stage I	Stage II	Stage III	Stage IV	
Stage I	17	0	0	0	17
Stage II	0	27	1	0	28
Stage III	0	1	23	1	25
Stage IV	0	0	0	14	14
Total	17	28	24	15	84

Note: CT: computed tomography; MRI: magnetic resonance imaging; VEGF-C: vascular endothelial growth factor-C; EGFR: epidermal growth factor receptor.

Secondary measurements: (1) Postoperative pathologic results were used as the gold standard to evaluate the accuracy of CT+MRI in the identification of lymph node metastasis, myometrial infiltration, and interstitial infiltration. (2) Positive rates of VEGF-C and EGFR expression were compared in patients with or without lymph node metastasis, with or without interstitial infiltration, and with different degrees of myometrial infiltration diagnosed by CT+MRI.

Statistical analysis

SPSS22.0 software was applied for data analysis. Graphpad prism 7.0 was used to make graphs. Counted data were expressed as the number of cases (percentage) (n (%)), followed by χ^2 test. $P<0.05$ indicated that a difference was significant.

Results

Identification of clinical stages

Pathologic results showed that among 84 patients, 17 were in stage I, 28 were in stage II, 24 were in stage III, and 15 were in stage IV. Given pathologic results as the gold standard, the diagnostic accuracy rates of CT, MRI, CT+MRI, CT+MRI+VEGF-C+EGFR for the identification of endometrial cancer were 70.24% (59/84), 77.38% (65/84), 91.67% (77/84), and 96.43% (81/84), respectively. The diagnostic accuracy rate of CT+MRI+VEGF-C+EGFR for endometrial cancer stages was significantly higher compared with CT+MRI, CT, and MRI ($\chi^2=5.621$, $P=0.011$; **Tables 1**-**4**).

Analysis of the relationship between the expression levels of VEGF-C and EGFR and stages identified by CT+MRI

The positive rates of VEGF-C and EGFR expression in patients with different endometrial cancer stages identified by CT+MRI were significantly different ($P<0.05$). The Spearman's rank correlation coefficient showed that the positive rates of VEGF-C and EGFR expression were positively correlated with stage ($r=5.362$, 4.111; $P=0.001$, 0.002; **Figure 1**).

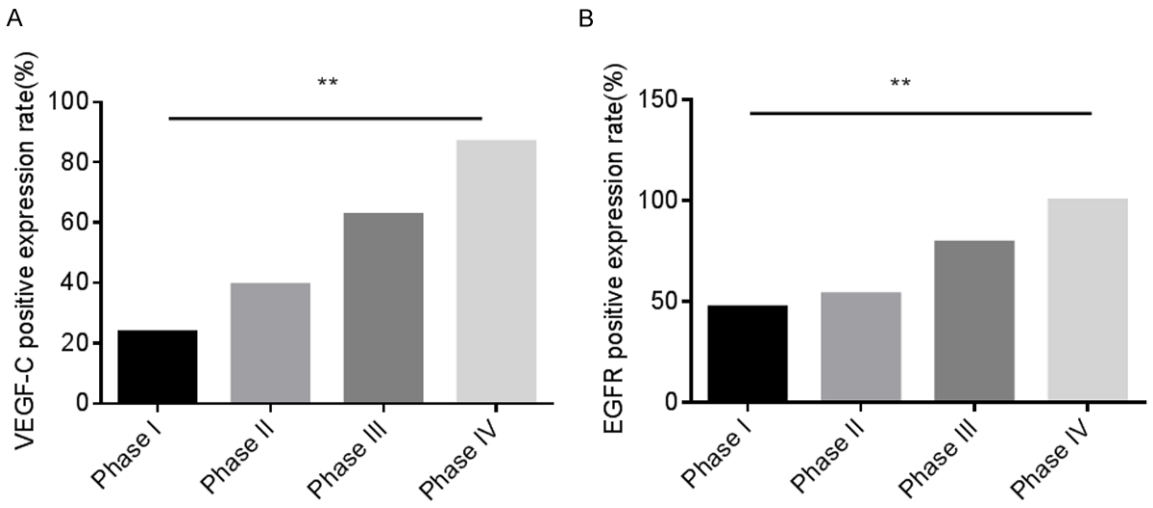

Figure 1. Analysis of the relationship between the expression levels of VEGF-C and EGFR and stage identified by CT+MRI. A: VEGF-C; B: EGFR. Compared with Phase I, **P<0.01. VEGF-C: vascular endothelial growth factor-C; EGFR: epidermal growth factor receptor.

Table 5. Comparison of the diagnosis of lymph node metastasis by CT+MRI and pathologic results (n)

CT+MRI	Pathologic result		Total
	Lymph node metastasis	No lymph node metastasis	
Lymph node metastasis	12	3	15
No lymph node metastasis	5	64	69
Total	17	67	84

Note: CT: computed tomography; MRI: magnetic resonance imaging.

Comparison of the diagnosis of lymph node metastasis, myometrial layer infiltration, and interstitial infiltration by CT+MRI and pathologic results

The pathologic results were applied as the gold standard. The accuracy of CT+MRI in the diagnosis of lymph node metastasis, myometrial layer infiltration, and interstitial infiltration was 90.48%, 92.86%, and 84.52%, respectively (**Tables 5**-**7**).

Analysis of the relationship between VEGF-C and EGFR expression levels and clinicopathologic features by CT+MRI

The positive rates of VEGF-C and EGFR expression were significantly higher for lymph node metastasis compared with no lymph node metastasis. The positive rates of VEGF-C and EGFR expression were significantly higher for deep myometrial infiltration compared with superficial myometrial layer infiltration. The positive rates of VEGF-C and EGFR expression were significantly higher if there was interstitial infiltration compared with no interstitial infiltration (P<0.05; **Table 8**).

Discussion

This study demonstrates that the identification of endometrial cancer stages by CT+MRI is significantly more accurate compared with CT or MRI identification alone. CT features a high spatial and density resolution, which can display the location, size, number of areas, and invasion of surrounding organs through enhanced scanning, thin-layer scanning, and three-dimensional reconstruction and has obvious advantages in determining whether or not there is metastasis and infiltration in tissues around the lesions [13-15]. MRI is characterized by good contrast and high resolution to visualize tissues. The lesions can be observed from multiple angles such as sagittal and coronal positions to achieve quantitative, qualitative, and localized diagnosis [16-18]. Although the use of CT or MRI alone is promising in the early diagnosis of endometrial cancer, they are still insufficient in terms of identification of clinical stages and diagnostic accuracy. Laifer-Narin et al. have reported that CT combined with MRI can improve the accuracy of the identification of endometrial cancer stages, with a rate of

Table 6. Comparison of the diagnosis of myometrial layer infiltration by CT+MRI and pathologic results (n)

CT+MRI	Pathologic result		Total
	Deep myometrial layer infiltration	Superficial myometrial layer infiltration	
Deep myometrial layer infiltration	25	1	26
Superficial myometrial layer infiltration	5	53	58
Total	30	54	84

Note: CT: computed tomography; MRI: magnetic resonance imaging.

Table 7. Comparison of the diagnosis of interstitial infiltration by CT+MRI and pathologic results (n)

CT+MRI	Pathologic result		Total
	Interstitial infiltration	No interstitial infiltration	
Interstitial infiltration	20	4	24
No interstitial infiltration	9	51	60
Total	29	55	84

Note: CT: computed tomography; MRI: magnetic resonance imaging.

90.5%, and can effectively determine the degree of endometrial invasion, which is in line with the results of our study, indicating that the combination of these two methods can improve the accuracy of the identification of endometrial cancer stage [19].

In this study, the combined application of CT+MRI and molecular analysis of VEGF-C+EGFR reveal a higher diagnostic accuracy for the identification of endometrial cancer stage than using the imaging approach alone. The positive rates of VEGF-C and EGFR expression in patients with different stages of this cancer are significantly different. They are significantly higher in lymph node metastasis compared with non-metastasis, are notably higher in deep myometrial layer infiltration than those of superficial myometrial layer infiltration, and are considerably higher in interstitial infiltration in comparison to without interstitial infiltration. This further suggests that the positive rates of VEGF-C and EGFR expression are closely related to the clinical stage of endometrial cancer and clinicopathologic features such as lymph node metastasis, depth of myometrial invasion, and interstitial invasion. Additionally, VEGF-C and EGFR measurement combined with imaging can improve the accuracy of the identification of endometrial cancer stage.

Cai et al. have shown that the positive rates of VEGF-C and EGFR expression in endometrial cancer are 64.47% and 82.24%, respectively, which is correlated with the degree of tumor differentiation, FIGO staging, lymph node metastasis, and depth of myometrial invasion [20]. These data are generally consistent with our results. The reason could be that overexpression of VEGF-C can increase the stimulation of tumor angiogenesis and change the permeability of blood vessels. After the injection of a paramagnetic contrast agent, the amount and speed of the agent entering blood vessels and intercellular spaces increase so that MRI enhancement is improved. In addition, VEGF-C overexpression indicates more neovascularization, a faster proliferation of cancer cells, more cervical involvement, greater metastasis, and malignancy of distant lymph nodes. Therefore, CT+MRI reveals that the blurrier the tumor boundary, the deeper the muscle layer invasion. The reason why EGFR is correlated with clinicopathologic features identified by CT+MRI may be explained by its participation in PI3K/AKT signaling pathway and mainly mediating cell division and proliferation signals, which convert normal endometrial cells into atypical hyperplastic endometrial cells, leading to tumor cell metastasis and proliferation [21].

There are some caveats in this study, such as a low number of sample size, single sample source, and retrospective analysis, which may cause data bias. Additionally, the relationship between disease malignancy predicted by a combination of imaging indicators and immunological biomarkers and prognosis has not been analyzed. Therefore, it is still necessary to expand the sample size in future studies and conduct multi-center and prospective research to validate the conclusion of this study.

In summary, preoperative CT combined with MRI can effectively identify the clinical stage of endometrial cancer. VEGF-C and EGFR can

Table 8. Analysis of the relationship between VEGF-C and EGFR expression levels and clinicopathologic features by CT+MRI (n (%))

Clinicopathologic feature	Identified by CT+MRI	Positive rate of VEGF-C expression	Positive rate of EGFR expression
Lymph node metastasis			
Yes	15	14 (93.33)	15 (100.00)
No	69	29 (42.03)***	42 (60.87)**
Myometrial layer infiltration			
Deep	58	23 (39.66)	3 (58.62)
Superficial	26	20 (76.92)**	23 (88.46)**
Interstitial infiltration			
Yes	24	19 (79.17)	21 (87.50)
No	60	24 (40.0)***	36 (60.00)*

Note: Compared with pathologic features, *P<0.05, **P<0.01, ***P<0.001. CT: computed tomography; MRI: magnetic resonance imaging; VEGF-C: vascular endothelial growth factor-C; EGFR: epidermal growth factor receptor.

reflect the biologic behavior of cancer cells and changes of genes and cells. Therefore, preoperative imaging in a combination of diagnostic methods and tumor biomarkers could be applied to gain insight into tumor diagnosis, treatment, and prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Zhexiang Fu, Department of Radiology, Hanchuan People's Hospital/Wuhan University People's Hospital of Hanchuan Hospital, Renmin Avenue 1st, Hanchuan 431600, Hubei Province, China. Tel: +86-17771215321; E-mail: fuzhexiang2020@sina.com

References

[1] Fadare O and Parkash V. Pathology of endometrioid and clear cell carcinoma of the ovary. Surg Pathol Clin 2019; 12: 529-564.

[2] Soslow RA, Tornos C, Park KJ, Malpica A, Matias-Guiu X, Oliva E, Parkash V, Carlson J, McCluggage WG and Gilks CB. Endometrial carcinoma diagnosis: use of FIGO grading and genomic subcategories in clinical practice: recommendations of the international society of gynecological pathologists. Int J Gynecol Pathol 2019; 38 Suppl 1: S64-S74.

[3] Murali R, Davidson B, Fadare O, Carlson JA, Crum CP, Gilks CB, Irving JA, Malpica A, Matias-Guiu X, McCluggage WG, Mittal K, Oliva E, Parkash V, Rutgers JKL, Staats PN, Stewart CJR, Tornos C and Soslow RA. High-grade endometrial carcinomas: morphologic and immunohistochemical features, diagnostic challenges and recommendations. Int J Gynecol Pathol 2019; 38 Suppl 1: S40-S63.

[4] Kulkarni R, Bhat RA, Dhakharia V, Kallur K and Gangoli A. Role of positron emission tomography/computed tomography in preoperative assessment of carcinoma endometrium-a retrospective analysis. Indian J Surg Oncol 2019; 10: 225-231.

[5] Albano D, Zizioli V, Odicino F, Giubbini R and Bertagna F. Clinical and prognostic value of (18)F-FDG PET/CT in recurrent endometrial carcinoma. Rev Esp Med Nucl Imagen Mol 2019; 38: 87-93.

[6] Rawish KR, Buza N, Zheng W and Fadare O. Endometrial carcinoma with trophoblastic components: clinicopathologic analysis of a rare entity. Int J Gynecol Pathol 2018; 37: 174-190.

[7] Farhane FZ, Alami Z, Bouhafa T, Elmazghi A and Hassouni K. Primary squamous cell carcinoma of endometrium: case report and literature review. Pan Afr Med J 2018; 30: 8.

[8] Oplawski M, Dziobek K, Zmarzły N, Grabarek B, Halski T, Januszyk P, Kuś-Kierach A, Adwent I, Dąbruś D, Kiełbasiński K and Boroń D. Expression profile of VEGF-C, VEGF-D, and VEGFR-3 in different grades of endometrial cancer. Curr Pharm Biotechnol 2019; 20: 1004-1010.

[9] Ramalingam P, Masand RP, Euscher ED and Malpica A. Undifferentiated carcinoma of the endometrium: an expanded immunohistochemical analysis including PAX-8 and basal-like carcinoma surrogate markers. Int J Gynecol Pathol 2016; 35: 410-418.

[10] Faria SC, Devine CE, Rao B, Sagebiel T and Bhosale P. Imaging and staging of endometrial cancer. Semin Ultrasound CT MR 2019; 40: 287-294.

[11] Bonatti M, Pedrinolla B, Cybulski AJ, Lombardo F, Negri G, Messini S, Tagliaferri T, Manfredi R

and Bonatti G. Prediction of histological grade of endometrial cancer by means of MRI. Eur J Radiol 2018; 103: 44-50.

[12] Zhou Q, Wu XH, Liu JH, Li L, Zhu JQ, Bai P and Sheng XG. Guidelines to the diagnosis and treatment of endometrial carcinoma (4th edition). Chin J Prac Gynecol Obstet 2018; 34: 880-886.

[13] Xu XJ, Li N, Chen Y, Ouyang H, Zhao XM and Zhou J. Diagnostic efficacy of MRI for pre-operative assessment of ovarian malignancy in endometrial carcinoma: a decision tree analysis. Magn Reson Imaging 2019; 57: 285-292.

[14] Hamm B and Pöllinger A. Cross-sectional imaging of endometrial carcinoma: MR imaging and CT. Zentralbl Gynakol 2002; 124: 27-31.

[15] Nougaret S, Horta M, Sala E, Lakhman Y, Thomassin-Naggara I, Kido A, Masselli G, Bharwani N, Sadowski E, Ertmer A, Otero-Garcia M, Kubik-Huch RA, Cunha TM, Rockall A and Forstner R. Endometrial cancer mri staging: updated guidelines of the european society of urogenital radiology. Eur Radiol 2019; 29: 792-805.

[16] Takagi H, Sasagawa T, Shibata T, Minato H and Takahashi T. Association between 18F-fluorodeoxyglucose-PET/CT and histological grade of uterine endometrial carcinoma. Taiwan J Obstet Gynecol 2018; 57: 283-288.

[17] Naaman Y, Pinkas L, Roitman S, Ikher S, Oustinov N, Vaisbuch E, Yachnin A and Ben-Arie A. The added value of SPECT/CT in sentinel lymph nodes mapping for endometrial carcinoma. Ann Surg Oncol 2016; 23: 450-455.

[18] Liu DD, Li J, Li X, Xie L, Qin L, Peng F and Cheng MH. Prognostic value of metabolic tumor volume and total lesion glycolysis from ^{18}F-FDG PET/CT in lymph node metastases and risk stratification of endometrial carcinoma. J Gynecol Oncol 2019; 30: e89.

[19] Laifer-Narin SL, Genestine WF, Okechukwu NC, Hecht EM and Newhouse JH. The role of computed tomography and magnetic resonance imaging in gynecologic oncology. PET Clin 2018; 13: 127-141.

[20] Cai S, Zhang YX, Han K and Ding YQ. Expressions and clinical significance of COX-2, VEGF-C, and EFGR in endometrial carcinoma. Arch Gynecol Obstet 2017; 296: 93-98.

[21] Du LX, Yu YQ, Wang YL, Xia J, Qiu XX and Lei Y. The diagnostic value of multimodality MRI in endometrial carcinoma staging. Acta Radiol 2017; 58: 609-616.