

Correlation between Ultrasound, Hysteroscopy and Histology in the Exploration of Postmenopausal Metrorrhagia (about 90 Cases)

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Abstract:

Introduction

Postmenopausal metrorrhagia (PMMs) is a common reason for consultation in gynaecology. It may reveal, during exploration, a benign or malignant pathology that must be differentiated following a para-clinical assessment with the main pathology to eliminate being endometrial cancer. The goal of our study was to assess the correlation between ultrasound, hysteroscopy and histology in the exploration of endo-cavitary lesions when faced with PMMs.

Materials and methods:

This is a retrospective descriptive and analytic study, based on 90 patients treated for postmenopausal metrorrhagia (PMM) in the department of Gynaecology and Obstetrics II of HASSAN II teaching hospital of FES, from January 2014 to January 2017.

Results: The mean age of the patients was 59 years. The correlation of the ultrasound and hysteroscopy data showed that the ultrasound presented sensitivity, specificity, PPV and NPV equal to 100% for endometrial atrophy. For hypertrophy, these values were respectively 74%, 95%, 88%, 87.5%. For the suspicion of cancer, the sensitivity was 100%, the specificity of 98.6%, the PPV of 93% and the NPV of 96%. As for the correlation between hysteroscopy-histology on biopsy, sensitivity, specificity, PPV and NPV were respectively 96.7%, 98.3%, 96.7% and 98.3% for hyperplasia and 94%, 100%, 100% and 98.6% for suspected cancer. The hysteroscopy-histology correlation on the surgical specimen showed 100% sensitivity, specificity, PPV and NPV for polyps and leiomyomas, respectively 96%, 92%, 83.8% and 98.3% for hyperplasia's and values of 72%, 100%, 100% and 92% for suspected cancer. The degree of performance of each means of exploration was variable according to the lesion in question of the metrorrhagia and generally, the hysteroscopy was more reliable in the exploration of the MMPs than the ultrasound: Kappa of 0.74 against 0.50.

Conclusion: Our results are consistent with the data in the literature, which attributes to hysteroscopy having a greater reliability compared to a pelvic ultrasound in the diagnosis of endo-cavitary lesions as the origin of postmenopausal metrorrhagia. An Ultrasound is the first-line examination in the exploration of PMMs, it should be coupled with diagnostic hysteroscopy and biopsy for better diagnostic accuracy.

Keywords: menopause; metrorrhagia; ultrasound; hysteroscopy; histology

Introduction

Postmenopausal metrorrhagia (MPM) is a frequent reason for consultation and also the main warning signal for endometrial cancer. 70% of gynaecological consultations during peri or post menopause are linked to bleeding [1].

Explorations can reveal benign or malignant pathologies and the methods available to assess endometrial lesions have evolved in recent years. Transvaginal ultrasound (coupled with colour Doppler) is accessible, non-invasive and has become the gold standard in cases of MPM as part of an

initial exploration, given the risk of endometrial cancer. The field of investigation has expanded in particular with the development of hysteroscopy.

The objective of our study was to evaluate the correlation between the results of ultrasound, hysteroscopy and histology in the exploration of these MPM, by evaluating for each its feasibility, sensitivity, specificity in the detection endocavitary lesions

Materials and methods:

This is a retrospective study describing and analysing over a 3year period (from January 2014 to January 2017), 90 cases of MPM treated in the Gynaecology Obstetrics II department at the UTH Hassan II in Fez.

We defined postmenopausal metrorrhagia as any abnormal uterine bleeding occurring in a woman who had not seen menstrual blood flow for at least 12 consecutive months.

The data was collected from department registers, clinical records, operating reports and the results of the anatomopathological study.

The analysis of the results was made using the IBM SPSS version 20 software. All the quantitative variables were expressed in the form of means and their standard deviation and all the categorical variables in the form of frequency. Then, a univariate analysis was done looking for sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and concordance. The Kappa test was used to measure the concordance between 2 independent judgments on the same endocavitary lesions. We agreed that the concordance is good if Kappa > 0.6, bad if Kappa < 0.3 and intermediate between the two.

Results:

I- Descriptive study

Epidemiology and clinical manifestation:

MPMs represent 62% of hospitalisations among postmenopausal women in the department. The average age of the patients was 59 years \pm 8.148 years [47 to 92 years]. 53.4% were between 47 and 59 years old and 35.5% between 60 and 69 years old.

Isolated MPMs represented the most frequent reason for consultation with a proportion of 82.20% followed by MPMs associated with pelvic pain (7.80%) and MPMs associated with leucorrhoea (5.60%). The association of pelvic pain – leucorrhoea and abdominopelvic mass represented respectively 2.20% of the reasons for consultation.

More than half of our patients had moderate obesity (57%) and 39% were overweight. The most documented medical history was hypertension in 21.10% of cases followed by Type 2 diabetes in 12.20% of cases. Hormone replacement therapy (HRT) was observed in one patient and tamoxifen treatment in 2 patients. Nulliparity was observed in 19% of cases. The average age of onset of menopause was 49.9 years \pm 4.3 years (36-62 years); 3% had had an early menopause (< 40 years old) against 6.6% with a late menopause (> 55 years old).

Ultrasound results:

This examination revealed endometrial hypertrophy with a thickness greater than 5 mm in 70 patients (78%), endometrial atrophy with endometrial thickness less than 5 mm in 15.5% of cases and myomas in 6.6% of cases.

The Doppler study was only specified in 4 patients among those who had an appearance with suspicion of malignancy. In these patients, neovascularization of the endometrium has been reported but without studies of the uterine artery.

Results of hysteroscopy:

Several lesions were sometimes found in the same patient. Certain procedures have been associated with hysteroscopy such as: endometrial biopsy (in 98.8% of cases), cervical biopsy in 13% of cases. The main lesions found were endometrial hypertrophy, polyps, suspected cancer, endometrial atrophy and uterine myomas with respective proportions of 34.4%, 22.2, 17.7, 15.5% and 8.8%.

Pathology: biopsy and surgical specimen

Biopsy histology revealed 15 cases of cancer (including 10 endometrioid adenocarcinomas, 2 cervical cancers and 3 other types).

The 28 cases of polyp and myomas found at hysteroscopy were resected by surgical hysteroscopy and the anatomopathological results confirmed their nature.

43.3% of the patients (39) underwent a surgical hysterectomy (HST) for therapeutic purposes and 11% underwent a diagnostic HST. The pathological results on surgical specimens are as follows: polyps (25.9%), hyperplasia with atypia (22%), endometrioid adenocarcinoma (19.4%), hyperplasia without atypia (12.9%), leiomyomas (10.9 %), cancers of the cervix (2.5%) and other types of cancers (6.4%).

Analytical study

Ultra Sound Performance					
Lesion measure	Atrophy	Hypertrophy	Polyp	Myoma	Suspicion of cancers
Sensibility	100%	74%	100%	100%	100%
Spécificity	100%	95%	88,5%	100%	98,6
VPP	100%	88%	71,4%	100%	93%
VPN	100%	87,5%	100%	100%	96%
Performance hysteroscopy and histology of the surgical specimen					
Sensibility	100%	96%	100%	100%	72%
Spécificity	85,3%	92%	100%	100%	100%
VPP	7,14%	83,8%	100%	100%	100%
VPN	100%	98,3%	100%	100%	92%
Performance of hysteroscopy compared to biopsy					
Sensibility	100%	96,7%			93,3%
Specificity	98,7%	98,3%			97,3%
VPP	92,8%	96,7%			87,5%
VPN	100%	98,3%			98,6%

Performance study between hysteroscopy and histology on the surgical specimen (Table 1).

The hysteroscopy-histology correlation on the surgical specimen was variable according to the aetiologies, with a good performance for the majority of the lesions.

Ultrasound		N	Hysteroscopy					
			Atrophy	Hypertropy	Polype	MSM	Suspicion of cancer	Impossible
Atrophy		14	14	0	0	0	0	0
Hypertrophy		26	0	23	0	0	3	0
Hypertrophy + suspicion of polyp		28	0	8	20	0	0	0
Myoma with submucosal component		8	0	0	0	8	0	0
+Hypertropy 2	+Atrophy 6							
Suspicious image		14	0	0	0	0	13	1

Table 2: Correlation between ultrasound and hysteroscopy

The correlation between ultrasound and hysteroscopy found a medium concordance with a Kappa of 0.50, so there is a medium concordance.

Hysteroscopy		N	Histology on biopsy					
			Atrophy	Hyperplasia	Polyp	Leiomyoma	Cancer	Not satisfying
Atrophy		14	13	1	0	0	0	0
Hypertrophy		31	0	30	0	0	1	0
Polyp		20	Biopsy not done					
MSM		8	Biopsy not done					
Suspicion of Cancer		16	0	2	0	0	14	0
Impossible		1	0	0	0	0	0	0

Table 3: Correlation between hysteroscopy and biopsy histology

The agreement between the results of hysteroscopy and histology on biopsy was good with a kappa value equal to 0.68.

Correlation between hysteroscopy and histology on surgical specimen (Table 4)

		Histology on surgical specimen				
Hysteroscopy	N	Atrophy	Hyperplasia	Polyp	Leiomyoma	Cancer
Atrophy	1	0	1	0	0	0
Hypertrophy	31	0	26	0	0	5
Polypes	20	0	0	20	0	0
MSM	8	0	0	0	8	0
Suspicion of cancer	16	0	0	0	0	16
Impossible	1	0	0	0	0	1

Table 4: Correlation between hysteroscopy and histology on surgical specimen

We noted a good correlation between the results of the hysteroscopy and the histology on the operating specimen with a Kappa value equal to 0.74.

Discussion

In the exploration of the uterus and its annexes in the event of uterine bleeding, ultrasound is an essential first-line examination. Its contribution to diagnostic research is widely demonstrated in the literature.

In post menopause, an ultrasound is considered normal when the endometrium is thin with an endometrial thickness of less than 5 mm in a woman without hormone replacement therapy (HRT) and less than 8 mm in a woman on HRT. Hypertrophy when the thickness of the endometrium is greater than or equal to 5mm in a woman without HRT and greater than 8mm in a woman on HRT [2-4]. The thresholds considered in our study for the diagnoses are similar to those used by these authors. Ultrasounds also makes it possible to visualize the signs of malignancy such as hypervascularization, myometrial invasion.

Okaro E and Bourne T [5], report that regardless of whether HRT is taken or not, considering a threshold greater than 4mm for abnormal endometrium makes it possible to detect 96% of endometrial cancers, and 92% of pathologies endometrial (hyperplasia, polyps), with respective false positives of 39 and 19%, while in two other studies conducted by Dorum A et al, [6] and Gupta JK et al [7], the authors explain that, used alone, this threshold value is not sufficient to exclude endometrial pathology. For the latter, ultrasound alone cannot replace histological examination in the evaluation of the endometrium in the event of postmenopausal metrorrhagia. Because of habit, we resort to other examinations as soon as abnormalities are detected on the ultrasound or when we find a discrepancy between the clinical picture of the patient and the results found on the ultrasound.

One study [8] reported a small proportion (0.1 to 1%) of cases of endometrial cancer with endometrial thickness less than or equal to 4mm. Despite this observation made by the authors of this study [8], other authors consider that additional examinations are not necessary in case of thickness less than 5 mm [9,10]. We also consider that there is no need to resort to further investigations when the thickness of the endometrium is less than 5 mm because in our study, we did not find any malignant pathology for thicknesses of the endometrium. endometrium less than 5 mm.

Correlation ultrasound and hysteroscopy and histology.

Hysteroscopy (HSC) is the examination of choice for exploring endocavitary lesions suspected on ultrasound or in the absence of individualized lesions by ultrasound [11]. It makes it possible to better visualize the signs of atypia such as anarchic vascularisation, the aspects in candle spots and thus to direct the biopsies.

The comparison of the different results observed on ultrasound and hysteroscopy allows us to say that these 2 explorations are 100% concordant for the diagnosis of atrophy.

On the other hand, among the 26 cases of hypertrophy found on ultrasound, only 23 were confirmed by hysteroscopy and 3 lesions were found to be suspicious of malignancy with a concordance of 74%. This could be explained by the fact that the study of the Doppler ultrasound of the endometrium and the uterine artery in search of signs of malignancy had not been done systematically.

The ultrasound had objectified 14 suspicious images among which 13 were confirmed by the hysteroscopy since in one woman the hysteroscopy could not be done which gives us a concordance of 100%.

Among the 28 cases of hypertrophy associated with a suspected polyp objectified on ultrasound, 20 cases of polyps were confirmed on hysteroscopy and the 8 other cases had returned in favor of polyploid hypertrophy plus candle spots and this with 75% accordance. So, ultrasound could not differentiate between polyploid hypertrophy and hypertrophy associated with polyps.

All of the myomas found on ultrasound were confirmed on hysteroscopy with 100% concordance. Thus, we can say that ultrasound is certainly a screening examination but not a diagnosis of endometrial pathologies.

Regarding the performance of endovaginal ultrasound for the diagnosis of MPM, the different specificities and sensitivities are variable and different from one series to another [7,9,12-16]. Our sensitivity is higher than those reported in studies [12,13,15] and yet lower than those reported by Alcazar JL et al. [14].

From the point of view of specificity, our results are superior to those reported by: N. Mathlouthi [13], Garuti G et al. [15], by Smith Bindman et al. [9] and Alcazar et al. [14] however lower than those reported by Barbero M et al [16].

Ultrasounds thus seemed to be quite efficient in the diagnosis of atrophy and cancers with sensitivities of 100% and specificities of 100% and 98.6% respectively. However, it was less effective in the diagnosis of hyperplasia with a specificity of 95% and a sensitivity of 74% since in 3 cases, the ultrasound was in favour of endometrial hypertrophy while the hysteroscopy had found signs suggestive of endometrial cancer. This could perhaps have been remedied by a better analysis of the endometrium, in particular its echo-structure, its vascularization but also its limits with the myometrium. Our data are similar to those of Mathlouthi N et al. [13] who prospectively analysed the results of transvaginal ultrasound and hysteroscopy in 80 patients with postmenopausal metrorrhagia. Ultrasound performed well when dealing with endometrial atrophy with a sensitivity and specificity of 87.5% and 93.75% or endometrial cancer with a sensitivity and specificity of 80%. and 100%. But on the other hand, the author does not report sensitivity for hyperplasia although 4 cases out of 6 were confirmed by hysteroscopy.

Ultrasound examination (ultrasound) has certain limitations in the exploration of post-menopausal metrorrhagia [8,17]. According to the authors of these two studies [8,17], in the event of endometrial hypertrophy, an ultrasound would be less effective in distinguishing between hyperplasia,

an endocavitary mucosal polyp, a suspicious lesion, between a fibroid less than 2cm and a polyp, or fails to accurately measure the thickness of the endometrium whose uterine cavity is deformed by fibroids or polyps. Hence the interest of supplementing any abnormal ultrasound with a hysteroscopy.

Correlation between hysteroscopy – histology on biopsy

While some authors recommend stopping the explorations if the thickness of the endometrium is < 5 mm [9,10], others, on the other hand, systematically recommend performing a diagnostic hysteroscopy [6,7].

Indeed, it has been reported in one study, a percentage of 0.1 to 1% of endometrial cancer in case of atrophy without the experience of the echographer being considered nor that the patients have benefited from hysteroscopy [8].

In our series, the sensitivity of hysteroscopy in the diagnosis of atypia was between 93.3% and 96.7%, which shows good accordance in the diagnosis of atypical hyperplasia.

Among the 16 suspected cancers on hysteroscopy, the biopsy revealed 14 cancers and 2 returned in favour of atypical complex hyperplasia.

The correlation between hysteroscopy – histology under biopsy shows a Kappa of 0.68 (significant P).

Our study shows that hysteroscopy is very effective in the diagnosis of endometrial atrophy, hyperplasia and in the suspicion of cancers with respective sensitivities of 100%, 96.7% and 93.3%.

Our sensitivity for detecting hyperplasia is better than that found by Garuti G et al. [15] who had reviewed the results of hysteroscopy in 323 patients with hyperplasia and whose sensitivity was only 63.7%.

Showkat MS et al. [18] did not establish a correlation between certain hysteroscopic aspects and the diagnosis of hyperplasia, so that this examination can only give a suspicion of hyperplasia which must be confirmed by biopsy.

Correlation hysteroscopy – histology on surgical specimen

There had been a total of 77 surgical procedures with histologies on the operating specimen in our series. The analysis showed that there is a good correlation between the hysteroscopic results and the histology on the surgical specimen with kappa equal to 0.74 (P significant). Hysteroscopy had presented a good performance in the diagnosis of polyps and myomas with a sensitivity and specificity equal to 100% for each. In hyperplasia, the sensitivity was 96% and the specificity 92%. Finally, in the case of cancer, the sensitivity of HSC is 72% with a specificity of 100%.

Sahbi K et al. [19] in a study of 82 cases of MPM, concluded that the sensitivity and specificity of hysteroscopy are low for diagnosing endometrial atrophy (about 49 and 68% respectively) with weak concordance, kappa equal to 0.17 (p not significant). This same study [19] showed that hysteroscopy has satisfactory sensitivity and specificity for the diagnosis of endometrial polyps (75 and 87% respectively); in only one woman, hysteroscopy was in favour of an endometrial polyp, while histology concluded to endometrial adenocarcinoma; in five cases, the hysteroscopy was in favour of a submucosal or intra-cavitary myoma, the histology concluded, however, to an endometrial polyp.

Conclusion

We separately studied the sensitivity, specificity, positive and negative predictive values of pelvic ultrasound and hysteroscopy in the exploration of postmenopausal metrorrhagia. The degree of performance of each means of exploration varied according to the lesion in question of metrorrhagia and in general hysteroscopy (Kappa 0.74) was more reliable in the exploration of metrorrhagia than ultrasound (Kappa 0.50). We believe that hysteroscopy may not be performed during the first episodes of MPM if the ultrasound shows endometrial atrophy, but it is important that the ultrasound is performed or supervised by an experienced operator. For endometrial hypertrophy, ultrasound must always be supplemented by Doppler in search of endometrial neovascularization plus the study of the uterine artery, which would improve the concordance between ultrasound and hysteroscopy in the

diagnosis of aspects of atypia. Hysteroscopy should be performed whenever ultrasound finds an abnormality, outside of atrophy.

Conflicts of interest: No conflict of interest between the different authors.

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