An audit of mismatch repair deficiency testing in endometrial cancers at St George's University Hospitals NHS Trust, London, UK

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Background

- NICE guidelines (October 2020) recommend offering Lynch syndrome testing to all women diagnosed with endometrial cancer, using immunohistochemistry (IHC) to identify mismatch repair (MMR) protein deficiency as the initial test.

- This audit compared the current practice at St George's Hospital (SGH) against the NICE guidelines.

Audit standards

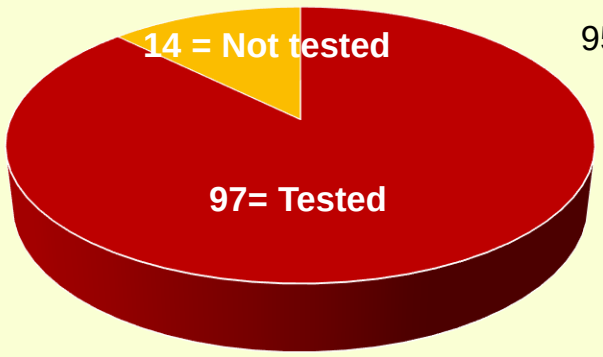
- All patients with endometrial cancer should have MMR protein IHC testing.
- All with MLH1 or PMS2/MLH1 loss should have MLH1 promotor hypermethylation testing.
- All with negative MLH1 promotor hypermethylation should be offered germline testing.
- All with MSH2/MSH6 loss and isolated MSH6 or PMS2 loss should be offered germline testing.

Methods

- We collected histopathology data on all endometrial biopsies and hysterectomies from 2/1/19 to 13/11/20, from our electronic histopathology database. Data on genetics referrals and germline testing were obtained from the clinical genetics team.

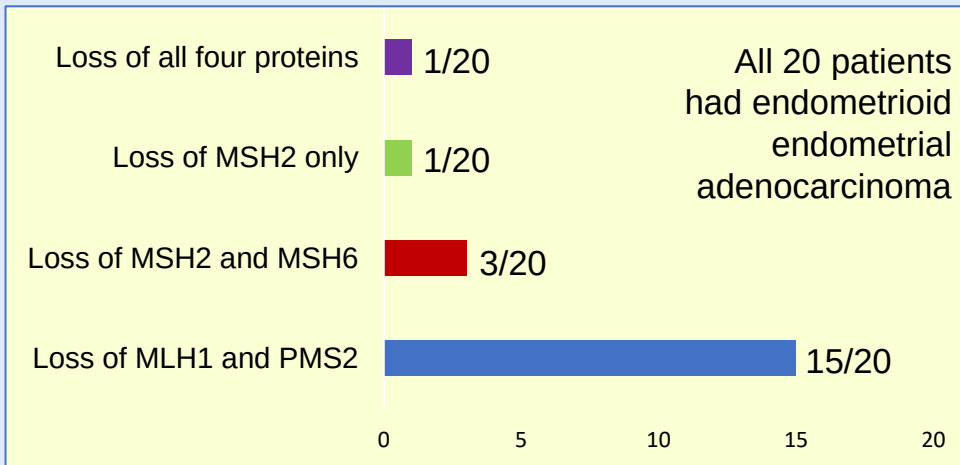
Results

- Out of the total 4366 endometrial biopsies, 111 patients were diagnosed with endometrial carcinoma.



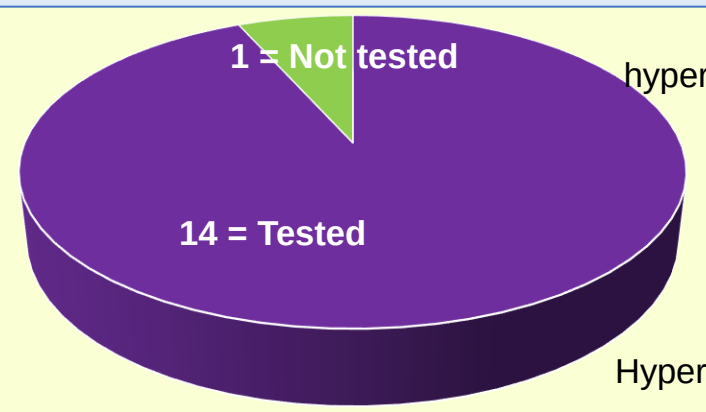
95.5% were tested for MMR protein deficiency

Fig. 1. MMR protein IHC testing for patients with endometrial cancer



All 20 patients had endometrioid endometrial adenocarcinoma

Fig. 2. 20 cases of MMR deficient endometrial carcinoma were identified



1- No hypermethylation

1- Lost to follow-up

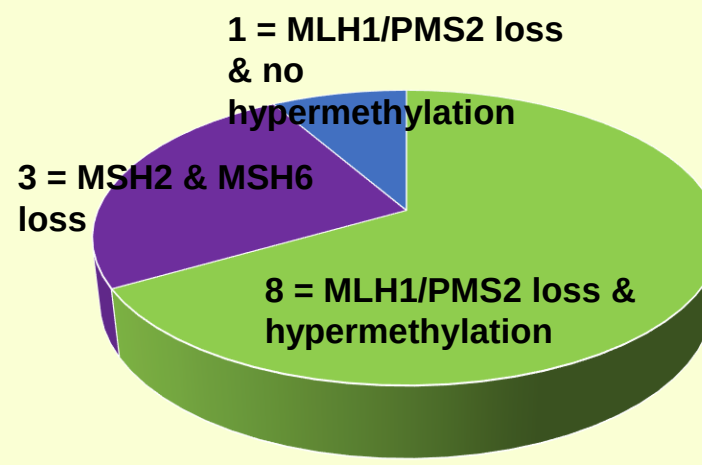
12- Hypermethylated

Fig. 3. MLH1 promotor hypermethylation testing in tumours with MLH1 and PMS2 loss

6 patients required germline testing and genetics referral:

- 1 patient with MLH1/PMS2 loss and absence of hypermethylation at the MLH1 promotor region
- 3 patients with MSH2 and MSH6 loss
- 1 patient with loss of MSH2 only
- 1 patient with loss of all four proteins

- A referral for germline testing was NOT made for 3/6 patients.
- Lynch syndrome was diagnosed in 1/6 patients (MSH6 pathogenic variant detected). Germline testing results are awaited for 1/6 patients.



12/20 patients were referred to clinical genetics

Fig. 4. Patients referred to clinical genetics team

Conclusions

- MMR IHC testing of endometrial carcinomas at SGH is nearly universal.
- Patients with MLH1 or MLH1/PMS2 loss and MLH1 promotor region hypermethylation do not require clinical genetics referral. Hypermethylation testing should be performed first.
- There is a need for a clear clinical referral pathway for suspected Lynch syndrome patients.
- A Trust guideline is currently under development by the genetics team to improve current practice. This includes a family history questionnaire for all patients (including those with normal MMR protein IHC).

References
1. The British Association of Gynaecological Pathologists. BAGP BGCS RCPath MMR pathway. Available from: https://www.thebagp.org/download/bagp-bgcs-nice-mmr-pathway/ [Accessed 9th May 2021].