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Comment

The enzyme linked immunoassay that we assessed is highly accurate in diagnosing childhood *H pylori* infection. The use of a grey zone may lower its accuracy, but the accuracy is satisfactory even with direct visual reading of the microwells without use of a plate reader; this makes it fairly cheap as a screening test (one determination cost is 22 euro (£14), half the average price of the urea breath test) and practical for epidemiological studies.

This study was approved by and conducted within the guidelines of the gastric disease section of the Italian Society for Paediatric Gastroenterology and Hepatology.

Contributors: GO designed and coordinated the study and wrote the article. AR and BR collected the data from each centre, analysed the faecal samples and did the statistical analysis. PL, MP, AS, GLde'A, and PS all participated in the discussion about the design of the study and approved the study proposal and the final draft; they also recruited all cases and collected data from patients from each centre, did endoscopy in children, and collected faecal samples to be sent to the coordinator centre. GO will act as guarantor for the paper.

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Competing interests: GO and AR have been reimbursed by Meridian Diagnostics, Europe (the manufacturer of HpSA) for attending a symposium on *H pylori* and gastroduodenal disease in Helsinki.

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Effect of hormone replacement therapy on the pathological stage of breast cancer: population based, cross sectional study

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Hormone replacement therapy is being used increasingly. Although it is known that the risk of developing breast cancer is slightly increased with long term use,[1] hormone replacement does not seem to adversely affect mortality from breast cancer.[2]

Studies have suggested that users of hormone replacement who get breast cancer develop tumours with "favourable" pathological features compared with non-users. One study included women who had been detected at screening and women who had presented with symptoms, with more screen detected women in the study group (users) than in the controls (non-users).[2] Another study compared type of tumour in users and non-users in a screen detected population alone[3] and showed that grade 1, node negative tumours were more common in the users.

Women with breast cancer who have used hormone replacement, however, may be more likely to have a cancer that was missed at screening; we have shown that women who develop such cancers (interval cancers) within a year of screening are twice as likely to have been using hormone replacement when they were screened.[4] We compared pathological features of tumours in both screen detected and interval cancers to assess whether previous use of hormone replacement therapy improves prognosis among women who develop breast cancer.

Patients, methods, and results

The study population comprised all 1130 women aged 50-64 years who underwent routine breast screening during May 1988 to December 1993 in the area of Scotland covered by the West of Scotland Breast Screening Unit and who either had a screen detected cancer or developed an interval cancer. Data on interval cancers were collected up to the end of 1996. Current use of hormone replacement (yes/no) had been recorded by radiographers at the time of screening and also at assessment for women with screen detected cancers. The case notes of half the women with interval cancers were reviewed to check whether use of hormone replacement at the time of presentation was the same as at their last screening. Seventeen women were excluded because use of hormone replacement was unknown, leaving 1113 patients for analysis.

Of the 815 women with screen detected cancers, 100 (12.3%) were using hormone replacement when they were screened. Of the 298 women with interval cancer, 66 (22.1%) were using hormone replacement; use at diagnosis was the same as at their previous screen. Of the total number of women studied, therefore, 166 (14.9%) were using hormone replacement at the time they developed breast cancer.

We found no difference in type, size, or grade of tumour in users compared with non-users (table). Twenty four per cent of users developed well differentiated tumours (tubular, mucoid, and invasive ductal grade 1 cancers) compared with 22% of non-users. This equates to an odds ratio of 0.98 (95% confidence interval 0.63 to 1.50). Seventy seven per cent of users were node negative compared with 67% of non-users. There was no difference in mean tumour size (mean difference 0.25 mm (-2.02 mm to 2.53 mm)) in users compared with non-users. No difference was seen in the distribution of the Nottingham prognostic index[5] between the two groups. Eight per cent of women using hormone replacement developed ductal carcinoma in situ compared with 15% of non-users. When

Pathological features of breast cancer by use of hormone replacement therapy. Values are numbers (percentages) unless stated otherwise

	All cancers (n=1113)		Screen detected cancers (n=815)	
	Users (n=166)	Non-users (n=947)	Users (n=100)	Non-users (n=715)
Type and grade				
Ductal carcinoma in situ	12 (7.9)	133 (14.9)	12 (12.5)	128 (18.3)
Invasive ductal cancer:				
Grade 1*	36 (23.7)	198 (22.2)	23 (23.9)	175 (25.1)
Grade 2	52 (34.2)	252 (28.3)	34 (35.4)	201 (28.8)
Grade 3	19 (12.5)	105 (11.8)	7 (7.3)	48 (6.9)
Grade not known	22 (14.5)	133 (14.9)	14 (14.6)	98 (14.0)
Lobular	11 (7.2)	59 (6.6)	6 (6.3)	39 (5.6)
Other	0	11 (1.2)	0	9 (1.3)
Missing data	14	56	4	17
Significance	χ^2=8.33, df=6, P=0.21		χ^2=4.26, df=6, P=0.64	
Size (mm)†				
<10	30 (23.4)	186 (25.3)	24 (31.6)	171 (31.0)
10-19	51 (39.8)	299 (40.7)	35 (46.1)	234 (42.4)
20-29	31 (24.2)	140 (19.1)	13 (17.1)	96 (17.4)
30-39	8 (6.3)	58 (7.9)	2 (2.6)	31 (5.6)
40-49	5 (3.9)	30 (4.1)	1 (1.3)	11 (2.0)
⩾50	3 (2.3)	21 (2.8)	1 (1.3)	9 (1.6)
Missing data	12	24	8	18
Significance	χ^2=0.01, df trend=1, P=0.92		χ^2=0.63, df trend=1, P=0.43	
No of nodes†				
None	96 (77.4)	437 (66.7)	58 (84.1)	354 (73.8)
<4	20 (16.1)	150 (22.9)	8 (11.6)	95 (19.8)
⩾4	8 (6.5)	68 (10.4)	3 (4.3)	31 (6.5)
Missing data	16	103	15	90
Significance	χ^2=5.09, df trend=1, P=0.03		χ^2=2.74, df trend=1, P=0.1	
Nottingham prognostic index‡				
Low	65 (62.5)	307 (57.5)	44 (74.6)	264 (67.2)
Medium	29 (27.9)	180 (33.7)	13 (22.0)	109 (27.7)
High	10 (9.6)	47 (8.8)	2 (3.4)	20 (5.1)
Significance	χ^2=1.34, P=0.51		χ^2=1.33, P=0.51	
Insufficient information	50	280	29	194

*Includes tubular and mucoid tumours.
†Excludes ductal carcinoma in situ and missing grades.
‡Nottingham prognostic index (in which a low score indicates a better prognosis than a high score) does not apply to cases of ductal carcinoma in situ.

screen detected cancers were analysed alone, no differences were found between the type, grade, size, or nodal status in users compared with non-users.

Comment

Our results do not support the commonly held view that women using hormone replacement therapy develop tumours with favourable prognostic features. Little information currently exists about the relation between the development of ductal carcinoma in situ and use of hormone replacement. Our numbers are small, and further studies are needed. We show, however, that women using hormone replacement do not develop poorer prognosis tumours, and this is reassuring to doctors prescribing hormone replacement therapy.

JCL, CMC, and HMD also work at the West of Scotland Breast Screening Centre, Glasgow.

Contributors: SS, JCL, and CMC initiated the present study, designed the project, collected data, and contributed to writing the paper. DH also helped to develop the original idea and study design. He carried out the statistical analysis and did the cross checks with the cancer registry. He has been closely involved in the writing and revising of the final paper. EAM reported the pathology of all the cases and was responsible for the pathology quality assurance in the screening cases. HMD discussed core ideas, collected data, helped in the interpretation of data, and is responsible for the quality assurance of the screening programme. WDG allowed his patients to be studied, discussed ideas and the interpretation of findings, and encouraged the project. SS is the guarantor for the paper.

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Endpiece

Religion

That very large part of mankind who have religion enough to make them uneasy when they do wrong, and not religion enough to keep them from doing wrong.

Lord Macauley