typical, 10 atypical and four carcinomas) classifications, we found that both classification systems were highly significantly ($P < 0.001$) correlated with overall survival, as well as tumour stage and complete resection (Figure 1). Both classifications were also statistically correlated each other ($P < 0.001$), but interobserver agreement was 0.57 and 0.97 within the WHO and Suster/Moran classifications respectively. Our results basically overlap with those previously published by Rieker *et al.*[8] (comparing the WHO and Barnatz classifications) and Sperling *et al.*[9] (comparing the WHO and Suster/Moran classifications).

The prognosis of thymomas depends mainly on tumour resectability and stage whatever classification system pathologists adopt. The Suster/Moran system seems less complex to learn and teach, is possibly more reproducible and also includes unusual thymoma variants not included in the WHO classification.

Finally, given the limited therapeutic options in patients with unresectable or metastatic thymomas,[10] it seems more helpful to spend time and effort in identifying molecular targets for therapy rather than validating or creating further classifications.

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Adiponectin and leptin expression in primary ductal breast cancer and in adjacent healthy epithelial and myoepithelial tissue

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Sir: Current hypotheses suggest that adiponectin and leptin, hormones synthesized predominantly by adipose tissue, could play a role in cancer development. Thus, several studies have demonstrated that low-serum adiponectin and high-serum leptin levels are associated with an increased risk for breast cancer.[1] Numerous *in vitro* studies have also shown that adiponectin mediates an antiproliferative response, whereas leptin enhances proliferation in numerous breast cancer cells.[2,3] These observations highlight the antagonistic properties of adiponectin and leptin and their potential involvement in breast cancer development.

Few studies have explored the expression of adiponectin or leptin in breast cancer. To the best of our knowledge, no study has simultaneously explored the expression of both adipokines in breast tissue. In order best to understand the involvement of these two antagonistic hormones in breast cancer development, we investigated adiponectin and leptin expression in the same human biopsy specimens of different grades of epithelial ductal breast cancer. We also analysed normal epithelial and myoepithelial tissue adjacent to ductal cancer. Myoepithelial cells form an almost continuous layer of cells that surround epithelial tissue and are known as a natural tumour suppressor.

Sections (4 μm) of alcohol–formalin–acetic acid paraffin-embedded primary breast ductal cancer ($n = 45$), *in situ* ductal carcinoma ($n = 14$) and normal breast tissue adjacent to breast cancer ($n = 40$) were stained using polyclonal biotinylated antibodies raised against adiponectin and leptin (1 μg/ml). In control samples, the specific antibody was omitted. The immunohistochemical procedure was realized as previously described.[4]

Immunoreactivity was assessed by a pathologist blinded to the clinical data. Adiponectin and leptin

expression in neoplastic and normal adjacent tissues was classified as either negative (<5% labelled cells) or positive (≥5% labelled cells). The intensity of expression was graded as 0 (none), 1+ (mild), 2+ (moderate) and 3+ (intense).

In normal tissue, cytoplasmic adiponectin expression was observed in myoepithelial cells (65% of cases studied) and to a lower extent in epithelial cells (15% of cases studied) (Table 1A; Figure 1B). The percentage of labelled cells in positive cases (65%) remained similar in these two cell types, but the intensity of immunoreactivity of myoepithelial cells was stronger (four cases with 3+) (Table 1B). Leptin expression was also identified in the cytoplasm of epithelial cells, and 80% of these cells in positive cases were labelled (Table 1A,B; Figure 1E). Adiponectin expression was noted in 15% of invasive ductal carcinoma samples (Table 1A; Figure 1C). Adiponectin immunoreactivity was localized in the cytoplasm of epithelial cells.

Leptin was expressed in 36 of the 45 (80%) invasive ductal lesions studied (Table 1A; Figure 1F). Leptin expression, which localized to the cytoplasm, was labelled in 85% of epithelial cells in positive cases (Table 1B). Similar observations were recorded for

Table 1. The expression of adiponectin and leptin (**A**), the percentage of labelled cells and staining intensity (**B**) in breast ductal cancer and in adjacent normal tissue

A

	Total number of cases studied	Adiponectin expression		Leptin expression	
Tissue	*n*	*n′*	%	*n″*	%
Normal tissue adjacent to breast cancer	40	30*	75	31	80
In epithelial cells	40	5	15	31	80
In myoepithelial cells	40	26	65	0	0
In-situ ductal carcinoma	14	0	0	11	80
Invasive ductal carcinoma	45	7	15	36	80
Grade 1	13	2	15	11	85
Grade 2	17	2	10	12	70
Grade 3	15	3	20	13	85

B

	Adiponectin					Leptin				
	Cases with adiponectin expression	Labelled cells	Staining intensity			Cases with leptin expression	Labelled cells	Staining intensity		
Tissue	*n′*	%	1+	2+	3+	*n″*	%	1+	2+	3+
Normal tissue adjacent to breast cancer	30*	70 ± 5	16	10*	4	31	80 ± 5	20	10	1
In epithelial cells	5	65 ± 10	2	3	0	31	80 ± 5	20	10	1
In myoepithelial cells	26	65 ± 5	14	8	4	0	0	0	0	0
In-situ ductal carcinoma	0	0	0	0	0	11	95 ± 5	6	5	0
Invasive ductal carcinoma	7	20 ± 10	3	4	0	36	85 ± 5	25	9	2

*For one patient, adiponectin expression was noted in both epithelial and myoepithelial cells.

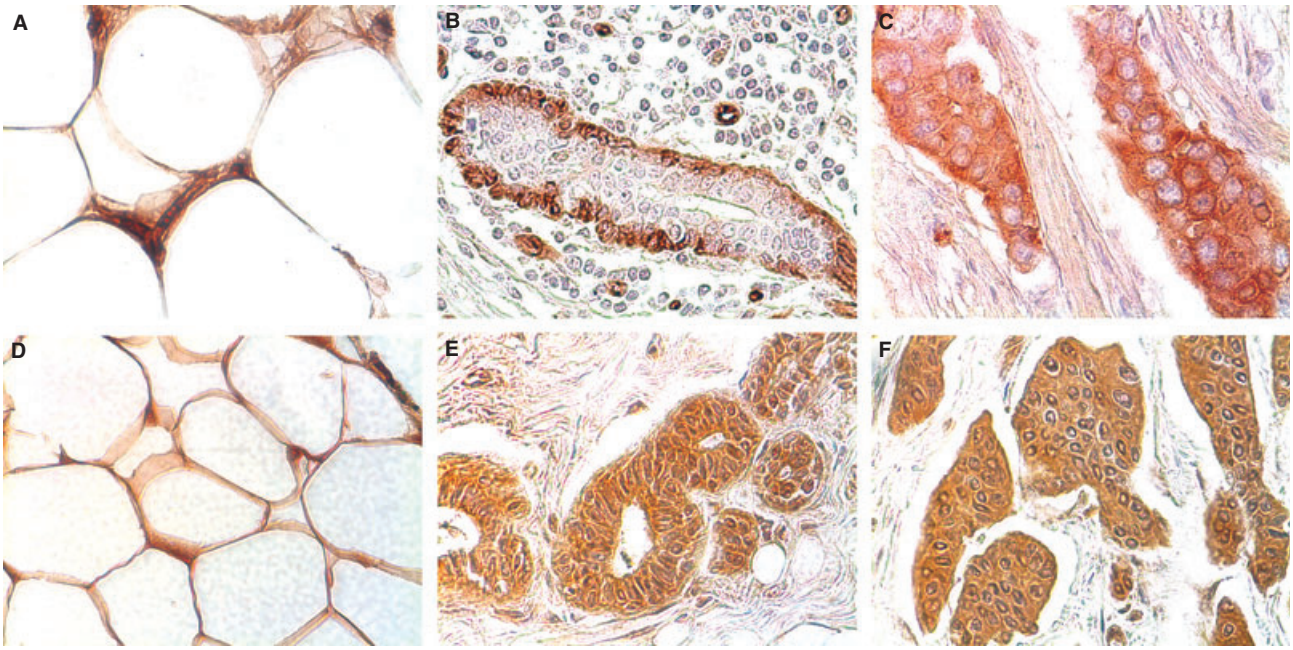

Figure 1. Immunohistochemical detection of adiponectin (**A–C**) and leptin (**D–F**). In these images, adiponectin can be seen in adipose tissue, used as a positive control (**A**), in normal myoepithelial cells (**B**) and in invasive breast ductal cancer cells (**C**). There is leptin immunopositivity in adipose cells (**D**), in normal tissue (**E**) and in invasive breast ductal cancer cells (**F**).

in situ lesions, since cytoplasmic leptin expression in epithelial tissue was noted in 80% of cases studied, with 95% of cells labelled in positive cases (Table 1A,B).

Thus, we observed that adiponectin and leptin are expressed in both breast cancer cells and adjacent normal epithelial tissue, signifying that these adipokines may act on mammary healthy and cancerous cells not only via an endocrine pathway but also locally via autocrine and/or paracrine activity. In addition, it was noted that these adipokines were inversely expressed in breast tissue, suggesting that normal epithelial and neoplastic cells are more heavily surrounded by leptin than by adiponectin.

Interestingly, this study has also provided the first evidence that normal myoepithelial cells strongly express adiponectin. Myoepithelial cells have been called 'natural tumour suppressors', due partly to their ability to inhibit the proliferation of breast carcinoma cells.[5] This effect has been attributed to paracrine factors secreted by myoepithelial cells. In this way, adiponectin, which inhibits proliferation and induces apoptosis in breast cancer cell lines, may act locally to protect normal epithelial breast cells or to inhibit the proliferation of cancer cells. The expression of adiponectin by myoepithelial cells may partially explain their tumour suppressor activity.

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Gross features of lobular endocervical glandular hyperplasia in comparison with minimal-deviation adenocarcinoma and stage Ib endocervical-type mucinous adenocarcinoma of the uterine cervix

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Sir: Lobular endocervical glandular hyperplasia (LEGH) was first described as a benign mimic of minimal-deviation adenocarcinoma (MDA), or 'adenoma malignum'.[1,2] Histopathological criteria for LEGH have well been established,[3,4] but the distinction between LEGH and MDA in imaging studies is still challenging for diagnostic radiologists. Appearance of a multicystic lesion on computed tomography and magnetic resonance imaging has been considered to be diagnostic for MDA,[5–9] but some authors have questioned this view, pointing out that cyst formation is rather uncommon in cases of MDA, but seems to be indicative of LEGH.

In order to elucidate the characteristic topological features of LEGH, we examined haematoxylin and eosin (H&E)-stained glass slides of cervical lesions in hysterectomy specimens from 31 patients, comprising 15 cases of LEGH, six cases of MDA and 10 cases of FIGO stage Ib common endocervical-type mucinous adenocarcinoma (EMA). On representative sagittal sections of these 31 cases, we determined the greatest longitudinal length and depth of the lesion, lesion location and the size and number of the cystic components and calculated the average values and standard deviation (Figures 1 and 2). The mean values were compared between groups by the Mann–Whitney *U*-test.

The mean longitudinal length and depth of MDA (62.3 and 21.8 mm, respectively) were obviously greater than those of LEGH (29.5 and 13.7 mm, respectively) ($P = 0.0022$ and 0.010) or common EMA (26.6 and 13.1 mm, respectively) ($P = 0.0048$ and 0.064) (Table 1). Indeed, all six MDAs extended widely from the vagina to the uterine corpus, occupying the entire uterine cervix.

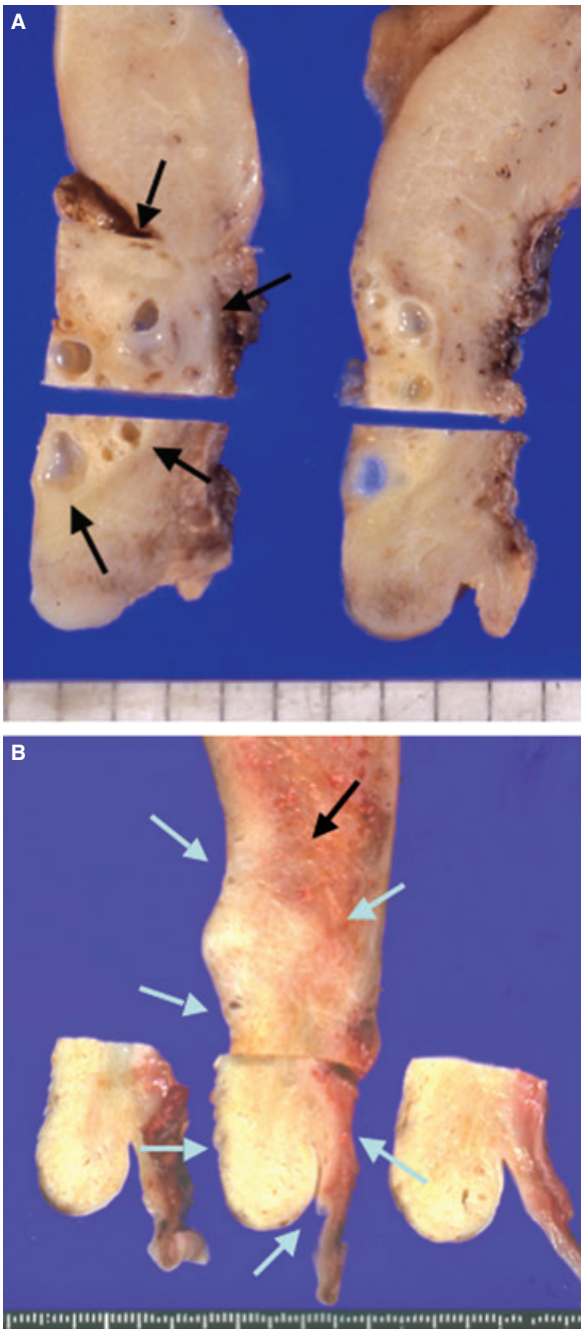

Figure 1. Gross features of surgically resected specimens of lobular endocervical glandular hyperplasia (LEGH) (**A**) and minimal deviation adenocarcinoma (**B**). Arrows indicate the area of tumours.