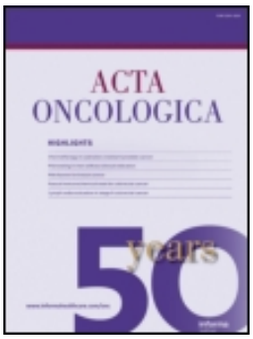

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QUALITY CONTROL OF PATHO-ANATOMICAL DIAGNOSIS OF CARCINOMA OF THE BREAST

H. KIÆR, J. A. ANDERSEN, F. RANK and B. V. PEDERSEN

Abstract

Three pathologists, especially interested in breast cancer, re-examined 379 random specimens of invasive breast cancer initially diagnosed at 27 pathological institutes; these were obtained from the computer register of the Danish Breast Cancer Cooperative Group (DBCG). The degree of variation between a) the primary diagnosis (the country as a whole) and each of the 3 pathologists and b) between the 3 pathologists mutually, has been studied with regard to the 2 main groups of carcinoma—infiltrating duct carcinoma (IDC) and infiltrating lobular carcinoma (ILC). The degree of variation was found to be similar between each of the 3 pathologists and the country as a whole, with a kappa value of approx. 0.3 for both types of carcinoma, and a considerably better interobserver variation between the 3 pathologists with a kappa value of approx. 0.7. The most important reason was that the 3 pathologists agreed on the occurrence of more than twice as many cases primarily diagnosed as ILC. A partial explanation is in fact that since the start of DBCG, reports have appeared of variants of ILC not previously known. The diagnosis of malignancy (carcinoma) was almost completely unambiguous.

Key words: Breast cancer, histopathology, quality control.

It is well known that there are variations in the detailed diagnosis of various pathologists.

In a country-wide, multicentre project, such as the Danish Breast Cancer Cooperative Group (DBCG), we have found it of interest to study how large the variations are in the typing of breast cancer by Danish pathologists as a whole as compared to the diagnosis of 3 pathologists with special interest in the subject, as well as to determine the variations between these 3 pathologists.

Presented at the DBCG meeting, Copenhagen, January 22–23, 1988.

Material and Methods

During the period 1979–1981, approximately 4000 patients were randomized in the DBCG register. All patients with birth dates on the 21st, 22nd or 23rd of each month were withdrawn from the DBCG computer register; this gave a sample of 420 patients. Requests to the 27 pathological institutes, where the cancer of the respective patients had been diagnosed, for specimens resulted in the receipt of slides from 384 patients. These were re-examined blind by 3 pathologists (HK, JA and FR) according to a standardized, computerized registration form which included compatibility of the diagnosis cancer and typing according to WHO (3). The final material fed into the computer included 379 patients.

The degree of agreement in the interobserver variation partly between the pathologists responsible for the initial

Table 1

The investigators' diagnosis as compared to the initial diagnosis (country as a whole)

	1	2	3	4	5	6	7
Pathologist 1	263	55	9	8	9	2	41
Pathologist 2	257	56	4	7	4	1	43
Pathologist 3	279	53	1	7	1	0	33
Whole country	318	16	10	6	10	8	9

1) Infiltrating duct carcinoma
2) Infiltrating lobular carcinoma
3) Mucinous carcinoma
4) Medullary carcinoma
5) Papillary carcinoma
6) Adenoid cystic carcinoma
7) Others (see text!)

Table 2

Degree of agreement with regard to individual cases in the diagnosis of the type of carcinoma

	The whole country	3 investigators agree with country	2 investigators agree with country	3 investigators mutually agree	2 investigators mutually agree
Infiltrating duct carcinoma	318	198	249	217	254
Infiltrating lobular carcinoma	16	13	13	35	42

diagnosis (country) and each of the 3 pathologists, and partly mutually between these pathologists 2 and 2, was evaluated by means of standard K values (kappa).

Results

The evaluation by the 3 pathologists as compared to the remainder of the country is shown in Table 1.

Concerning infiltrating carcinoma, the 3 pathologists all had a somewhat smaller number of infiltrating duct carcinoma than the country as a whole and all 3 had far more cases of infiltrating lobular carcinoma. Even though there was good agreement between the 3 pathologists regarding the absolute numbers of these types of cancer, a study of the individual cases showed considerable interobserver disagreement between the pathologists (Table 2).

The 'others' group included types of cancer which were not specified in the computer form, types of carcinoma which could not be determined with certainty (owing to sparse amounts of tumour tissue or too poor quality of the slides), and a number of cases of carcinoma in situ; the latter category amounted to 9 cases for the country as a whole, but 10–12 cases for the 3 pathologists. The group contained in addition a few cases of atypical ductal epithelial hyperplasia and a few cases with incomplete information on the type of cancer.

The interobserver variation between the country as a whole and each of the 3 pathologists and between the 3 pathologists mutually, 2 and 2, was analyzed for the diagnoses infiltrating duct carcinoma and infiltrating lobular carcinoma; the results are shown in Tables 3 and 4.

The absolute value of kappa compares pairs of observers, but does not provide information as to the capability of the observer, as this value is dependent on the prevalence. The quantity K, as well as the estimated K, comes between minus 1 and plus 1. The agreement is no better than would be expected from chance for a K value = 0. A K value of 1 corresponds to complete agreement.

It can be seen from Tables 3 and 4 that concerning both infiltrating duct carcinoma and infiltrating lobular carcinoma, the 3 pathologists had equal agreement with the country as a whole, but their mutual agreement was considerably closer than their agreement with the country as a whole.

Table 3

Interobserver variation in the diagnosis infiltrating duct carcinoma. Estimated kappa value ± estimated spread

	Pathologist 1	Pathologist 2	Pathologist 3
The whole country	0.276±0.074	0.276±0.069	0.240±0.077
Pathologist 1		0.699±0.050	0.640±0.054
Pathologist 2			0.688±0.050

Table 4

Interobserver variation in the diagnosis infiltrating lobular carcinoma. Estimated kappa value ± estimated spread

	Pathologist 1	Pathologist 2	Pathologist 3
The whole country	0.346±0.093	0.311±0.095	0.330±0.096
Pathologist 1		0.743±0.053	0.666±0.059
Pathologist 2			0.753±0.051

Discussion

The three investigators had considerably fewer cases of infiltrating duct carcinoma and considerably more cases of infiltrating lobular carcinoma than the country as a whole. An explanation is presumably the publication of a number of reports on variants of infiltrating lobular carcinoma not previously recognized (1, 2).

Even though the investigators closely agreed on the total number of cases of infiltrating lobular carcinoma, there was less agreement in the individual cases (Table 2), and the interobserver variation increased with the number of investigators. Complete agreement with regard to the diagnosis of infiltrating duct carcinoma and infiltrating lobular carcinoma cannot be expected, as there exists a group of small-cell infiltrating breast carcinomas without

an in situ component, the diagnosis of which is fairly subjective. The fact that the K value, as regards infiltrating duct carcinoma (Table 3) for the country as a whole as compared to the individual investigators, lies nearer chance can be explained by the fact that the number of cases of infiltrating duct carcinoma in the material represented between 68 and 84% of the total number. Due to the large number there is a great possibility that chance played a considerable role for the agreement. The K value for the investigators mutually 2 and 2 lies nearer perfect agreement than would be expected from chance alone. Similar K values were obtained for infiltrating lobular carcinoma (Table 4).

The results for infiltrating duct carcinoma and infiltrating lobular carcinoma are not completely independent of each other, inasmuch as good agreement in the diagnosis of infiltrating duct carcinoma will increase the agreement with regard to the diagnosis of infiltrating lobular carcinoma.

In the study there were few cases of special types of infiltrating carcinoma, such as medullary carcinoma and mucinous carcinoma. There was extremely good agreement regarding the diagnosis medullary carcinoma, while the variation in the diagnosis of mucinous carcinoma presumably resulted from varying opinions as to how much mucin a cancer must contain before it should be classified as typical mucinous carcinoma. The demonstrated difference in the typing of carcinoma did not influence the treatment of patients, as in the treatment protocols no stratification was made with regard to the histologic type of invasive carcinoma. The investigators interpreted two cases, initially diagnosed as duct carcinoma in situ, as being atypical ductal epithelial hyperplasia. Furthermore, 3 cases, initially interpreted as infiltrating duct carcinoma with a dominating intraductal component, were diagnosed by the investigators as ductal carcinoma in situ. On the whole, however, the diagnosis of invasive carcinoma was almost unambiguous.

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