



The prognostic value of histological grade determined after neoadjuvant chemotherapy of breast cancer

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ABSTRACT

Histological grade is a validated prognostic factor of breast cancer but may show alterations following neoadjuvant chemotherapy (NACT). Its reporting after NACT is recommended by several guidelines, but evidence of its retained prognostic impact is scarce. Patients treated with NACT followed by surgery and having sufficient residual tumour for the determination of grade were analysed for the survival effects of posttreatment grade (yG). Kaplan-Meier analyses and the log-rank test were applied, followed by the univariable and multivariable Cox proportional hazards models. The cohort comprised 355 patients with known yG, and 320 of them had also a pretreatment grade available. Pretreatment grade changed in 99/320 (31 %) cases following NACT, and downgrading was more common (n=78/320, 24 %) than upgrading (21/320, 7 %). Among 355 breast cancer patients, those with yG3 (poorly differentiated) tumours (n=155) had worse 5-year relapse-free and overall survival estimates than those with yG2 (n=169) or yG1 (n=31) tumours. This was also substantiated by univariable analysis; however, yG lost its significance in the multivariable model. Post-NACT histological grade has a prognostic impact, but does not seem to be an independent prognosticator in the post-NACT setting; however, these results lend support for its reporting by pathologists after primary systemic treatment.

1. Introduction

Breast cancer is a heterogeneous disease that can be stratified along multiple features. Its prognosis is dependent on several factors, traditional ones, like age of the patient, nodal status, tumour size, histological grade, vascular invasion [1–4], and newer ones which require molecular techniques for assessment, like scores derived from gene expression profiles [3,5]. The differentiation of malignant tumours generally reflects their biological behaviour, and the beginning of cancer grading can be traced back to the end of the 19th century, when David von Hansemann published his *Die mikroskopische Diagnose der bösartigen Geschwülste*, linking mitoses and atypia to disease outcome; this was followed by Broders' milestone papers correlating the differentiation of

squamous cell carcinomas with their outcome [6]. A three-tiered histological parameter-based grading system of breast cancers was published by Greenhough in 1925 [6,7], and this can be considered the ancestor of the Bloom and Richardson grading system [8] or of the presently used Nottingham or Elston and Ellis histological grading [9] advocated by most current guidelines on reporting breast carcinomas [10–15], because of its well-established prognostic and ensuing treatment influencing role. The histological grade of breast cancer is derived from scoring gland (tubule) formation, nuclear pleomorphism as well as mitotic activity on a 1- to 3-point scale, adding the relevant ordinal values to get a sum, and classify tumours as well, moderately or poorly differentiated, i.e. belonging to grade I, II or III, (G1, G2, G3) respectively.

Abbreviations: 5FU, 5-fluoro-uracil; BxG, core needle biopsy based histological grade; CNB, core needle biopsy; ER, oestrogen receptor; HER2, human epidermal growth factor receptor-2; HR, hazard ratio; NACT, neoadjuvant chemotherapy; OS, overall survival; PR, progesterone receptor; RFS, recurrence-free survival; yG, posttreatment histological grade, 1–3, referring to grades 1–3.

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Table 1

Basic clinicopathological characteristics of included patients (NST: breast carcinoma of no special type, IDC: invasive ductal carcinoma, ILC: invasive lobular carcinoma, BxG: grade in the core needle biopsy, ER: oestrogen receptor, PR: progesterone receptor, HER2: human epidermal growth factor receptor-2, NACT: neoadjuvant chemotherapy, yG: grade in the resection specimen after neoadjuvant therapy).

Histological type	n	%
NST (IDC)	298	84
ILC	36	10
others	21	6
BxG		
G1	19	5
G2	109	31
G3	192	54
No data	35	10
ER		
Positive	225	63
Negative	127	36
No data	3	1
PR		
Positive	193	54
Negative	158	45
No data	4	1
HER2		
Positive	52	15
Negative	280	79
Unknown	23	6
Molecular subtypes		
Triple (ER/PR/HER2) negative	88	25
HER2 positive (ER and PR negative)	26	7
HER2 positive (ER or PR positive)	26	7
“Luminal-like” (ER and/or PR positive)	192	54
Unclassifiable (missing data)	23	6
NACT		
Taxane-based	285	80
Anthracycline-based	57	16
Other	8	2
Not specified	5	1
Anti-HER2 treatment (mostly trastuzumab alone, or with pertuzumab) (added)	35	10
Surgery		
Excision	105	30
Mastectomy	250	70
yG		
yG1	31	9
yG2	169	48
yG3	155	43
Lymphovascular invasion		
Positive	100	28
Negative	250	71
No data	5	1
ypT		
ypT1a-b	59	16
ypT1c	81	23
ypT2	127	36
ypT3	50	14
ypT4	10	3
ypTx	28	8
ypN		
ypN0	109	31
ypN0(i+)/1 mi	14	4
ypN1	113	32
ypN2	73	21
ypN3	37	10
ypNx	9	2

Neoadjuvant treatment is often used to downstage locally advanced breast cancers to allow breast-conserving surgery and is also helpful in reflecting the response of the tumour to the given treatment. Histological grade has some role in advocating the type of neoadjuvant chemotherapy (NACT), e.g. G1 tumours with low proliferation are unlikely to benefit from classical chemotherapy. It is also known that the grade assessed on pretreatment core needle biopsies (CNBs) most commonly matches the grade established from excisional specimens and when

there is a mismatch, most of the time, CNBs underestimate tumour grade [16,17]. In keeping with this finding, we also demonstrated that the correspondence between biopsy grade (BxG) and grade of residual breast carcinoma after NACT (yG) is somewhat lower, and when there is a discrepancy between the two, the yG is generally lower, as a consequence of decreased proliferation, i.e. lower mitotic scores [17].

Most studies reporting on breast cancer patients treated with primary systemic treatment report the initial prognostic profile of their patients, and pathology-based prognosticators of breast cancer in such instances derive from the pretreatment CNBs. Residual tumours are also required to have their grade assessed. The International Collaboration on Cancer Reporting lists this feature as a core element, i.e. an obligatory part of the histopathology report [18], but little is known about yG as a prognostic factor. In the present work, we looked at the prognostic role of histological yG in residual tumours following NACT.

2. Materials and methods

The analysis included a retrospectively collected consecutive series of breast cancer patients treated with NACT followed by surgery at the Departments of Oncotherapy and Surgery, Albert Szent-Györgyi Faculty of Medicine, University of Szeged between 1999 and 2018 and at the Bács-Kiskun County Teaching Hospital, Kecskemét, between 2000 and 2018. Exclusion criteria were the lack of the relevant prognostic parameters (including lack of sufficient residual tumour or poor fixation to determine yG), detection of distant metastasis within 6 months from diagnosis, or lack of follow-up data from the patients' digital charts.

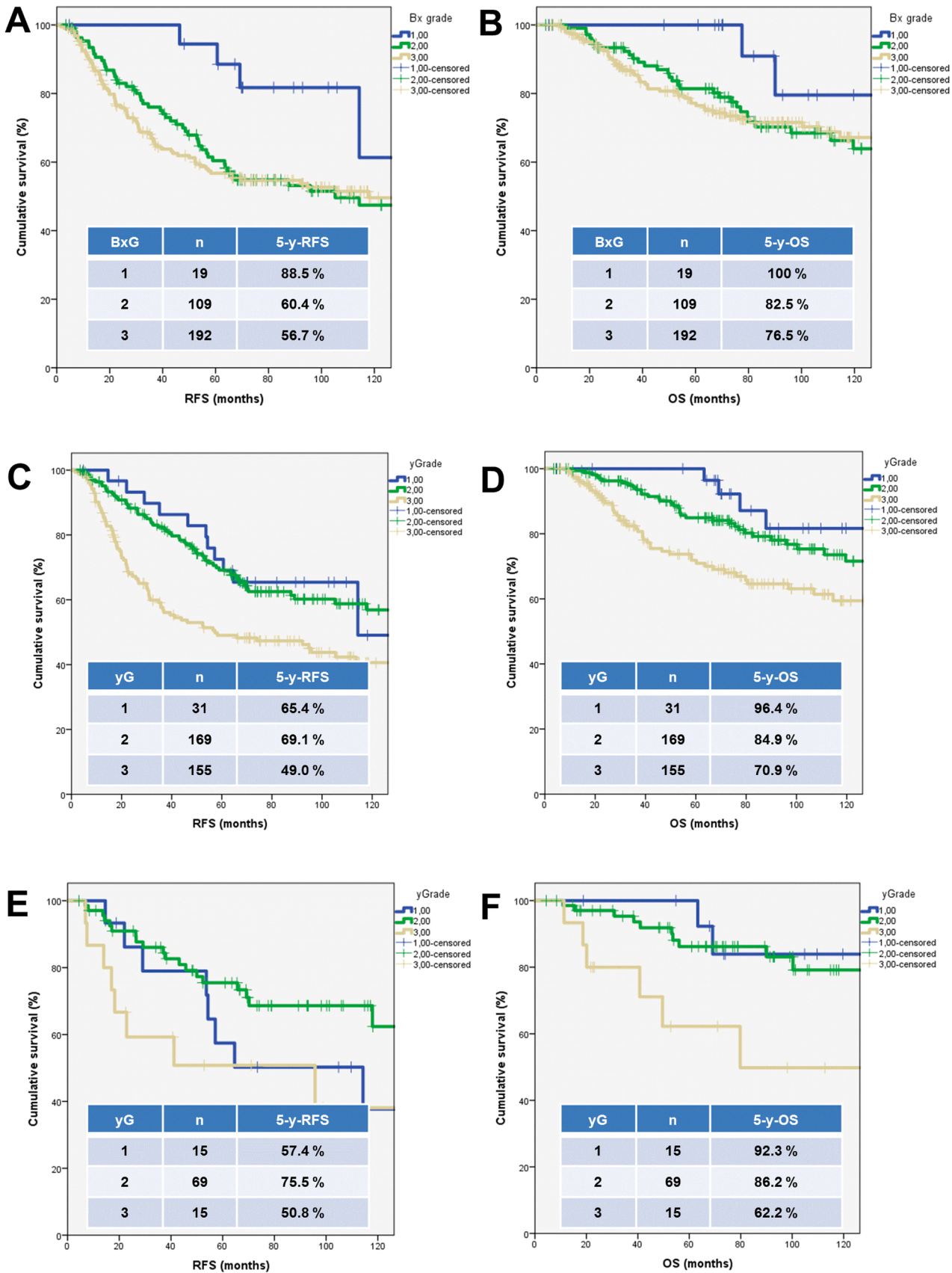
The clinicopathological parameters, namely gender, age, histological diagnosis/histological type [12] from the CNB, BxG of the tumour, type of NACT, type of surgery, completeness of resection, biopsy based oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER2) status, presence of vascular invasion, yG, ypT and ypN categories, finally follow-up data as overall survival (OS) and recurrence-free survival (RFS) were collected from medical charts; these were defined as time from the initiation of NACT to the last follow up or event. There were many chemotherapy regimens used at the two sites during this relatively long period, and therefore the type of NACT was broadly classified as taxane-based (mostly combined with an anthracycline; including docetaxel-epirubicin/doxorubicin ± cyclophosphamide, paclitaxel-epirubicin-capecitabine, paclitaxel-cisplatin, consecutive epirubicin/doxorubicin-cyclophosphamide or cyclophosphamide-epirubicin-5FU and docetaxel, mono paclitaxel); anthracycline-based (when anthracyclines were not combined with taxanes; including cyclophosphamide-epirubicin-5FU, epirubicin/doxorubicin-cyclophosphamide) and others (including few instances of cyclophosphamide-methotrexate-5FU or mitoxantrone-methotrexate ± Mitomycin-C). Trastuzumab (generally alone, on occasion with pertuzumab) was added to NACT in 35/52 HER2-positive cases (Table 1). All patients had regular follow-ups. The follow-up period ended in December 2023.

The proportion of grade changes on NACT was evaluated with contingency tables and the chi-square test.

To evaluate the impact of histological grade on prognosis, Kaplan-Meier analyses and the log-rank test were applied. For further investigations, the univariable Cox proportional hazards model was applied. Factors found significant in the univariable analyses were entered into the multivariable Cox proportional hazards model. Statistical models were fitted using SPSS Statistics V 23.0 software (Armonk, USA). The study was approved by the institutional ethical committee of the Albert Szent-Györgyi Clinical Centre of the University of Szeged.

3. Results

Altogether 355 patients diagnosed with breast cancer, receiving NACT and having residual invasive carcinoma on excision were included. All but one patient were female and the median age was 53



(caption on next page)

Fig. 1. The results of the Kaplan-Meier analyses

A and B: Regarding BxG, significant differences were identified among the RFS estimates of BxG 1 vs. 2 ($p_{\text{RFS}}=0.022$) and BxG 1 vs. 3 ($p_{\text{RFS}}=0.019$) but not those of BxG 2 vs. 3 ($p_{\text{RFS}}=0.356$). Furthermore, significant differences were identified between the OS estimates of BxG 1 vs. 3 ($p_{\text{OS}}=0.05$) but not among BxG 1 vs. 2 ($p_{\text{OS}}=0.075$) and BxG 2 vs. 3 ($p_{\text{OS}}=0.518$), respectively. C and D: Concerning yG, significant differences were defined among RFS estimates of yG 1 vs. 3 ($p_{\text{RFS}}=0.010$) and yG 2 vs. 3 ($p_{\text{RFS}}<0.001$) but not those of yG 1 vs. 2 ($p_{\text{RFS}}=0.788$). Significant differences were demonstrated among OS estimates of yG 1 vs. 3 ($p_{\text{OS}}=0.008$) and yG 2 vs. 3 ($p_{\text{OS}}<0.001$) but not between yG 1 vs. 2 ($p_{\text{OS}}=0.185$), respectively. E and F: Subgroup analysis of the cases where BxG and yG were different ($n=99$). Significant differences were found among RFS estimates of yG 2 vs. 3 ($p_{\text{RFS}}=0.022$), but not among yG 1 vs. 2 ($p_{\text{RFS}}=0.213$) and yG 1 vs. 3 ($p_{\text{RFS}}=0.463$). Furthermore, significant differences were found among OS estimates of yG 1 vs. 3 ($p_{\text{OS}}=0.048$), and yG 2 vs. 3 ($p_{\text{OS}}=0.008$) but not between yG 1 vs. 2 ($p_{\text{OS}}=0.555$), respectively.

Table 2
Grade changes per molecular subtypes.

Type	All/ assessable*	Grade changes (%)**	Grade decrease/increase ***
Triple-negative	88/78	15 (19 %)	9 (0.6) / 6 (0.4)
HER2+ (HR-)	26/23	5 (22 %)	4 (0.8)/1(0.2)
HER2+ (HR+)	26/25	17 (68 %)	17 (1.0)/0
HR+ (HER2-)	192/175	61 (35 %)	47 (0.77)/14(0.23)
Unclassified	23/19	1 (5 %)	1 (1.0)/0

HR: hormone receptor, i.e. oestrogen receptor and/or progesterone receptor, HER2: human epidermal growth factor receptor-2

* assessable: having both BxG and yG values;

** percent of assessable cases;

*** proportion of grade changes in parentheses

years (range 26–81 years). Basic clinicopathological characteristics are summarised in Table 1. Most patients had ER-positive breast carcinoma of no special type with BxG 3. Most of them received taxane-based NACT and were treated with mastectomy. Approximately 40 % and 70 % of patients were diagnosed with the ypT1 and ypN1–3 categories, respectively. Regarding yG, the grade 1 category was barely identified; whereas the frequency of the grade 2 and 3 categories was almost similar. The median follow-up was 73 months (range: 3.5–236 months); 86 patients died, and 155 experienced disease recurrence.

As the Kaplan-Meier analyses of Fig. 1 demonstrate (Fig. 1 A-D), several significant differences in RFS and OS estimates were found among different comparisons of BxG and yG categories. In general, the higher grade categories of BxG and yG were related to more unfavourable prognoses regarding RFS and OS estimates, respectively. Of the 320 tumours with both BxG and yG data available, the histological grade did not change in 221 (69 %), and there was an increase in grade in 21 (7 %) and a decrease in 78 (24 %) cases. Table 2 displays the distribution of grade changes according to molecular subtypes of breast cancers. As shown in the table, hormone receptor (ER and/or PR) and HER2-positive tumours had the highest rate of grade change on NACT among classifiable cases (chi-square: 22.26, degrees of freedom: 3, $p<0.0001$), followed by hormone receptor-positive and HER2-negative cases. When these luminal-like tumours were lumped together, their proportion of grade change was still significantly higher than that of triple-negative cancers or HER2-positive hormone receptor-negative cancers (Table 2, chi-square: 11.32, degrees of freedom: 2, $p=0.004$).

In the subgroup analysis of cases with different BxG and yG (Fig. 1 E-F), the higher categories of yG had an adverse impact on both RFS and OS estimates.

Table 3 displays the results of univariable and multivariable Cox proportional hazards models. Concerning OS, in the univariable analysis, significant adverse prognostic parameters were older age, lack of ER and PR expressions, presence of lymphovascular invasion, incomplete resection, and higher ypT, ypN and yG categories. Regarding RFS, in univariable models, poor prognosis was associated with lack of ER and PR expressions, mastectomy, presence of lymphovascular invasion, and higher ypT, ypN, BxG and yG categories.

In multivariable analysis, regarding OS and RFS estimates, significant independent prognosticators were ER status (HR_{OS} : 2.71, 95 % CI: 1.74–4.20, $p_{\text{OS}}<0.001$; HR_{RFS} : 1.72, 95 % CI: 1.14–2.59, $p_{\text{RFS}}=0.009$),

lymphovascular invasion (HR_{OS} : 2.26, 95 % CI: 1.42–3.58, $p_{\text{OS}}=0.001$; HR_{RFS} : 1.84, 95 % CI: 1.27–2.69, $p_{\text{RFS}}<0.001$) and the ypN category (Table 3), respectively.

The univariable subgroup analysis of cases with different BxG and yG categories (data not shown) demonstrated that older age (HR_{OS} : 5.83, 95 % CI: 1.69–20.06, $p_{\text{OS}}=0.005$) and higher yG (HR_{OS} : 5.13 95 % CI: 1.03–25.88 $p_{\text{OS}}=0.045$) category had an adverse impact on prognosis. None of them proved to be independent in multivariable analysis.

The results of the Kaplan Meier subgroup analyses focusing on the prognostic impact of yG and molecular subtypes are displayed in Supplementary Figures 1 and 2. Among hormone receptor (ER and/or PR) positive HER2- breast cancer cases, significant differences were found between the RFS and OS estimates of yG1 vs. yG3 and yG2 vs. yG3 categories (p_{RFS} yG1 vs. yG3=0.021; p_{RFS} yG2 vs. yG3=0.002; p_{OS} yG1 vs. yG3=0.005; p_{OS} yG2 vs. yG3=0.001).

4. Discussion

Histological grade is a well-established traditional prognostic factor of breast cancer either alone [9,12] or in combination with other prognosticators [19–22]. A higher BxG (i.e. G3) is associated with pCR and its effect is independent on the basis of multivariable analysis [23]. Although most of the time, BxG matches the grade established from surgical excision specimens, there is a tendency to underestimate the grade in CNBs. NACT has effects on mitotic activity and nuclear pleomorphism, reducing the first and potentially increasing the second (Fig. 2). Our previous findings suggest that changes in mitotic scores from CNBs to excision specimens (where a reduction was more prevalent after NACT) were significantly different from those seen in the non-NACT setting (where an increase was most common); but no significant differences were demonstrated in nuclear pleomorphism scores [17]. As most breast cancers treated with NACT are of high grade, and reflect subscores 3 for most assessed parameters, aggravation cannot occur in most cases, but a reduction in proliferation can lead to decreased grade in the residual tumour [17]. Whether this change is associated with increased prognosis is not well known.

Although several recommendations prescribe the reporting of histological grade in the post-neoadjuvant setting [18,24,25], a survey among 23 US academic pathologists with breast pathology experience suggested that grade was not reported by 6/23 (26 %); their added comments included the lack of evidence on correlation of yG and prognosis in the post-NACT setting and the drop of mitotic scores with potential senseless downgrading. Those who provided a grade in their reports also made comments and one included that the majority of cases had identical grades but some had a changed grade, with no known evidence (by the responder) of the prognostic impact this could have [26]. Indeed, the prognostic impact of yG has not been widely studied.

The extent of residual disease after NACT has been proven to be of prognostic relevance as reflected by the residual cancer burden (RCB) [27–30], but the addition of Ki67 proliferation index, ER status and yG further improves prognostication [31], suggesting that yG has prognostic importance, too. It should be noted, that the cases analysed in this study have not reached pathological complete regression (pCR), and therefore represent a cohort of patients with worse prognosis than cohorts including pCR patients.

Changes in nuclear atypia after chemotherapy have been described before [32,33], but have not been linked to changes in outcome. On the

Table 3

Results of univariable and multivariable Cox proportional hazards models regarding OS and RFS estimates. (HR: hazard ratio, CI: confidence interval, BxG: grade in the core needle biopsy, ER: oestrogen receptor, PR: progesterone receptor, HER2: human epidermal growth factor receptor-2, NACT: neoadjuvant chemotherapy, yG: grade in the resection specimen after neoadjuvant therapy).

Variable	OS						RFS					
	univariable			multivariable			univariable			multivariable		
	HR	95 %CI	p	HR	95 %CI	p	HR	95 %CI	p	HR	95 %CI	p
Age (years)												
<53	reference						reference					
≥53	1.59	1.034–2.45	0.034				1.23	0.90–1.69	0.188			
BxG												
1	reference						reference					
2	2.90	0.69–12.17	0.144				2.75	1.01–7.61	0.050			
3	3.06	0.74–12.60	0.121				2.86	1.05–7.82	0.040			
ER												
positive	reference			reference			reference			reference		
negative	1.90	1.24–2.90	0.003	2.71	1.74–4.20	<0.001	1.70	1.24–2.34	0.001	1.72	1.14–2.59	0.009
PR												
positive	reference						reference					
negative	1.71	1.12–2.61	0.013				1.57	1.14–2.15	0.005			
HER2												
negative	reference						reference					
positive	1.189	0.90–1.55	0.208				0.97	0.77–1.22	0.81			
NACT												
Taxane	reference						reference					
Anthracyclin	1.05	0.61–1.81	0.864				1.04	0.69–1.57	0.833			
Others	1.61	0.51–5.11	0.421				1.16	0.42–3.14	0.772			
Surgery												
Breast-conserving surgery	reference						reference					
Mastectomy	1.33	0.82–2.11	0.251				1.63	1.13–2.35	0.009			
yG												
1	reference						reference					
2	1.87	0.66–5.27	0.235				1.07	0.57–1.99	0.822			
3	3.39	1.22–9.41	0.019				1.88	1.02–3.45	0.041			
Complete resection												
R0	reference						reference					
R1	1.94	1.13–3.30	0.014				1.34	0.86–2.09	0.192			
Lymphovascular invasion												
Absent	reference			reference			reference			reference		
Present	2.94	1.90–4.51	<0.001	2.26	1.42–3.58	0.001	2.18	1.57–3.02	<0.001	1.84	1.27–2.69	0.001
ypT												
ypT1a	reference						reference					
ypT1b	0.42	0.11–1.59	0.205				0.27	0.07–0.93	0.039			
ypT1c	1.19	0.54–2.59	0.658				1.42	0.77–2.61	0.262			
ypT2	1.17	0.55–2.46	0.676				1.33	0.73–2.38	0.344			
ypT3	1.34	0.58–3.08	0.482				1.61	0.84–3.09	0.150			
ypT4	4.27	1.42–12.83	0.009				4.2	1.59–11.05	0.004			
ypN												
ypN0	reference			reference			reference			reference		
ypNmi	1.11	0.14–8.50	0.919	1.75	0.23–13.39	0.591	0.98	0.23–4.12	0.983	2.26	0.52–9.74	0.274
ypN1a	3.32	1.75–6.28	<0.001	2.95	1.52–5.73	0.001	2.46	1.58–3.84	<0.001	2.36	1.42–3.92	0.001
ypN2	3.50	1.76–6.97	<0.001	3.03	1.46–6.24	0.003	3.06	1.90–4.94	<0.001	3.33	1.93–5.75	<0.001
ypN3	5.11	2.39–10.92	<0.001	4.29	1.88–9.79	0.001	3.16	1.78–5.57	<0.001	3.10	1.61–5.97	0.001

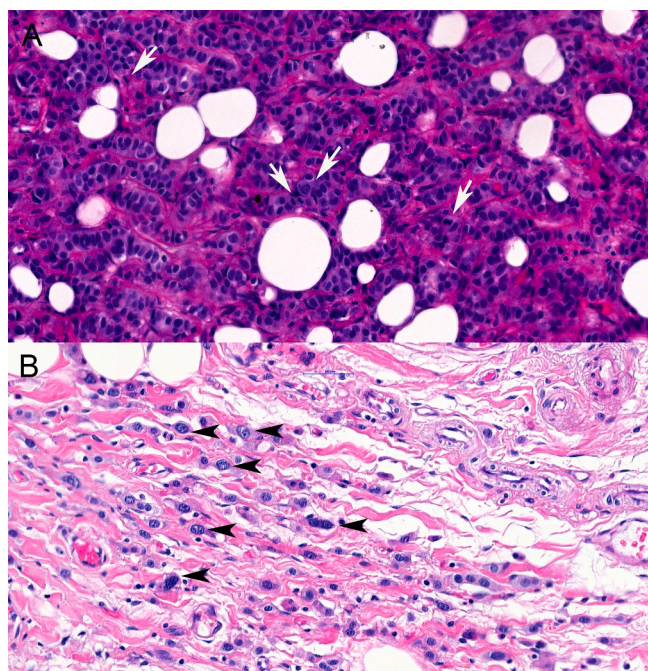


Fig. 2. An example of change in pretreatment grade after neoadjuvant chemotherapy. A: pretreatment BxG3 stemming from tubule formation score 3, nuclear pleomorphism score 2 and mitotic rate score 3. Note mitotic figures highlighted by arrows. B: The patient received NACT consisting of 3 cycles of epirubicin and cyclophosphamide followed by 3 cycles of docetaxel and there was a downgrading occurring, as yG was G2 stemming from tubule formation score 3 (unchanged), nuclear pleomorphism score 3 and mitotic rate score 1. There was cytorreduction, nuclear pleomorphism increased (arrowheads highlight some pleomorphic cells) and there was a significant reduction in mitotic activity. Note, taxanes cause a mitotic arrest, and often this leads to the formation of larger nuclei characterised by polyploidy.

other hand, post-NACT changes in mitotic indices were found to be prognostic [34,35], and this may infer a prognostic value for yG of which this is one of the scored components. Our previous results also point to the fact that whenever there is a change in grade in the pretreatment and posttreatment specimens, this is more likely to be a decrease, and is related to a drop in mitotic activity [17]. In our previous work from a single institution, 24 % (95 % CI: 18–32 %) of breast cancers showed a decrease in grade, which is comparable to this series from 2 institutions, where 24 % (95 % CI: 20–29 %) showed this decrease. An earlier French study documented 34/171 assessable cases (20 %; 95 % CI: 14–27 %) to have a reduction in yG [36]. In the latter study, this improvement in yG was seen more often in responsive tumours and was therefore interpreted as being associated with a benefit from NACT, though survival was not analysed [36].

A previous study of 485 patients treated with anthracycline or anthracycline and taxane-based NACT showed the prognostic impact of both BxG and yG, the impact being greater in the yG setting. The series included 8 % G1, 41.5 % G2 and 50.5 % G3 tumours; with 115 cases (23.7 %) showing pathological complete regression, the remaining 370 residual tumours showed a split of 12 %, 55 % and 33 % between yG1, yG2 and yG3, respectively. The Cox proportional hazards model demonstrated a significant overall and distant disease-free survival disadvantage for yG3 (but not yG1 and yG2) compared to yG0 (reflecting pathological complete regression). However, yG was not assessed separately for cases with residual tumours only [28].

5. Conclusions

Our analysis demonstrates that yG3 is associated with worse RFS and OS than yG1 or yG2, therefore a reduction in grade may be associated

with a better prognosis. This is substantiated by the univariable Cox regression analyses, too. However, this role in prognostication does not seem independent, as significance is lost in the multivariable model. Consistent with scarce reports on the prognostic value of yG, these results point to the appropriateness of recommending the determination of histological grade in the post-NACT setting.

Ethical statements

All procedures were performed in compliance with relevant laws and institutional guidelines. This study was approved by the institutional ethical committee of the Albert Szent-Györgyi Clinical Centre of the University of Szeged (91/2021 SZTE-RKEB), the approval includes a waiver of informed consent for this retrospective study; the privacy rights of human subjects was granted by anonymizing data before analysis, as specified in the approval.

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CRediT authorship contribution statement

Zsuzsanna Kahán: Writing – review & editing, Supervision, Methodology. **Tamás Lantos:** Writing – review & editing, Methodology, Formal analysis. **Gábor Csérni:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ádám Ferenczi:** Writing – review & editing, Investigation. **Tamás Zombori:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Szintia Almási:** Writing – review & editing, Data curation. **Anita Sejbén:** Writing – review & editing, Data curation, Conceptualization. **Renáta Kószó:** Writing – review & editing, Data curation. **Veronika Szelestei:** Writing – review & editing, Data curation.

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AI use. No AI was involved in the writing of this manuscript.

Declaration of Competing Interest

The authors have no conflict of interest. This is also expressed as part of the manuscript.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.prp.2024.155732](https://doi.org/10.1016/j.prp.2024.155732).

Data Availability

There have been no computerized data produced in connection with this study. Anonymized data collected and analysed are stored in an Excel file with Hungarian labels and are available from the

corresponding author or first author on reasonable request.

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Glossary

breast cancer: histological grade, neoadjuvant chemotherapy, post-treatment histological grade, prognosis.