Impact of anaemia on tumor response to neoadjuvant chemotherapy in breast cancer patients

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Background

- Pathological complete response (pCR) to neoadjuvant systemic therapy (NST) in patients with breast cancer (BC) predicts long-term outcomes.
- Anaemia is one of the most common side effects of cytotoxic drugs. Biologically, anaemia induces adaptive responses due to the low intra-tumoral oxygen levels that may be responsible for increase chemotherapy resistance. In literature, data regarding this issue are lacking.

Aim

- To evaluate the influence of anaemia throughout treatment course on tumour shrinkage induced by NST.

Methods

Patients - 317 patients diagnosed with stage I-III BC treated with NST and with available blood tests were included. Patients and tumor characteristics and treatments information were collected. We focused on Haemoglobin (Hb) level (at baseline, at the end of NST, drop in Hb throughout treatment and duration of anaemia) and its correlation with pCR rate. Anaemia was defined as a drop of Hb under the local limit of normal in women (12 mg/dl).

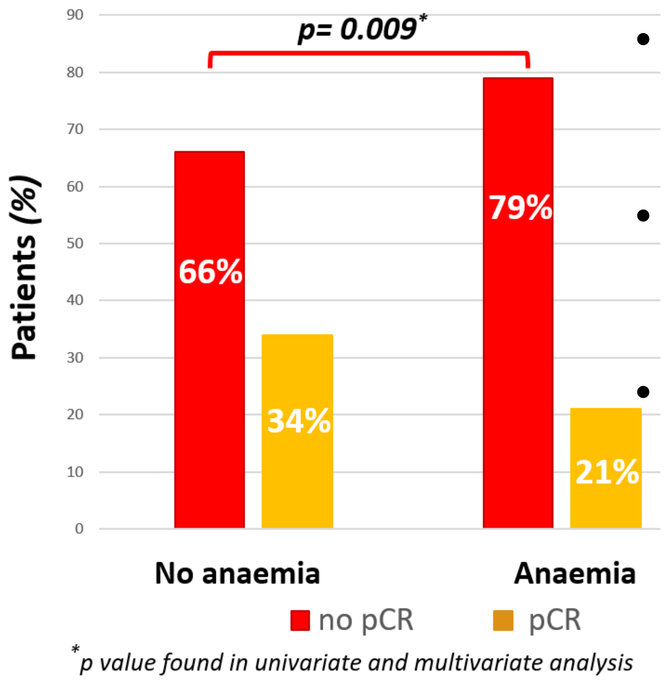
Statistical analysis - Categorical variables were analyzed using chi-square test or Fisher's exact test, continuous variables using t test. Univariate and multivariate analyses were fit to determinate the association between anaemia and pCR rate. A p-value < 0.05 was considered statistically significant; hazard ratio was estimated with 95% of confidence limits.

Patients' characteristics

Characteristics	All patients 317	No Anaemia 126	Anaemia 191	*p-value*
Age at diagnosis, median (range)	49.5 (26.1-80.2)	50.5 (29.1-80.1)	48.3 (26.1-80.2)	*0.905*
Clinical stage				*0.933*
I	6	2 (1.6)	4 (2.1)	
II	235	95 (75.4)	140 (73.3)	
III	76	29 (23.0)	47 (24.6)	
BC subtypes				*0.710*
Hormone receptors positive	124	46 (36.5)	78 (40.8)	
HER2 positive	111	47 (37.3)	64 (33.5)	
Triple negative	82	33 (26.2)	49 (25.7)	
Grade				*0.723*
1-2	37	9 (7.1)	28 (14.7)	
3	280	117 (92.9)	163 (85.3)	
Neoadjuvant chemotherapy				*0.132*
Anthracycline	26	16 (12.7)	10 (5.2)	
Anthracycline + Taxane	259	98 (77.8)	161 (84.3)	
Taxane	9	3 (2.4)	6 (3.1)	
Platinum + Taxane	23	9 (7.1)	14 (7.3)	
Pre-treatment anaemia				*<0.0001*
Absent	286	126 (100)	160 (83.8)	
Present	31	0	31 (16.2)	

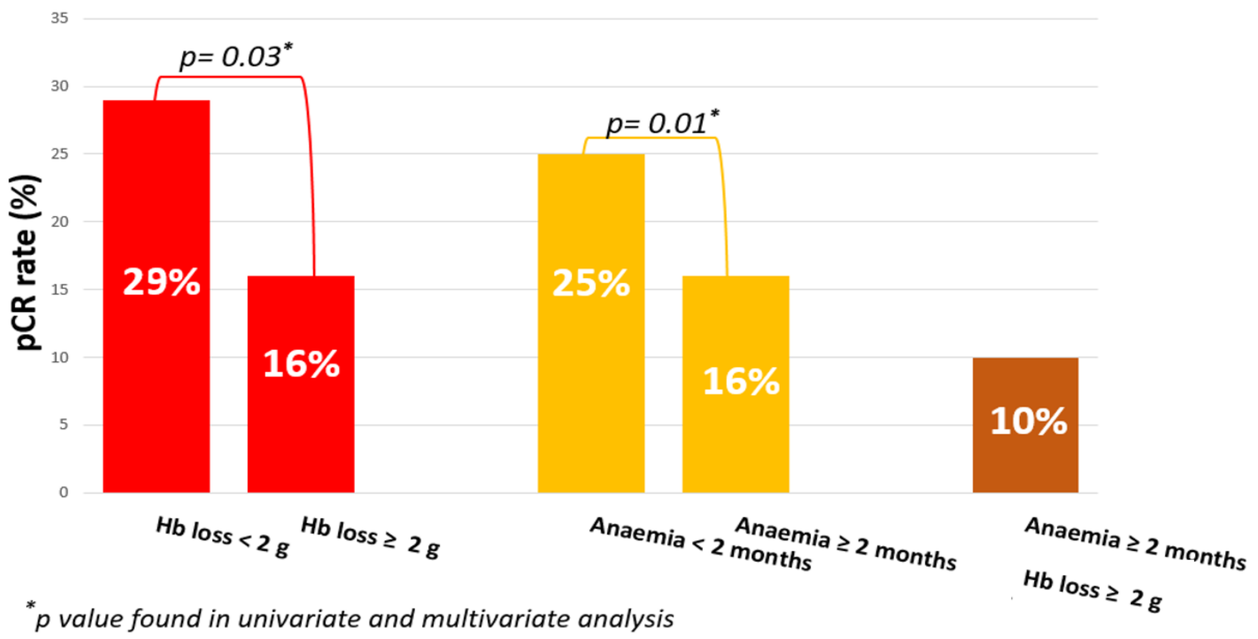
Results

- No difference in Hb levels was observed stratifying patients according to nuclear grade, tumor stage, cancer subtypes and chemotherapy regimens.
- Median baseline Hb was 13.3 g/dl while median Hb level at the end of NST was 10 g/dl.
- 31 patients had pre-treatment anaemia. 60% of patients developed anaemia during NST period.



*p value found in univariate and multivariate analysis

- 83 patients (26%) achieved pCR.
- pCR rate was not influenced by baseline Hb level.
- Anaemia was an independent negative predictive factor for pCR in univariate and multivariate analysis *(p=0.009).*
- In the subgroup of anaemic patients, who had a decrease in Hb ≥ 2 g/dl from baseline or anaemia longer than two months, a lower rate of pCR was observed (16% vs 29%, *p=0.03* and 16% vs 25%, *p=0.01*, respectively). Patients with both these characteristics had the lowest rate of pCR (10%, *p=0.01*).



*p value found in univariate and multivariate analysis

Conclusions

- Anaemia is a negative predictive factor for tumor response in women treated with NST for BC.
- This evidence suggests that anaemia should be improved in order to improve response to NST.