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Prediction of pathologic complete response after neoadjuvant chemotherapy in breast cancer patients according to different biological subtypes and imaging signs

Neoadjuvant chemotherapy (NACT) is a therapeutical approach for breast cancer patients with inoperable, locally advanced, and chemosensitive breast cancer. The main advantages of chemotherapy treatment prior to surgery are the achievement of operability and improved breast conservation by downsizing the tumor and to address systemic disease as early as possible. In order to plan the surgical procedure, reliable breast imaging is necessary. The prediction of pathologic complete response (pCR) is of special surgical interest because it might define the extend of surgery.

Physical examination, mammography, breast ultrasound and breast magnetic resonance imaging may be used to monitor and to evaluate clinical tumor response and therefore to predict pCR.

So far there is only limited data regarding the accuracy to predict pCR by using different examination modalities.

In this monocenter, retrospective, exploratory study, we included invasive breast cancers (the breast is the reference parameter, not the patient), diagnosed histologically by core cut or vacuum biopsy, from January 2006 to December 2011 and which received NACT and a breast magnetic resonance imaging (MRI) after NACT according to clinical routine procedures. A total of 150 invasive breast cancers met these inclusion criteria out of a prospectively followed-up cohort of 250 breast cancers treated by NACT during the same period of time.

We wanted to analyze if there is any reliable possibility to predict pCR in breast cancer patients after NACT according to different breast cancer subtypes (triple negative, HER2

positive and HR+/HER2 negative tumors) in combination with different imaging signs using mammography, breast ultrasound, breast magnetic resonance imaging, and physical examination. Clinical, radiological, surgical and histopathological variables of these cases were assessed in order to identify predictors of pathologic complete response in final pathology.

The univariate logistic regression analysis revealed a number of statistically significant associations between the finding of pCR in the final pathology and the tumor characteristics. The most significant associations were found between the finding of pCR in the final pathology and the absence of clinically palpable suspicious findings after NACT (OR 7.171, P=0.000), the absence of fast enhancement pattern after NACT (OR 5.630, P=0.000), a weak sign on MRI ISO series after NACT (OR 11.860, P=0.000), the absence of suspicious findings on MRI SUB after NACT (OR 25.912, P=0.000), the absence of sonographically detectable suspicious findings after NACT (OR 4.276, P=0.000), the absence of mammographically detectable suspicious findings after NACT (OR 3.804, P=0.001). Further indications for pCR were found for mammographically detectable mass and suspicious microcalcification before chemotherapy whereas after NACT only suspicious microcalcification was present (OR 2.706, P=0.029), a Ki67 status >50% (OR 3.040, P=0.004), a weak sign on MRI ISO series after the second cycle of chemotherapy (OR 5.775, P=0.003), a G3 WHO Grading (OR 2.274, P=0.025), a triple negative receptor status (OR 2.185, P=0.044), the absence of suspicious findings after NACT on MRI SUB and ISO series (OR 5.050, P=0.027) and the absence of a washout enhancement pattern after NACT (OR 5.768, P=0.022).

In multivariate logistic regression analysis a Ki67 status >50 % (OR 5.496, P=0.005) and the absence of suspicious findings on MRI SUB series after NACT (OR 19.267, P<0.001), remained statistically significant independent pCR predictors. The identified predictors indicate an increased possibility for the prediction of pCR in patients with invasive breast cancer.

We further characterized the tumors by radiological presentation before and after NACT and calculated its probability of pCR in combination with different tumor biology. It showed that similar biological tumors have different pCR probabilities depending on imaging findings: e.g. triple negative tumors (TNBC) presented as unifocal mass by MRI achieved higher pCR rates than TNBC with multifocal presentation by MRI (46% vs. 36%).

Moreover (near) complete remission (cCR) assessed by MRI in TNBC is predictive to pCR in 92.9% of cases whereas (near) cCR by MRI in HER2 positive is only 68% and in HR+/HER2-only 27.8%. We showed that the combination of biological subtype and radiological presentation may add valuable information to estimate pCR probabilities.

Our study principally confirmed the existing knowledge about histopathological pCR predictors in invasive breast cancer patients after NACT. To quantify the impact of the pCR predictors, we analysed them univariate and multivariate, included them in a prediction model and evaluated them in combination with different breast cancer subtypes. This prediction model led to better possibility of pCR prediction.

MRI variables are stronger pCR predictors than breast ultrasound-, mammography-, and clinical examination variables. Breast imaging, especially breast MRI is helpful to further improve pCR prediction. Knowledge of tumor biology combined with breast imaging, especially breast MRI, improves pCR prediction. Nevertheless pCR prediction through tumor biology and breast imaging is up to now far from perfect. Therefore pathological evidence is still necessary to prove pCR.