Do We Still Need Estrogen and Progesterone Receptor Measurements for Breast Cancer?

D.		Lüftner
K.		Possinger

Medizinische Klinik und Poliklinik II, Universitätsklinikum Charité, Humboldt-Universität zu Berlin

Dr. med. Diana Lüftner, Medizinische Klinik und Poliklinik II, Universitätsklinikum Charité, Humboldt-Universität zu Berlin, Schumannstraße 20-21, D-10117 Berlin (Germany)

The interpretation of tumor-associated factors is changing with time. This is true even for the commonly used estrogen and progesterone receptor status. We are going to point out that, although having been put aside as an indicator for long-term overall survival in breast cancer, the steroid hormone receptor determination has a predominant role in predicting a patient's chance of response to hormonal treatment and helps to estimate the individual risk of relapse.

At the St. Gallen Consensus Conference in 1995, a stratification of breast cancer patients based on steroid hormone receptor status was recommended [1]. These therapeutic recommendations based on studies throughout the 1980s, which had shown an early advantage in terms of disease-free survival and overall survival for estrogen receptor(ER)-positive patients. After 5 years, however, the difference in the annual hazard rates of relapse between ER-positive and ER-negative patients becomes small with the two Kaplan-Meier-curves tending to converge [2]. This result generally determines the time of observation as an outstanding factor for the quality and outcome of clinical trials on prognostic factors. Furthermore, one must hypothesize that the prognostic relevance of the hormone receptor status may be related to (temporary) benefits from palliative treatment. Recently, the ASCO Expert Panel Team summarized clinical practice guidelines on the interpretation of the hormonal receptor status in breast cancer [3]. They stated that 'in both premenopausal and post-menopausal patients, steroid hormone receptor status may be used to identify patients most likely to benefit from endocrine forms of adjuvant therapy and therapy for recurrent or meta-static disease.' Estrogen and progesterone receptors were classified as 'relatively weak predictors of long-term relapse and breast cancer related mortality rates', and were 'not recommended to be used alone to assign a patient to a prognostic group.'

This exemplary statement relates to the clinical observation that the course of breast cancer varies considerably from patient to patient, making a prominent influence of a single factor improbable. The more, it seems necessary and difficult to identify patient subsets with different risks of disease recurrence and prognosis. While most former results on prognostic factors based on multivariate Cox regression analysis partly supplemented by subgroup analyses, modern mathematical methods allow a new approach. Own results from machine learning techniques (automatical generation of classification trees, optimal arrangement of parameters by neural networks) indicated that for instance in node-negative patients with grade I and grade II tumors, a PR expression < 20% of all cells identifies a patient subpopulation with a > 85% risk to die within 60 months [4]. Tumor size in this context ranked last in the automatical risk

evaluation. On the other hand, node-positive patients with the same constellation of grading (I and II) and PR staining (< 20% of cells) had a low risk to die within 40 months if the tumor size as leading parameter in classification tree was < 2 cm. Thus, in distinct patient subsets prognostic factors have different relative meaning. These results show that computer-derived classification helps to predict a patient's individual prognosis with a confidence > 85%. As in any laboratory data, the determination of steroid hormone receptor positivity is complicated by the multiplicity of assay techniques. Traditionally, the receptor status was evaluated using labelled hormone in binding assays. More recent techniques use immuno(histo)chemical assays even in frozen sections or formalin-fixed, paraffin-embedded tissue [5]. These assays generally correlate well with each other. The intra- and interobserver reliability varies as the cut-off level of receptor positivity in immunohistochemical assays is difficult to define. Nevertheless, this problem can be overcome by adequate quality control.

One must conclude that the favorable courses of receptor-positive patients most probably depend on a combination effect from endocrine therapy and tumor-related biological factors. Although this effect declines with time, the steroid hormone receptor status is a very important information for selecting a particular type of therapy which then might improve a patient's prognosis. Patients with metastatic breast cancer who are steroid hormone receptor-positive have an approximately 50% chance to respond to front-line endocrine therapy. The relationship between tumor-related variables and individual risk evaluation may translate into therapeutic decisions for high-risk patient subsets.

KÄRGER

© 1997 S. Karger GmbH, Freiburg Fax (0761)4520714 <http://www.karger.ch>

References

Goldhirsch A, Wood WC, Senn HJ: International consensus panel on the treatment of primary breast cancer. Eur J Cancer 1995;31A:1754-1759.

Hilsenbeck SG, Ravdin PM, de Moor CA, Osborne CK, Clark GM: Paradoxical decreased in prognostic utility as data sets mature: Time-dependent lack of proportional hazards in prognostic factors in primary breast cancer. Breast Cancer Res Treat 1995;37:35.

ASCO Expert Panel Team: Clinical practice guidelines for the use of tumor markers in breast and colorectal cancer: Report of the American Society of Clinical Oncology Expert Panel. J Clin Oncol 1996;14:2843-2877.

Possinger K, Wischnewsky M, Schönborn I, Lichtenegger W: What can we do with prognostic and predictive factors in breast cancer? European Society for Medical Oncology: 21st ESMO Congress, Vienna Austria, November 1-5, 1996. Educational Book: 3-9.

Andersen J: Determination of estrogen receptors in paraffin-embedded tissue. Acta Oncol 1992;31:611-622.

öeler,

in der Krebsther

Tumoren, bei denen sich die antioxidative Therapie mit Sel

af Ovarialkarzinom (2,6,8,9) Kolontumoi

f Mammakarzinom (2,7,9) f Leberkrebs

:Æ Uterustumoren (8) * Hirtumore

M Prostatakrebs (9) Leukämie (i

M Hodentumor (4) Malignes AJ

Cefasel-

Wirkstoff: Natriumselenit

20 % w/v. 50 ml. 10 Amp. 50 Amp.

D L D D

Anwendungsgebiete: Nachgewiesener Selenmangel, der ernährungsmäßig nicht behoben werden kann auftreten bei Malabsorptions- und Malabsorptionszuständen (Verdauungs- und Ver-

Mangelernährung (z.B. totale parenterale Ernährung). Zusammensetzung: Ampullen: 1

Arzneilich wirksamer Bestandteil: Natriumselenit 5 % 0,333 mg (entsprechend 100 µg

Natriumchlorid, Wasser für Injektionszwecke; Tropfen: 1 g (=1,02 ml) enth.: Arzneilich wirksa:

5 H₂O 0,1 mg. Sonstiger Bestandteil: Ethanol 18,5 % V/V 999,9 mg; Tabletten: 1 Table

Bestandteil: Natriumselenit 5 % 0,333 mg (entsprechend 100 µg Selen). Sons

Magnesiumstearat. Gegenanzeigen: Selenintoxikationen (Selenvergiftungen). Zusätzlich auch in

der Vorgeschichte; nicht anwenden bei Kindern unter 12 Jahren. Nebenwirkungen Gebrauch

bisher nicht bekannt. Wechselwirkung mit anderen Mitteln: Die gleichzeitige unterbleiben, da

dann eine Ausfällung von elementarem Selen nicht auszuschließen ist. Die Medien nicht löslich

und nicht bioverfügbar. Ampullen: Bei parenteraler Verabreichung als Zu sichergestellt sein, daß

keine unspezifischen Ausfällungen auftreten. Es ist darauf zu achten, daß keine

Mischung mit Reduktionsmitteln wie z.B. Vitamin C erfolgt, da dann ein Selen nicht

auszuschließen ist. Warnhinweis: Cefasel® forte Tropfen enthält Verschreibungspflichtig

Erstattungsfähig! Cefak Arzneimittel ■ Postfach 13 60 ■ 87403 Kempt

Quelle: (1) Yu, S.Y. et al, Biol. Trace Elem. Res. 29, 289-294 (1991) (2) Wischnik, A. et al. (3)

Rheinhold, U. et al, Acta Derm Venerol (Stockh) 69, 132-136 (1989) (4) Vernie, L.N. et al. (5)

Philipov und Tzatchev, Zent. bl. Neurochirur. 49, 344-347 (1988) (6) Das, N.P. und C. Research

10, 215-222 (1986) (7) Fishbein, L, Arch. Geschwulstforsch. 56, 1, 53-78 (1986) Dao, H. ed.,

Eicosanoids and Cancer. Raven Press, NY, 263 (1984) (9) Schrauzer et al 23-24 (1977)

Do We still Need Steroid Receptor Measurements for Breast Cancer?

HI

Der Partner in der Selentherapie