Strahlenther Onkol 2012 · 188:782–787
DOI 10.1007/s00066-012-0118-z
Received: 20 January 2012
Accepted: 23 March 2012
Published online: 1. August 2012

A.-C. Müller[1] · C. Gani[1] · H.M.E. Rehm[1] · F. Eckert[1] · M. Bamberg[1] · T. Hehr[2] · M. Weinmann[1]

[1] Department of Radiooncology, Eberhard-Karls-University Tübingen

[2] Department of Radiooncology, Marienhospital Stuttgart

Are there biologic differences between male and female breast cancer explaining inferior outcome of men despite equal stage and treatment?!

Breast cancer is the most common cancer in women with a lifetime probability of one of seven according to Surveillance, Epidemiology, and End Results (SEER) program [13]. Due to the overwhelming relevance and frequency of this disease, current treatment of breast cancer in women is well defined and optimized. A comprehensive framework of guidelines for diagnosis and treatment exists for this entity [3, 12, 15, 31, 33], which is based on a large body of data from randomized, controlled trials. Beneficial and adverse effects of standard treatment are well characterized [10, 35, 36]. In contrast, male breast cancer is a rare and often overlooked disease which represents <1% of all breast cancer cases [1]. Despite possible differences in pathogenesis, biology and genetics between both sexes, the treatment strategies for male breast cancer have been extrapolated from the large body of knowledge for female breast cancer [7, 37].

However, recent studies using large cancer registries or multi-institutional databases have only marginally increased knowledge about breast cancer in men. It has been assumed that male breast cancer carried a worse prognosis compared to breast cancer in women [1, 9]. These differences in prognosis have mainly been attributed to delays in diagnosis, higher stages and later ages associated with increased co-morbidity rather than to differences in tumor biology or to systematic differences in patterns of care between both groups [2, 9, 14].

Therefore, the aim of the present study was to analyze disease characteristics and treatment strategies of male breast cancer in a single institution over the last 25 years. In this regard, prognosis in terms of overall survival (OS), disease-free survival (DFS), and distant metastasis-free survival (DMFS) as well as adverse effects of treatment were evaluated. Furthermore, an estimated outcome was calculated for a "virtually" matched pair cohort of women by the Adjuvant!Online® 8.0 algorithm and compared to outcome of men in this series with no, same, and optimal adjuvant treatment from current point of view.

Patients and methods

Patient characteristics

To be included in this retrospective analysis, the following conditions had to be fulfilled: all men had to suffer from invasive breast cancer curatively treated with (modified radical) mastectomy and postoperative radiotherapy. Patients presenting with metastases, recurrences or second cancers were excluded. Men fulfilling these criteria were identified by the departmental database. Therefore, 21 out of an initial cohort of 61 patients were excluded due to the following reasons: palliative treatment (n=9), no postoperative radiotherapy (n=7), recurrence (n=1) or second cancers (n=4). After discussing the intended analysis, the institutional review board (ethics committee of our institution) had no objections (No. 395/2011A). Thus, 40 men—treated between 1982 and 2007—fulfilled the conditions and were analyzed. The median age of the cohort was 62 years (range 35–80 years). Tumor stages of all patients were converted to the seventh edition of AJCC classification [6] for easier comparison of prognosis. According to tumor and nodal stages most patients were classified as AJCC stage II and IIIb. Details of patients' characteristics considering tumor and treatment-related factors are displayed in Tab. 1.

Surgery

A total of 37 patients (92.5%) were treated with a modified radical mastectomy, the remaining 3 patients underwent a simple mastectomy. No breast conserving surgeries were performed. Mastectomy provided clear margins in almost all patients (n=38). Only 2 patients were classified having microscopic residual tumor (R1). Thirty-seven men (92.5%) received an axillary lymphadenectomy and 3 patients a sentinel lymphadenectomy (7.5%). A mean of 13 lymph nodes (range 1–33) were removed, while four (range 0–24) were affected. Of these patients, 65% (n=26) presented with pathologically confirmed positive lymph nodes (**Tab. 1**).

Tab. 1 Patients' characteristics

Characteristic	Value	Percentage
Patients (n)	40	100
Age (years)		
Range	35–80	
Median	63	
pT stage (n)		
1	11	27.5
2	18	45.0
3	0	0.0
4	11	27.5
pN status (n)		
0	14	35.0
1	16	40.0
2	5	12.5
3	5	12.5
pR status (n)		
R0	38	95.0
R1	2	5.0
UICC stage		
0	0	0.0
I	5	12.5
IIA	11	27.5
IIB	10	25.0
IIIA	2	5.0
IIIB	12	30.0
IIIC	0	0.0
IV	0	0.0
Grading (n)		
I	0	0.0
II	23	57.5
III	12	30.0
Unknown	5	12.5
Hormone receptor expression (n)		
ER-positive	26	65.0
PR-positive	24	60.0
Negative	7	17.5
Unknown	7	17.5
cERB status (n)		
Positive	6	15.0
Negative	8	20.0
Unknown	26	65.0
Surgery of primary breast cancer (n)		
Simple mastectomy	3	7.5
Modified radical mastectomy	37	92.5
Adjuvant radiation treatment (n)	40	100.0
Median total chest wall dose in Gy (range)	50 (45–66.4)	
Lymph node irradiation to 50 Gy (n)	22	55.0
Supra-/infraclavicular fossa	22	55.0
Axillary nodes	9	22.5
Parasternal nodes	19	47.5
Adjuvant systemic treatment (n)		
Chemotherapy	9	22.5
Hormonal treatment	22	55.0

Radiotherapy

Postoperative radiotherapy to the chest wall was fractionated with single doses of 1.8–2.5 Gy to a median dose of 50 Gy (range 45–50.4 Gy) either with tangential photon fields (n=19) or by an electron beam rotational technique (n=21) as described elsewhere [19]. Eleven patients (27.5%) received an additional boost to the tumor region of median 10 Gy (range 5–16 Gy). In 22 men (55%) regional lymphatics were included to a total dose of 50 Gy (Tab. 1). Supra-/infraclavicular fossa (n=22) was treated by an anterior oblique field. Axillary nodes (n=8) were included in the supra-/infraclavicular field or tangential fields. Additional treatment of parasternal nodes (n=19) was performed using the mixed beam technique by extension of tangential fields and subsequently irradiated by a smaller tangential field plus a separate anterior electron field. Acute toxicity (within 90 days) and late toxicity after 90 days was assessed using RTOG criteria [4].

Systemic treatment

Further adjuvant treatment consisted of chemotherapy in 22.5% of patients (n=9). Three different schedules were administered: CMF (cyclophosphamide, methotrexate, 5-fluoruracil), (F)EC (5-fluoruracil, epirubicin, cisplatinum), TAC (docetaxel, adriamycin, cyclophosphamide). Adjuvant antihormonal therapy was given in 55% (n=22) of men and mainly performed with tamoxifen alone (n=17). A few patients received aromatase inhibitors (n=4) or a switch from tamoxifen to an aromatase inhibitor (n=1).

Generating virtual matched pairs by Adjuvant!Online® 8.0

To compare outcome of men with that of women, an online calculator for overall survival of female breast cancer was employed (http://www.adjuvantonline.com). This evidence-based calculator was developed to evaluate benefits of receiving adjuvant therapy, i.e., chemotherapy, antihormonal therapy, or both. The origins of Adjuvant!Online® 8.0 were San Antonio Data Base, SEER database, and clin-

Abstract · Zusammenfassung

Strahlenther Onkol 2012 · 188:782–787 DOI 10.1007/s00066-012-0118-z

A.-C. Müller · C. Gani · H.M.E. Rehm · F. Eckert · M. Bamberg · T. Hehr · M. Weinmann

Are there biologic differences between male and female breast cancer explaining inferior outcome of men despite equal stage and treatment?!

Abstract

Background. Reasons for inferior outcome of male compared to female breast cancer are still under debate. Therefore, we retrospectively analyzed male breast cancer cases to figure out possible treatment- and gender-related differences.

Patients and methods. A total of 40 men (median age 62 years) were curatively treated with mastectomy and postoperative radiotherapy from 1982–2007. They presented predominantly in stages II and IIIb. Postoperative radiotherapy was applied with doses of 1.8–2.5 Gy to a median of 50 Gy including regional lymphatics in 22 patients. Adjuvant systemic treatment consisted of chemotherapy (22.5%) and antihormonal treatment (55%). For reasons of comparison, we estimated outcome of a virtual female matched cohort for no/equal to men/optimal adjuvant treatment with the Adjuvant!Online® 8.0 algorithm.

Results. After a median follow-up of 47 months, the estimated 5-year local control rate was 97%, disease-free and distant metastasis-free survival rates reached 79% and 82%, respectively. With update of survival data by tumor registry, mean overall survival reached 120 months with 5- and 10-year overall survival rates of 66% and 43%, respectively. Predominant prognostic factor was T-stage for overall survival (T1/2 vs. T4: >80% vs. 30%). The generated virtual matched cohorts of women with equal characteristics reached superior 10-year-overall survival for no/equal to men/optimal adjuvant treatment with 55/59/68%.

Conclusion. Compared to historical and virtual matched cohorts of women, male breast cancer patients had inferior outcome despite of equal stage and treatment which indicates that biological differences (of tumor or population) may contribute to worse prognosis.

Keywords

Male breast cancer · Radiotherapy · Mastectomy · Adjuvant treatment

Bestehen biologische Unterschiede zwischen männlichem und weiblichem Brustkrebs, die das schlechtere Überleben von Männern trotz gleichen Stadiums und gleicher Behandlung erklären?!

Zusammenfassung

Hintergrund. Die Ursachen für eine schlechtere Prognose von Männern mit Brustkrebs verglichen mit Frauen sind noch nicht abschließend geklärt. Wir analysierten daher retrospektiv männliche Brustkrebsfälle hinsichtlich möglicher behandlungs- und geschlechtsbedingter Unterschiede.

Patienten und Methoden. Von 1982 bis 2007 wurden 40 Patienten (medianes Alter 62 Jahre) hauptsächlich im Stadium II und IIIb mit Mastektomie und postoperativer Bestrahlung (Einzeldosis 1,8–2,5 Gy, Gesamtdosis 50 Gy) kurativ behandelt. Die Lymphabflusswege wurden bei 22 Patienten eingeschlossen. Die adjuvante Systemtherapie bestand aus Chemotherapie (22,5%) und/oder antihormoneller Therapie (55%). Zur besseren Vergleichbarkeit berechneten wir das Überleben für eine virtuelle weibliche „Matched-pair"-Gruppe mit keiner/gleicher/optimaler adjuvanter Therapie mit dem Programm Adjuvant!Online® 8.0.

Ergebnisse. Nach einem medianen Nachbeobachtungszeitraum von 47 Monaten erreichte die geschätzte 5-Jahres-Lokalkontrolle 97%, das krankheitsfreie Überleben 79% und das metastasenfreie Überleben 82%. Unter Hinzunahme der Überlebensdaten aus dem Tumorregister erreichte das mittlere Überleben 120 Monate und die geschätzte 5-/10-Jahres-Überlebensrate 66% bzw. 43%. Prädominanter Prognosefaktor für das Gesamtüberleben war das T-Stadium (T1/2 vs. T4: >80% vs. 30%). Die mit Adjuvant!Online® 8.0 ermittelten 10-Jahres-Überlebensraten für Frauen mit gleicher Charakteristik und keiner/gleicher/optimaler adjuvanter Behandlung lagen über den Raten der Männer mit 55/59/68%.

Schlussfolgerung. Verglichen mit historischen und virtuell gematchten Kontrollen mit gleichen Tumorstadien und Behandlungen scheint das Überleben von Männern mit Brustkrebs trotzdem schlechter zu sein. Möglicherweise erklären biologische Unterschiede (von Tumor oder Population) diese Diskrepanz.

Schlüsselwörter

Männlicher Brustkrebs · Radiotherapie · Mastektomie · Adjuvante Therapie

ical trials as described elsewhere [32]. Matched pair survival data for female breast cancer patients were generated according to patient characteristics defined by age, receptor status, grading, size of tumor, and number of positive nodes. The 10-year overall survival was calculated for no/same like men/optimal adjuvant treatment.

Statistical analyses

OS, DFS, and DMFS were calculated using the Kaplan–Meier method from time of diagnosis [23]. Local failure was defined as any recurrence of tumor in the ipsilateral chest wall or in mastectomy scars. Recurrence at any other site was considered as distant failure (DMFS). Any event, i.e., local or distant failure, defined DFS.

Actuarial curves were compared by the two-tailed log-rank test. Statistical comparison of female matched pair survival data was performed with the paired t-test. A p value ≤ 0.05 was considered significant for both tests. The statistical analysis was done with the software package PASW 18.0 (SPSS Inc., Chicago, IL, USA).

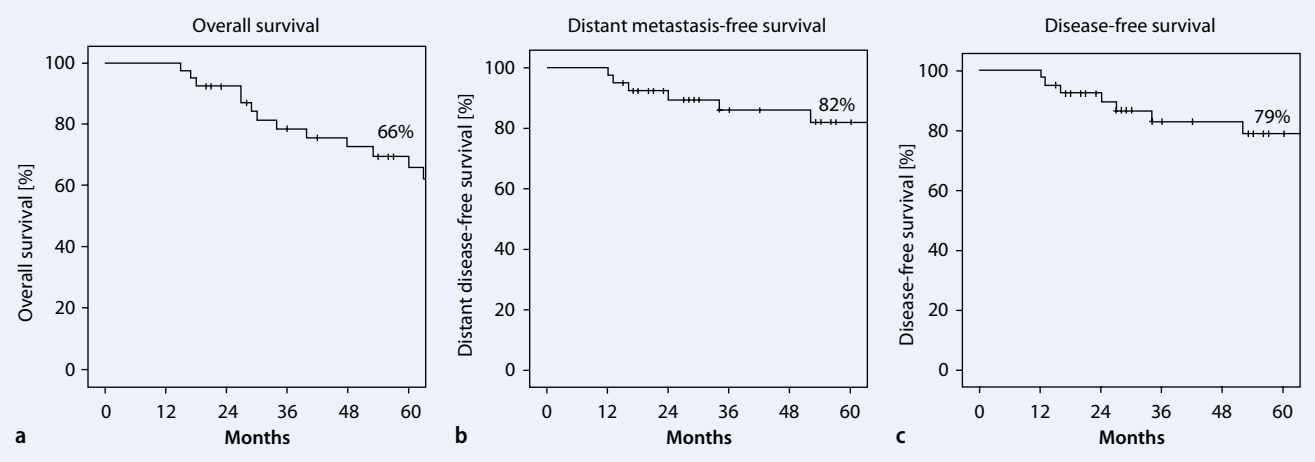

Fig. 1 ▲ Survival parameters. **a** Overall survival, **b** distant metastasis-free survival, and **c** disease-free survival were estimated using Kaplan–Meier method after a median follow-up of 47 months. Data on overall survival were updated with the tumor registry leading to a mean overall survival of 120 months (median 84 months) and an estimated 10-year overall survival of 43%

Results

Acute and late radiation toxicity

Radiation treatment was completed as planned in all patients. Higher graded acute toxicities did not occur. Acute radiation dermatitis of grade 1 and 2 was detected in 32.5% (n=13) and 45.0% (n=18) patients, respectively. Nine patients developed no acute side effects. Esophagitis of grade 1 was detected in 2 men receiving radiotherapy of supraclavicular fossa. After a median follow-up of 47 months no late toxicity of G3+ was observed. Radiation atrophy and moderate teleangiectasia were detected in 30.0% (n=12) and 7.5% (n=3) of patients, respectively. Radiation fibrosis of grade 1 was determined in 5% (n=2) of men.

Local control and survival figures

Local failure occurred in 1 patient resulting in an estimated 5-year local control rate of 96.2%. Local recurrence was treated by excision and adjuvant tamoxifen leading to no further evidence of disease in this man. At last follow-up, 8 patients experienced distant metastasis with predominance of bone (n=7). In 3 patients, bony lesions were combined with lung or liver metastases. One additional man experienced lung metastases only.

The estimated OS, DMFS, and DFS at 5 years were 66%, 82%, and 79%, respectively (**Fig. 1**). The median follow-up of 47 months applies for toxicity, information on recurrences and metastases. Information on overall survival was updated by the tumor registry of our Comprehensive Cancer Center. Therefore, mean overall survival reached 120 months with a median of 84 months. Estimated 10-year overall survival was 43%.

Subanalyses of factors potentially influencing overall survival (OS)

To further investigate relevance of tumor- and treatment-related factors on OS the following subanalyses were performed. Impact of T-stage on OS was significant. Estimated 5-year OS for T1 and T2 were 81.8% and 80.4%, respectively, versus 30.3% for T4 stages (**Fig. 2a**). Presence of node-negative disease resulted in an estimated 5-year OS of 68.8% vs. 63.1% for node-positive breast cancer (p=0.08; **Fig. 2b**). Given chemotherapy was associated with 100% 5-year OS compared to 58.2% without chemotherapy reaching a trend with p=0.06 (**Fig. 2c**). In contrast, administration of antihormonal treatment had no impact on OS with p=0.516 (**Fig. 2d**).

Matched pairs by Adjuvant!Online® 8.0

To evaluate, whether male and female breast cancer had a similar outcome, matched pairs of males with virtual females were generated. The 10-year OS was calculated for the 40 male characteristics (defined by five items as described above) of this series with Adjuvant!Online® 8.0 in combination with two variables, i.e., adjuvant chemotherapy and/or antihormonal therapy. We used three constellations of both variables: no adjuvant systemic treatment, treatment as performed in this series, and optimal adjuvant treatment. For each characteristic (n=40) of this series, three rates depending on adjuvant therapy were generated. Mean 10-year OS for virtual women without adjuvant treatment reached 55%, for virtual women with a treatment as performed in this male cohort 59% and for virtual women with optimal treatment 68%. Comparison of these OS rates by paired t-test was significant (p<0.001). Regarding the 10-year OS of our cohort with estimated 43%, same postulated treatment in women according to Adjuvant!Online® 8.0 resulted in a 16% better OS.

Discussion

The outcome of the present male cohort of breast cancer patients in terms of OS was inferior to women as expected from some literature data [14] and confirmed by our matched pairs with virtual women. The main reason for treatment failure was distant metastases. The main prognostic factor for DFS and OS was T-stage. Unlike in

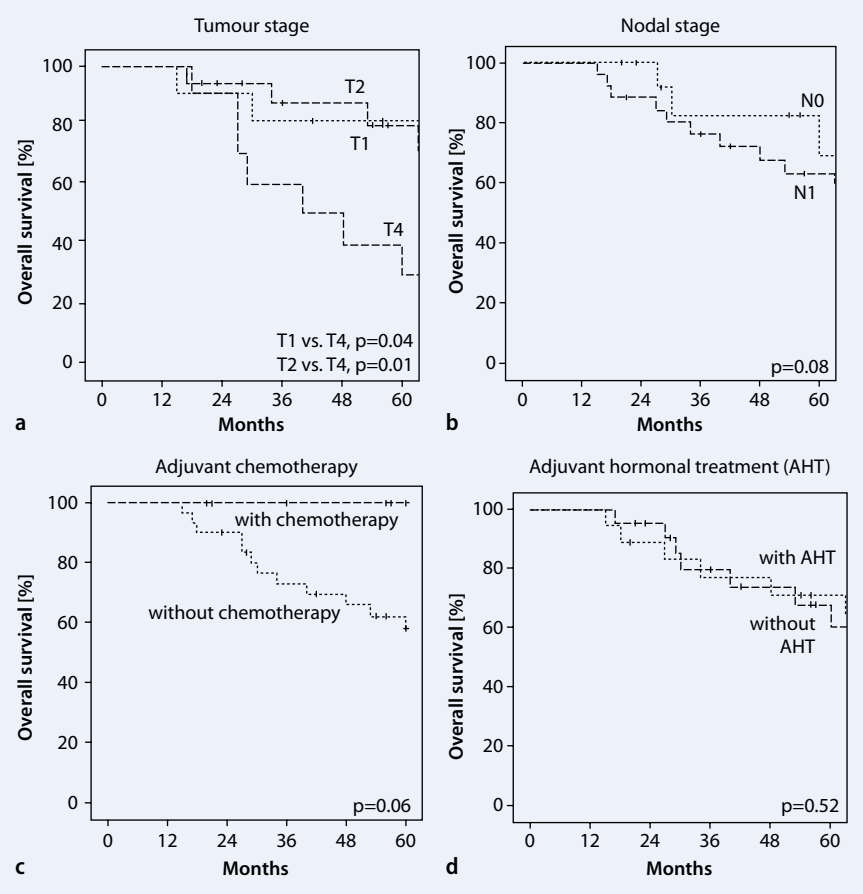

Fig. 2 ▲ Relevance of tumor- and treatment-related factors on overall survival (*OS*). Five-year OS rates were estimated using Kaplan–Meier method. **a** Lower T-stage was associated with superior survival (T1: 81.8%, T2: 80.4% vs. T4:30.3%; p<0.05), while **b** node-negativity reached only a trend to better outcome (pN0: 68.8% vs. pN+: 63.1%; p=0.08). **c** Regarding treatment related factors, there was a trend to improved overall survival at 5 years for adjuvant chemotherapy (100% vs. 58.2%; p=0.06). **d** Adjuvant antihormonal treatment (AHT) had no impact on overall survival with 60.4% vs. 71.1% (p=0.516)

larger series [1, 5, 11], the effect of T-stage was much more pronounced than the effect of nodal status. We only observed a trend toward inferior outcome for node-positive men. However, lower impact of nodal stage might also be caused by low number (35%) of node-negative men. Possibly due to anatomical differences in men, larger tumors tend to metastasize more frequently directly by a hematogenic pathway [22]. The relevance of control of micrometastases is further emphasized by the fact that given chemotherapy was a strong positive prognosticator in this group.

This historical cohort was definitely undertreated when current state-of-the-art adjuvant treatment for breast cancer is used as a measure for optimal therapy [3, 12, 15, 31, 33]. But the 25% inferior survival of men (43% versus 68%) in this series compared to women with optimal treatment in randomized trials according to the Adjuvant!Online® 8.0 algorithm might not only be attributable to suboptimal adjuvant treatment as further indicated by the fact that there was a difference of 12% in survival between the sexes with same adjuvant treatment. However, this comparison has to be used with caution since direct statistical comparison of real matched pairs was not available. Furthermore, all adjuvant assessment tools for prognosis including Adjuvant!Online®, the St Gallen Consensus, Oncotype DX®, and MammaPrint® have limitations [29]. Consideration of biological markers like Her2-neu, Mitotic Index, and Ki67 were not possible leading to an overestimation of survival in patients <40 years old [18]. But, only 1 patient was <40 years in this series, limiting the possible relevance of this confounder. Another limitation of the comparison is the given radiotherapy in all male patients, while radiotherapy is not taken into consideration in Adjuvant!Online®. However, as all of our male patients had standard indication for radiotherapy, treatment without radiation in the respective female groups would have to be rated as undertreatment and would suggest a worse outcome of the female comparison. As Adjuvant!Online® comprises randomized data published from the early 1970s [16, 17, 32] to the present, the time period of this study is completely matched compensating for potential influence of historical radiation treatment techniques which could be associated with increased cardiotoxicity.

A population-based comparison of SEER data also demonstrated superior survival of 10% for women with breast cancer compared to men [1]. These SEER data may reflect differences in pattern of care between men and women, but it may also point to systematic and relevant biological differences between both groups. A recently published matched pair analysis from Sweden further corroborates this theory with a 14% inferior survival in men [28]. But, radiation treatment was significantly less often delivered in male patients. Therefore, the current series clearly substantiates that even with maximal local treatment (all patients received mastectomy and radiotherapy) outcome of men with breast cancer is inferior compared to virtual matched women treated in randomized trials. We first used the evidence-based calculator Adjuvant!Online® 8.0 for comparison of survival of men and women with breast cancer. Even considering the known limitations of such a tool, the fact that calculated OS of women of same stage and treatment was clearly superior compared to men and the predominant influence of T-stage point to more aggressive tumor biology or other biological differences between the two groups.

Recent studies documented improved survival rates over recent decades for both male and female breast cancer, but progress for men has lagged behind that for women [1]. In this series, the same effect was seen mainly attributable to appli-

cation of chemotherapy which predominately was administered in the last decade. An additional reason for slower increase of survival figures or different biological features in men could be a limited benefit from antihormonal treatment [8, 30]. Thus, it is uncertain whether hormone receptor positivity has the same prognostic implication in male as in the female disease [27, 37].

In female breast cancer, durable local control is the precondition for long-term survival and leads to a reduction of distant metastases [34]. Excellent local control in men was achieved in this intermediate to high-risk population comparable to other trials of both genders [25, 26, 38]. Moreover, local treatment was as well tolerated as in women [1, 20, 21]. Therefore, intensification of systemic treatment is a viable option to further increase cure rates for men.

Conclusion

Compared to historical and virtual matched cohorts of women our male breast cancer patients had inferior outcome suggesting that not only undertreatment, but also biological differences either of tumor or of population may contribute to the worse prognosis. This assumption is supported by the predominant impact of T-stage on prognosis, while nodal stage did influence outcome to a much lesser extent and the limited effect of adjuvant endocrine therapy. It is unclear whether inferior prognosis could be completely compensated by the indicated more frequent use of chemotherapy. Therefore, further treatment- and outcome-related investigations including multi-institutional clinical trials are necessary [24].

Corresponding address

Dr. C. Gani
Department of Radiooncology,
Eberhard-Karls-University Tübingen
Hoppe-Seyler-Str. 3, 72076 Tübingen
Germany
cihan.gani@med.uni-tuebingen.de

Conflict of interest. On behalf of all authors, the corresponding author states that there are no conflicts of interest.

References

1. Anderson WF, Jatoi I, Tse J et al (2010) Male breast cancer: a population-based comparison with female breast cancer. J Clin Oncol 28:232–239
2. Andrykowski MA (2011) Physical and mental health status and health behaviors in male breast cancer survivors: a national, population-based, case-control study. Psychooncology doi: 10.1002/pon.2001
3. Carlson RW, Hudis CA, Pritchard KI (2006) Adjuvant endocrine therapy in hormone receptor-positive postmenopausal breast cancer: evolution of NCCN, ASCO, and St Gallen recommendations. J Natl Compr Canc Netw 4:971–979
4. Cox JD, Stetz J, Pajak TF (1995) Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 31:1341–1346
5. Cutuli B, Le-Nir CC, Serin D et al (2010) Male breast cancer. Evolution of treatment and prognostic factors. Analysis of 489 cases. Crit Rev Oncol Hematol 73:246–254
6. Edge S, Byrd D, Compton C (2009) American Joint Committee on Cancer: AJCC cancer staging manual, 7th edn, Springer, New York
7. Erlichman C, Murphy KC, Elhakim T (1984) Male breast cancer: a 13-year review of 89 patients. J Clin Oncol 2:903–909
8. Everson RB, Lippman ME, Thompson EB et al (1980) Clinical correlations of steroid receptors and male breast cancer. Cancer Res 40:991–997
9. Fentiman IS, Fourquet A, Hortobagyi GN (2006) Male breast cancer. Lancet 367:595–604
10. Fisher J, Scott C, Stevens R et al (2000) Randomized phase III study comparing best supportive care to biafine as a prophylactic agent for radiation-induced skin toxicity for women undergoing breast irradiation: Radiation Therapy Oncology Group (RTOG) 97–13. Int J Radiat Oncol Biol Phys 48:1307–1310
11. Giordano SH, Cohen DS, Buzdar AU et al (2004) Breast carcinoma in men: a population-based study. Cancer 101:51–57
12. Glen H, Jones RJ (2003) Eight international conference: primary therapy of early breast cancer, St Gallen, Switzerland, March 12–15 2003. Breast Cancer Res 5:198–201
13. Gloeckler Ries LA, Reichman ME, Lewis DR et al (2003) Cancer survival and incidence from the Surveillance, Epidemiology, and End Results (SEER) program. Oncologist 8:541–552
14. Gnerlich JL, Deshpande AD, Jeffe DB et al (2011) Poorer survival outcomes for male breast cancer compared with female breast cancer may be attributable to instage migration. Ann Surg Oncol 18:1837–1844
15. Goldhirsch A, Ingle JN, Gelber RD et al (2009) Thresholds for therapies: highlights of the St Gallen International Expert Consensus on the primary therapy of early breast cancer 2009. Ann Oncol 20:1319–1329
16. Early Breast Cancer Trialists' Collaborative Group (1998) Polychemotherapy for early breast cancer: an overview of the randomised trials. Lancet 352:930–942
17. Early Breast Cancer Trialists' Collaborative Group (1998) Tamoxifen for early breast cancer: an overview of the randomised trials. Lancet 351:1451–1467
18. Hajage D, Rycke Y de, Bollet M et al (2011) External validation of Adjuvant! Online breast cancer prognosis tool. Prioritising recommendations for improvement. PLoS One 6:e27446 [Epub ahead of print]
19. Hehr T, Classen J, Huth M et al (2004) Postmastectomy radiotherapy of the chest wall. Comparison of electron-rotation technique and common tangential photon fields. Strahlenther Onkol 180:629–636
20. Hemati S, Asnaashari O, Sarvizadeh M et al (2012) Topical silver sulfadiazine for the prevention of acute dermatitis during irradiation for breast cancer. Support Care Cancer 20:1614–1618
21. Jensen JM, Gau T, Schultze J et al (2011) Treatment of acute radiodermatitis with an oil-in-water emulsion following radiation therapy for breast cancer: a controlled, randomized trial. Strahlenther Onkol 187:378–384
22. Joshi MG, Lee AK, Loda M et al (1996) Male breast carcinoma: an evaluation of prognostic factors contributing to a poorer outcome. Cancer 77:490–498
23. Kaplan EL, Meier P (1958) Nonparametric estimation from incomplete observations. JASA 53:457–481
24. Korde LA, Zujewski JA, Kamin L et al (2010) Multidisciplinary meeting on male breast cancer: summary and research recommendations. J Clin Oncol 28:2114–2122
25. Liukkonen S, Saarto T, Maenpaa H et al (2010) Male breast cancer: a survey at the Helsinki University Central Hospital during 1981–2006. Acta Oncol 49:322–327
26. Marchal F, Salou M, Marchal C et al (2009) Men with breast cancer have same disease-specific and event-free survival as women. Ann Surg Oncol 16:972–978
27. Nahleh ZA (2006) Hormonal therapy for male breast cancer: a different approach for a different disease. Cancer Treat Rev 32:101–105
28. Nilsson C, Holmqvist M, Bergkvist L et al (2011) Similarities and differences in the characteristics and primary treatment of breast cancer in men and women—a population based study (Sweden). Acta Oncol 50:1083–1088
29. Oakman C, Santarpia L, Di Leo A (2010) Breast cancer assessment tools and optimizing adjuvant therapy. Nat Rev Clin Oncol 7:725–732
30. Pich A, Margaria E, Chiusa L et al (1999) Androgen receptor expression in male breast carcinoma: lack of clinicopathological association. Br J Cancer 79:959–964
31. Rabaglio M, Aebi S, Castiglione-Gertsch M (2007) Controversies of adjuvant endocrine treatment for breast cancer and recommendations of the 2007 St Gallen conference. Lancet Oncol 8:940–949
32. Ravdin PM, Siminoff LA, Davis GJ et al (2001) Computer program to assist in making decisions about adjuvant therapy for women with early breast cancer. J Clin Oncol 19:980–991
33. Sautter-Bihl ML, Budach W, Dunst J et al (2007) DEGRO practical guidelines for radiotherapy of breast cancer I: breast-conserving therapy. Strahlenther Onkol 183:661–666
34. Sautter-Bihl ML, Sauer R (2007) One more change of paradigm in breast cancer treatment. Postmastectomy radiotherapy for patients with one to three lymph node metastases? Strahlenther Onkol 183:357–359
35. Schmidt ME, Chang-Claude J, Vrieling A et al (2012) Fatigue and quality of life in breast cancer survivors: temporal courses and long-term pattern. J Cancer Surviv 6:11–19
36. Sharp L, Johansson H, Landin Y et al (2011) Frequency and severity of skin reactions in patients with breast cancer undergoing adjuvant radiotherapy, the usefulness of two assessment instruments: a pilot study. Eur J Cancer 47:2665–2672
37. Wang-Rodriguez J, Cross K, Gallagher S et al (2002) Male breast carcinoma: correlation of ER, PR, Ki-67, Her2-Neu, and p53 with treatment and survival, a study of 65 cases. Mod Pathol 15:853–861
38. Willsher PC, Leach IH, Ellis IO et al (1997) A comparison outcome of male breast cancer with female breast cancer. Am J Surg 173:185–188