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Original article

Changes in body weight during various types of chemotherapy in breast cancer patients

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SUMMARY

Background & aims: Weight gain is a common problem for breast cancer patients treated with chemotherapy. It increases the risk of several comorbidities and possibly cancer recurrence. We assessed whether weight gain depends on the type of chemotherapy.

Methods: In a retrospective study among 739 breast cancer patients, we assessed whether change in body weight during chemotherapy differed between types of chemotherapy. Information about weight, clinical and personal factors was retrieved from medical records of breast cancer patients treated with chemotherapy between 2001 and 2010 in 4 different hospitals.

Results: Body weight information was complete in $n = 483$ patients (66%). There was substantial between-patients variability in weight change during chemotherapy: within the upper quintile of weight change, median weight gain was +6 kg, while in the bottom quintile median weight loss was of −3 kg. Adjusted multivariate regression analysis showed that change in weight differed between types of chemotherapy: women treated with anthracyclines + taxanes gained +0.9 kg (95%CI 0.1, 1.7) more than women treated with anthracyclines only. This differential change in weight was no longer statistically significant after taking into account that regimens with anthracyclines + taxanes have a longer duration than regimens with anthracyclines only.

Conclusion: There was more weight gain among patients treated with anthracyclines + taxanes than among patients treated with anthracyclines-only. This is partly explained by the longer duration of regimes with anthracyclines + taxanes.

1. Introduction

The majority of breast cancer patients are treated with adjuvant chemotherapy often in combination with other systemic treatment.[1] Weight gain during and after chemotherapy is highly prevalent: it has been reported that at least 35% of breast cancer patients gain weight after diagnosis, with an overall mean gain in weight of 1.4–5.0 kg.[2–11] Weight gain has been mainly associated with chemotherapy with or without other systemic therapies.[5,12] Weight gain negatively affects quality of life and it may also increase the risk of comorbidities, such as cardio-vascular disease and diabetes.[12,13] Moreover, it has been suggested that even modest amounts of weight gain (increases in BMI of 0.5 kg/m^2 or more) are associated with a higher risk of disease recurrence or death compared to those who remained weight stable.[14]

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Abbreviations

AC	adriamycin and cyclophosphamide
AC + T	adriamycin and cyclophosphamide, followed by paclitaxel (a specific taxane)
BMI	body mass index
CMF	cyclophosphamide, methotrexate and 5-fluorouracil
FAC	5-fluorouracil, adriamycin and cyclophosphamide
FEC	5-fluorouracil, epirubicin and cyclophosphamide
TAC	taxotere (docetaxel, a specific taxane), adriamycin and cyclophosphamide
ER	oestrogen receptor
PR	progesterone receptor

Whether weight gain occurs during chemotherapy may depend on the type of chemotherapy that is used. Currently, 2nd and 3rd generation regimens are mostly used; examples of 2nd and 3rd generation schemes for breast cancer are anthracyclines based schedules with or without taxanes.[15] Body weight gain has been associated with 1st generation chemotherapy regimens, which is mainly the combination of cyclophosphamide, methotrexate and 5-fluorouracil (CMF)[8,16,17]; the use of 1st generation schedules has decreased, as 2nd and 3rd generation schedules proved to have better survival.[15] There is some evidence suggesting that weight gain is less prevalent in 2nd and 3rd generation schemes, although the evidence is not consistent.[9,12]

Over the past years, the use of taxanes in chemotherapy regimens for breast cancer has become more widespread.[18] The use of taxanes will become even more abundant in the coming years, as taxanes proved to be effective in high-risk node-negative, early stage breast cancer.[19] It is not clear whether taxane-use is associated with body weight gain.

Therefore, we conducted a retrospective study among women treated with adjuvant chemotherapy for breast cancer. The main aim of this study was, to assess whether weight change during chemotherapy differed between chemotherapy regimens. Moreover, we assessed whether any association was confounded by clinical or patient characteristics.

2. Method

2.1. Data collection

We retrospectively collected information on body weight during adjuvant chemotherapy for breast cancer. We only included data from adult patients with newly diagnosed, stage I–III breast cancer. Data were retrieved from four regional non-academic Dutch hospitals (Hospital Gelderse Vallei, Ede; Maxima Medical Centre, Eindhoven/Veldhoven; Catharina Hospital, Eindhoven; Rijnstate Hospital, Arnhem/Zevenaar). For the hospital in Ede, the pharmacy of the hospital provided information about patients treated with adjuvant chemotherapy in the period from Oct-2004 until July-2010. In the other hospitals the Cancer Registries of the Comprehensive Cancer Centres the Netherlands provided the information which breast cancer patients were treated with adjuvant chemotherapy in the period from Jan-2001 until Dec-2004 (Arnhem/Zevenaar) and in the period from Jan-2008 until July-2010 (Eindhoven/Veldhoven). With this information, we retrieved the medical records in the participation hospitals. From medical records, we extracted: age, date of diagnosis, body weight before and after chemotherapy (see below for more details), body height, type of chemotherapy, date and duration of chemotherapy, patient-reported menopausal status (pre, peri, postmenopausal), type of surgery (lumpectomy vs. mastectomy), date of surgery, receptor status (oestrogen, progesterone, her2/neu), stage of disease (stage I, IIa, IIb, III). If menopausal status was missing ($n = 60$), we assumed that patients were premenopausal if they were younger than 50 years, and postmenopausal if they were 50 years or older.[5]

Body weight prior to the start of chemotherapy was defined as weight used to calculate dose of chemotherapy. If this weight could not be retrieved, we used weight at the start of the first cycle of chemotherapy and if this was not available, we used weight at diagnosis. Body weight at the end of chemotherapy was defined as weight at the start of the last cycle of chemotherapy. If this was not available, we used weight at the second last cycle of chemotherapy. Duration of chemotherapy was calculated as the number of days between the assessment of weight prior to and at the end of chemotherapy.

Chemotherapy regimens were divided into 4 categories, 1: Anthracyclines-based schedules, 2: Anthracyclines-based schedules with taxanes, 3: CMF, 4: other regimens see Table 1. If patients were her2/neu-positive, chemotherapy was mostly combined with immunotherapy: trastuzumab. Trastuzumab was always given as part of an anthracyclines-based schedule with taxanes, see Table 1. Usually the schedule was 4xAC (Adriamycin and Cyclophosphamide), followed by 12xpaclitaxel (a specific taxane) in combination with trastuzumab, followed by 13xtrastuzumab-monotherapy: 4*AC + 12*T/trastuzumab + 13*trastuzumab. As the focus of this study was chemotherapy and not immunotherapy, we retrieved information on body weight from the start of chemotherapy until the end of chemotherapy and not during the period of 13xtrastuzumab-*mono*therapy.

As this was a retrospective study, the medical ethical review board declared that it was not necessary to obtain medical ethical approval for the study.

Table 1
Overview of categorisation of chemotherapy used in this observational study among breast cancer patients.

4 Categories of chemotherapy	Contains:	Number of patients in final analysis
1: Anthracyclines-based schedules	• FAC: 5-Fluorouracil, Adriamycin and Cyclophosphamide • FEC: 5-Fluorouracil, Epirubicin and Cyclophosphamide • AC: Adriamycin and Cyclophosphamide	$n = 289$ (59%)
2: Anthracyclines-based schedules with taxanes (T)	• TAC: Taxotere (docetaxel), Adriamycin and Cyclophosphamide • AC + T: Adriamycin and Cyclophosphamide, followed by paclitaxel • AC + T/trastuzumab + trastuzumab[a]: Adriamycin and Cyclophosphamide, followed by paclitaxel in combination with trastuzumab, followed by trastuzumab-monotherapy	$n = 170$ (35%) • 125 of 170 did not receive trastuzumab • 45 of 170 did receive trastuzumab
3: CMF	• CMF: Cyclophosphamide, Methotrexate and 5-Fluorouracil	$n = 10$ (2%)
4: Other	Combinations of several schedules, usually because patients did not respond well to the first choice chemotherapy	$n = 14$ (3%)

[a] Trastuzumab is prescribed only for Her2-positive tumours. Usually the schedule is 4 × AC, followed by 12 × paclitaxel in combination with trastuzumab, followed by 13 × trastuzumab-monotherapy.