

Obesity and diabetes have adverse effects on cancer outcomes

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Both obesity and diabetes have adverse effects on outcomes in breast cancer patients who receive chemotherapy as primary treatment before surgery (neoadjuvant chemotherapy), according to research to be presented at the 9th European Breast Cancer Conference (EBCC-9) tomorrow (Friday). Although a high body mass index (BMI) is known to have a negative impact on cancer development and prognosis, until now there has been uncertainty as to whether having a high BMI had an equal effect on patients with different types of breast tumours.

Dr Caterina Fontanella, MD, a trainee in medical oncology from the University of Udine (Italy) and a research fellow with the German Breast Group, based in Neu-Isenburg, near Frankfurt am Main (Germany), will present an analysis based on nearly 11,000 patients with early [breast cancer](#) treated with [neoadjuvant chemotherapy](#). She will show that a high BMI adversely affects the chances of surviving without the breast cancer recurring or spreading to other parts of the body, , although this detriment was not seen in those women had been diagnosed with HER2-positive disease.

"Although the overall survival of patients with [metastatic breast cancer](#) has increased over the past few decades, it remains an incurable disease," Dr Fontanella will say. "So preventing disease relapse after primary treatment of early breast cancer is fundamentally important in oncology daily practice. Considering that about one-third of the worldwide population has a [body mass index](#) higher than 25 kg/m², investigating the possible higher risk of relapse that affects overweight and [obese patients](#)

compared with normal weight patients should be a priority."

The researchers studied data from 8,872 early [breast cancer patients](#) from the German Breast Group, and 1,855 from a joint EORTC/BIG[1] trial. All had received a modern treatment consisting of an anthracycline/taxane-based neoadjuvant chemotherapy, anti-HER-2 drugs, or hormone therapy according to tumour type and national guidelines.

The vast majority of the patients in this study received chemotherapy doses capped at a body surface area (BSA) of 2.0m^2 , which is often the limit when calculating doses. "Obese patients may have a BSA of more 2.0m^2 , but the chemotherapy dose they receive will not reflect this. It is a very common practice in these patients for fear of overdosing, but of course it means that they will often receive a relatively lower quantity of chemotherapy," Dr Fontanella will say. "In my opinion, a deeper understanding of chemotherapy metabolism and distribution in patients with high BMI and with increased adipose tissue is needed."

"We already know that obese hormone receptor-positive tumour patients respond less well to aromatase inhibitors as adjuvant treatment, and this underlines a key role of higher aromatase activity in patients with increased adipose tissue." Aromatase is an enzyme that synthesises oestrogen, and blocking it is important in cancers where oestrogen encourages tumours to grow.

Final analysis of outcomes from the two groups in the joint study showed a significant decrease in survival without the cancer spreading (metastasising) – distant disease-free survival (DDFS) – or the cancer recurring – distant relapse-free survival (DRFS) – in patients with increased BMI in all tumour types, apart from those with HER2-positive tumours.

"The exception in this group can probably be explained by the impressive impact of anti-HER2 treatment," Dr Fontanella will say.

"Given the significant proportion of the world's population with a BMI higher than recommended for good health, it is vitally important that we find a way to treat overweight and obese cancer patients that combines maximum efficacy with the avoidance of unnecessary side-effects."

In a second study, Dr Fontanella and colleagues investigated the incidence of Type 2 (adult onset) diabetes in patients with early breast cancer at the time of diagnosis, as well as its effect on the outcome after neoadjuvant chemotherapy. Diabetes has been reported in 15%-20% of elderly breast cancer patients, although in the group of just over 4,000 patients studied it was considerably lower. "This was probably because these patients were enrolled in clinical trials and were therefore selected to be in good physical condition without other illnesses that could complicate procedures and outcomes," Dr Fontanella will say.

"However, we did find that patients with diabetes were more likely to have their cancer diagnosed at a more advanced stage, and this suggests that diabetes may affect the size of the tumour. We also found that patients with diabetes had worse distant disease free survival rates."

Diabetes is currently believed to be associated with a 49% increased risk of death from all causes in breast cancer patients, as well as being an independent prognostic factor for the risk of recurrence and metastasis. Increased insulin levels seem to be related to a high risk of recurrence after primary treatment, and an increase in C-peptide [2] levels has been associated with an increased risk of cancer-related deaths, particularly in hormone receptor-positive tumours.

"We think that hyperinsulinemia – where there are increased levels of insulin circulating in the blood – may encourage the growth of tumour cells by providing them with large amounts of glucose. We therefore

believe that strict control of blood sugar levels is essential to the successful treatment of breast cancer," she will conclude.

Professor David Cameron, from the University of Edinburgh (Edinburgh, UK), who is a member of the EBCC-9 executive scientific committee, commented: "The growing epidemic of obesity needs to be given greater attention as a risk factor for developing breast cancer, and in how we treat [patients](#) in routine practice. The data presented by Dr Fontanella are important as they challenge not only the concept of 'chemotherapy dose capping' but also highlight how much we need to learn about the interaction between obesity and the biology of breast cancer."

More information: Abstract: O-417 "Influence of body mass index on long-term outcome of breast cancer patients receiving neoadjuvant therapy – Combined results from the GBG (German Breast Group) and the EORTC cohorts" and O-416 "Effect of diabetes mellitus on early breast cancer patients receiving neoadjuvant therapy" Friday 10.30-11.30 hrs GMT, poster discussion "Elderly and Lifestyle", Lomond Auditorium.

[1] European Organisation for the Research and Treatment of Cancer 10994/Breast International Group 1-00 trial.

[2] C-peptide is an amino-acid protein involved in the production of insulin

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