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COGNITIVE FUNCTION IN CANCER PATIENTS

Significant proportions of cancer patients report cognitive changes following therapy that interfere with their daily life activities and that can persist well into the survivorship period. The projects and collaborations constituting this research line center around the investigation of the prevalence, nature and cause of cognitive problems associated with systemic therapies. Understanding who is at risk and the emotional, cognitive and biological mechanisms associated with the development and maintenance of these effects is critical to treatment and prevention.

Late effects of chemotherapy on cognitive functioning in the elderly. NKI-Erasmus MC It is still largely unknown if chemotherapy induced cognitive changes observed several years after administration are persistent in the long term. We conducted a cross-sectional study comparing cognitive functioning of breast cancer patients who had undergone six cycles of CMF chemotherapy on average 21 years ago ($n=196$) to a population-based sample of women without a history of cancer ($n=1509$). All participants were between 50 and 80 years of age. Exclusion criteria were endocrine treatment, development of a secondary malignancy after the primary breast cancer, breast cancer relapse and metastasis. Chemotherapy-exposed women performed significantly less well than the reference group on cognitive tests covering the domains of immediate ($p=.015$) and delayed verbal memory ($p=.002$), attention ($<.001$), executive functioning ($p=.013$) and psycho-motor speed ($p=.001$). Chemotherapy-exposed women presented with less symptoms of depression ($p<.001$) but had significantly more memory complaints which were not associated with cognitive performance. The pattern of cognitive problems in these patients resembled the pattern seen in patients shortly after cessation of treatment.

Incidental findings on brain MRI in long-term survivors of breast cancer treated with adjuvant chemotherapy NKI-Erasmus MC Incidental brain findings are defined as previously undetected abnormalities of potential clinical relevance that are unexpectedly discovered and unrelated to the purpose of the examination. They are common in the general population. Because it is unclear whether the prevalence of incidental findings in cancer patients is similar to that in the general population we compared the prevalence in a population-based sample of women without a history of cancer with that in breast cancer survivors treated with chemotherapy and radiotherapy.

We compared 191 female CMF chemotherapy-exposed invasive breast cancer survivors with 1590 non-exposed control subjects without a history of cancer from a population-based cohort study. All subjects were between 50 and 80 years of age. Structural brain MRI (1.5T) was performed according to a standardized protocol. Five trained reviewers recorded all brain abnormalities. An experienced neuro-radiologist reviewed all incidental findings.

On average, cancer survivors had completed chemotherapy 21 years earlier. There was no difference in prevalence of meningiomas and aneurysms between the groups. The prevalence of pituitary macro adenomas in chemotherapy-exposed breast cancer survivors (1.57%) was higher than the prevalence in the reference group (0.06%) (OR=23.7; 95% c.i. 2.3 – 245.8).

Breast cancer patients who had been treated with adjuvant chemotherapy more on average than two decades earlier are at higher risk of developing pituitary macro adenomas. This elevated risk might be related to differences in exposure to sex hormones, as a result of chemotherapy induced menopause.

International Cognition and Cancer Task Force Recommendations to Harmonize Studies of Cognitive Function in Cancer Patients NKI, MDACC, MSKCC, Sydney Cancer Centre In the past years it has become increasingly apparent that cytotoxic agents delivered systemically for non Central Nervous System tumors may have cognitive side-effects, but many fundamental questions require further elucidation. Answering these questions will benefit from larger samples collected over multiple institutions. The International Cognition and Cancer Task Force brought together experts in the field of cancer and cognition to create research recommendations and guidelines with the specific aim to increase the homogeneity of study methodology.

Suggestions are formulated by two working groups for a core set of neuropsychological tests, a common criterion for defining cognitive impairment and cognitive changes, and common methodological approaches that will provide a basis for combining data across studies. These recommendations will improve research design and facilitate between study comparisons and meta-analyses, which will help determine more accurate estimates of incidence, severity, individual risk factors and causes of cognitive problems associated with chemotherapy for non-CNS tumors.

Information about chemotherapy-associated cognitive problems contributes to cognitive problems in cancer patients NKI-VU University While increasing attention is directed at identifying biological mechanisms underlying cognitive changes observed in cancer patients without CNS disease following chemotherapy, psychological factors that can contribute to these cognitive changes are much less studied.

In an online experiment, the influence of informing patients about the association between cognitive problems and chemotherapy on self-reported cognitive functioning and neuropsychological test performance was investigated. Cancer patients treated with chemotherapy ($n=148$) reported higher levels of cognitive complaints after receiving such information ($M = 21.20$) than without such information ($M = 19.00$; $p = .032$). No difference was found for chemotherapy-naïve patients ($n=88$; $M = 18.85$ vs. 20.08 ; ns). A similar interaction pattern was observed on a word learning test. Patients treated with chemotherapy recalled fewer words after being informed about the association between cognitive problems and chemotherapy ($M = 24.44$) than without such information ($M = 27.63$; $p = .010$). No difference was found for chemotherapy-naïve patients ($M = 26.35$ vs. 25.39 ; ns). Patient information may induce a stereotype threat, which affects self-reported cognitive function and neuropsychological test performance in cancer patients for whom this information is relevant.

Key publications

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