EDITORIAL

# Long-Term Structured Follow-up Is Essential After Curative Cancer Treatment

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Editorial to accompany the article "Breast Cancer in Young Women After Treatment for Hodgkin's Disease During Childhood or Adolescence" by Schellong et al. in this issue of Deutsches Ärzteblatt International

In this issue of the *Deutsches Ärzteblatt International*, Schellong and co-authors report on the increased incidence of breast cancer in young women who as children or adolescents were treated for Hodgkin's disease (1). As early as 1993, the first report was published on the increased incidence of breast cancer after Hodgkin's disease (also known as Hodgkin's lymphoma) (2). Because the inner quadrants of the chest are included in the radiation field during mediastinal irradiation to treat Hodgkin's lymphoma, it was rapidly suspected that the increased incidence of breast cancer was due to the combination of chemo- and radiotherapy. The association was confirmed in 2003 (3), which formed the basis for studies into the stepwise reduction and eventual elimination altogether of radiation in the primary treatment of Hodgkin's disease.

## Implications for follow-up

Two main points in this study (1) are of particular importance and have significant implications, not just for the long-term follow-up of patients after treatment for Hodgkin's disease, but also in general for the long-term follow-up of all patients after curative treatment for malignant disease:

- Breast cancer is not the only late sequela of radio- and chemotherapy.
- The study (1) underlines the great importance (already known about for several years) of long-term follow-up after curative cancer treatment (4).

The primary reports of treatment trials do not, naturally, include late complications occurring after 20 years or even more, so there is a limit to how far survival probabilities after various treatment approaches to potentially curable diseases can be genuinely compared (5). This is particularly important because different philosophies about the aggressiveness of the primary treatment have led to differing strategies around the world (6).

In Germany, for more than 30 years we have had a unique tradition of carrying out long-term tumor follow-up, thus identifying late sequelae of curative cancer treatment at an early stage. The decisive contribution to the systematic acquisition of knowledge has been from collaborations such as, not just the Hodgkin's study groups, but also working groups on leukemia, breast cancer, testicular cancer, and other entities. Experiences of systematic follow-up after curative radiotherapy and stem cell transplantation have also contributed to systematic knowledge acquisition. In pediatric oncology, integrating the German Childhood Cancer Registry (Deutsches Kinderkrebsregister) in Mainz has proved to be an essential part of learning about late sequelae. All systematic analyses showed an increase in certain specific malignant tumors and other diseases that were not cancers associated with the index malignancy, but appeared to be connected to the tumor therapy. Only systematic, long-term follow-up spanning decades allows late consequences of various components of the curative treatment for the malignancy to be identified and appropriately treated, as well as having an essential influence on the continuous further development of the primary therapy.

Against this background, long-term support for the collaborating working groups must be secured, and multidisciplinary follow-up must be improved.

## Systematic data collection on late sequelae

As already mentioned, follow-up after curative cancer treatment needs to be continued for decades because of the varying kinetics of the secondary diseases, and the data collected during the follow-up must continue to be systematically collated and evaluated. Schellong and co-authors describe a screening project for breast cancer after treatment for Hodgkin's disease that is extremely useful and worthwhile, but is insufficient on its own to ensure comprehensive care of patients with curatively treated Hodgkin's disease and to document the sequelae of the continually developing treatment protocols. For example, at present in the curative primary therapy of Hodgkin's disease, different cytostatics are used to those previously employed (especially etoposide), requiring a renewal of long-term documenting of any late sequelae. Associations between late sequelae and etoposide and other cytostatics were identified when these had been combined with radiotherapy. After 5 to 10 years, 0.5% to 2.6% of patients developed acute leukemia (3, 4, 9, 10). Some cytostatics are suspected of triggering myelodysplasia

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within 10 to 15 years in about 1% of those treated (3, 4, 9, 10). Skin cancer, melanoma, and thyroid cancer show a particularly long latency. For these cancers, peak incidences in cohort studies were only reached after 23.1 years. Between 18% and 27% of patients affected develop a secondary cancer (4, 8). Besides cardiotoxicity—which generally manifests in 30% of cases after anthracycline treatment and radiotherapy, but only after more than 5 years (4, 5, 7)—patients need long-term follow-up for pulmonary and neurological toxicity, infertility, and hormonal dysfunction.

Apart from being necessary in patients with Hodgkin's disease, targeted and appropriate follow-up is essential in all patients with curatively treated cancer who have undergone radio- and/or chemotherapy. This is particularly true for leukemia and non-Hodgkin lymphoma, sarcoma, testicular cancer, breast cancer, cancer in children and adolescents, and in general for all patients who have received curative radiotherapy or hematopoietic stem cell transplantation. In Germany at present, the funding of some collaborating groups (centers of excellence) is coming to an end or has already ended. We therefore need to think about how systematic follow-up and documentation are to be continued. Perhaps collaboration between study groups and the clinical cancer registry just being developed would be well suited to the systematic collection and evaluation of follow-up data.

## Multidisciplinary follow-up is needed

One further problem relates to the need for multidisciplinary follow-up. Because of the variety of different diseases and different organ systems affected, collaboration between several medical specialties is required, which must work together in coordination if the necessary tests are to be carried out in good time while at the same time avoiding overdiagnosis. Follow-up is particularly important in the case of patients who have undergone curative cancer treatment as children—and the numbers of these patients are increasing. Often, the follow-up is coordinated on a multidisciplinary basis in pediatric departments even after the patients have reached adulthood, while some of it is done by the family doctor, or even does not take place at all. Particularly in the case of patients given curative treatment for cancer in childhood, adolescence, or early adulthood, who need to be observed for decades, interdisciplinary follow-up appointments are very important. Coordination of the various specialties required for this multidisciplinary follow-up could be handled by the initially treating hospital. Probably, comprehensive cancer centers are the best suited to offering such interdisciplinary follow-up appointments, or to coordinating them within a region.

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**Conflict of interest statement**
The authors declare that no conflict of interest exists.

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