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EDITORIAL

Late effects – the new focus of follow-up

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Following cancer treatment with curative intention, the primary clinical focus is on possible local recurrence (R), metastasis (M), or a new secondary malignancy (S) in the patient. The aim is to secure detection and continued survival. However, quality of life is often given less focus. Across countries in the industrialized world, comprehensive follow-up programs have been established aiming at these outcomes. However, as illustrated in a recent Cochrane review of the entire area of follow-up [1], the scientific evidence for success in reaching this goal is weak, if not absent.

This cannot come as a surprise, as the organization of follow-up is dictated by the calendar and not by any events related to the cancer in a meaningful, biologically plausible way, despite in diseases with specific tumor-markers. It is implausible that signs of RMS will emerge on or just before the date of the follow-up visit, and it is doubtful that the mutation rates will increase close to the date of the examination. Such events and thus the possibility of (re)discovery of cancer are more likely to occur between scheduled visits [1].

In this conflict between insufficient evidence for our current follow-up practices and the need to continuously monitor the possible development of cancer, two complementary approaches appear on the horizon. First is the need to involve the patients themselves in aspects of the surveillance by implementing patient-reported outcomes (PROs). Second is the necessity of increasing focus on late effects after cancer treatment among the exponentially growing survivor population due to the improvements in treatment options.

PROs are important tools for monitoring patient health status in collaboration between patients and clinicians. Health systems are continually looking for ways of reducing admissions, avoiding hospital stays, and enforcing rapid discharge for medical as well as economic reasons, while maintaining quality of treatment and care. This demands an increased focus on the collaboration between healthcare providers and patients, with the latter required to assume greater responsibility. PRO-based communication is one important tool in this emerging alliance. Most cancer patients and survivors will benefit from communicating with their healthcare providers through PRO systems, which present a practical method for reporting symptoms and having them evaluated by health professionals, without the need for an appointment. The European Society of Medical Oncology just recently published guidelines for the application of PRO in cancer care [2].

Late effects have been known since the dawn of modern cancer treatment, beginning with late effects of surgery and radiation on to the long-term adverse effects of systemic chemotherapy and, possibly, today's immune therapy. Today, surveillance of adverse events during and immediately following cancer treatment is an integral part of the treatment of cancer patients. The first late effects to be addressed were consequences of surgery; the need for stoma bandaging following rectosigmoid resections, the need for compression when lymphedema occurred in women treated for breast cancer and gynecological cancers, and the need for a voice when laryngectomized. Radiation causes other types of late effects, e.g., fibrosis and changes in tissue functions leading to diarrhea when radiation fields include the intestine, pneumonitis in lung cancer patients, or reduced fertility when exposing the gonads. Systemic treatment with chemotherapy may disrupt yet other physiological functions, e.g., the heart, the endocrine system, or the senses. Today's immunotherapies present with new challenges, e.g., skin rash or itching, muscle and joint pain, cramping, or nervous system damage.

In addition to these specific late effects, which are related to individual cancer sites and treatments, many patients also suffer from general late effects. In particular depression, fear of recurrence, cognitive impairment, sleep disturbances, fatigue, and pain issues [3]. Compared to the more specific late effects, these general symptoms and diseases are prevalent across all cancer survivors and thus influence more patients in their daily life. Furthermore, general late effects are often correlated, and patients rarely experience only one [3].

The situation calls for a new model of follow-up, which considers both: (A) the need for keeping an eye on RMS and for educating patients to take on some of the observations of symptoms associated with RMS; and (B) the need for

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prevention, early detection, and treatment of late effects. How may this be orchestrated?

PROs provide an educational opportunity to support the patient in the ability to interpret symptoms, which may help patients treated for cancer become familiar with the most common symptoms of RMS as well as late effects. We suggest the introduction of mandatory cancer late effect information policies linked directly to the treatment protocol information to support this patient education. The information should not only be based on the treatments and their known late effects, but also on the patients' characteristics, including somatic or psychological comorbidities that may place patients at particular risk of certain late effects. We are aware that – to some extent – such policies are already in place. We argue that such educational perspectives may be included and further prioritized if linked to the well-established information procedures. Online programs providing a thorough overview of symptoms made available for patients on demand will reinforce the suggested information policies.

We also need to improve the patients' self-care skills. This calls for education. Having this in mind, we do have to acknowledge the social inequality in all aspects of cancer - the prevention, the incidence, and the prognosis. Across all cancer sites, we do observe a continuing and indeed increasing difference in survival, when comparing socioeconomic status – no matter which factor we include in the equation [4].

Currently, the necessary range of programs is not available. However, more studies have implemented various techniques, e.g., nurse navigators, problem-solving instructions to patients and numerous PRO tools [5–7]. In our perspective, the oncologist, surgeon or radiation specialist takes on some teaching responsibilities in collaboration with nurses at the hospital. The time saved by minimizing direct physical contact during follow-up is transferred to these kinds of activities. We anticipate that such changes may only function if dedicated staff is assigned to the training of patients in the use of PRO.

This is a shared-care model, sharing tasks between the healthcare provider and patient, assigning various responsibilities to either the health system, e.g., diagnostic decisions, imaging, and biological sample analysis and other chunks to the patient, e.g., conducting regular examination of a list of symptoms relevant for this patient/cancer, and some biological analyses. This division between healthcare provider and the patient will change rapidly over time along with the development of technological possibilities for 'home-based medicine'. No matter the stage of development, such an organization calls for communication tools between the two partners in health, and for educational activities that support patients in taking on these responsibilities, to the degree they are able. Outsourcing such tasks to patient's risks overburdening some patients, as well as their family caregivers, and must be accompanied by differentiated support measures taking into account the above-mentioned need for helping patients with fewer socioeconomic resources.

Which health professionals should be responsible for the monitoring and management of late effects? In our view, the responsibility should be shared between the highly specialized hospital department and the general practitioner (GP), with the GP as the triaging officer in charge of referring patients to health professionals with the relevant level of specialty depending on the symptoms and diseases occurring along the survivorship trajectory. Such assignments of responsibility to the GP probably call for a number of educational initiatives to secure timely action in case of RMS. A model allowing patients' self-referral might even be considered. While the organization of follow-up will most likely differ between countries and take on various forms based on the local healthcare provider system, we believe that the cornerstone of future survivorship care should be patient education and follow-up-care prompted by the patients themselves, e.g., through PRO reporting, the organization needed will most likely differ between countries and take on various forms based on the local healthcare provider system.

Disclosure statement

No potential conflict of interest was reported by the authors.

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