

# Adolescents and Young Adults with Cancer: The Pathway of Care

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## Overview

- Cancer in adolescents and young adults (AYAs) is a major global health issue
- Studies indicate that both 'patient delay' and 'referral delay' are increased in AYAs, therefore the pathway of referral to a specialised centre can be long and sometimes complicated
- All patients should be referred to a specialised centre experienced in diagnosing and treating cancer in AYAs
- A complete work-up and diagnostic procedure should be performed including histological confirmation and staging of the tumour burden
- It is crucial that all the caregivers work together as a team, to provide the optimal care for the patient

Cancer in AYAs represents a distinct disease constellation in which progress in diagnosis and management lags behind that of children and older adult patients. Moreover, it has been shown that in this patient

group, there is a substantial delay in diagnosis of the tumour, which is clinically relevant considering that these malignancies have a particular biological behaviour and subsequently different sensitivities to treatment as compared with other patient age groups. Often, AYAs with cancer face numerous psychosocial, educational and professional challenges during this period of their life, which may lead to poor adherence to their proposed treatment plan. In addition, they are often under-represented in clinical trials and their management usually takes place in centres with a low number of AYA cancer cases. Unfortunately, it is only in the last 20 years that the oncology community has acknowledged the significant care gap for this age group and focused on the particular difficulties in AYA cancer management. This has led to the significant conclusion that universal protocols for AYAs should be created and that centres of excellence with specialised AYA cancer services should be implemented throughout Europe.

## Definitions

Traditionally, AYAs have been considered as the ‘older’ patients in paediatric oncology and haematology practice and the ‘younger’ patients in adult practice. This perception led to a general confusion with AYAs being treated in both adult and paediatric cancer wards by either adult or paediatric oncologists, based on the primary tumour location and ‘type’ of malignancy, rather than the patient’s age.

At present, there are no universally accepted limits that define the AYA age range because the interface between adult and children’s services varies across healthcare systems. According to the World Health Organization (WHO) definition, teenage years are between 13 and 19 years of age, inclusive, and older patients, from 20 to 39 years of age, are generally considered ‘young adults’. Moreover, in most healthcare systems, the upper limit for paediatric patients is 14 years of age. Thus, it would be logical to conclude that the AYA age group ranges from 15 to 39 years of age. Most international guidelines and reviews on AYAs with cancer use the aforementioned age spectrum, although regional and national deviations exist worldwide, since the exact timepoint of transition from childhood to adulthood differs from culture to culture.

## Particular Aspects of Cancer in AYAs

Cancer in AYAs is a major global health issue. It represents the main cause of death for medical reasons (other than accidents, homicides and suicides) in 18-40-year-olds (Table 1). More details regarding the disease spectrum and the epidemiology of malignancies in AYAs are provided in Chapter 2.

*Table 1 Leading Causes of Death in Young Adults Between 20-39 Years in the United States in 2005 (Excluding Accidents and Homicides) According to the Surveillance, Epidemiology and End Results (SEER) Database of the National Cancer Institute.*

*From: Bleyer A, Barr R. Cancer in young adults 20 to 39 years of age: overview. Semin Oncol 2009; 36:194-206.*

	Males and Females	Deaths	Females	Deaths	Males	Deaths
1	Suicide	10482	<b>Neoplasms</b>	<b>4888</b>	Suicide	8520
2	<b>Neoplasms</b>	<b>9310</b>	Heart disease	2519	Heart disease	5536
3	Heart disease	8055	Suicide	1962	<b>Neoplasms</b>	<b>4442</b>
4	HIV disease	3142	HIV disease	1069	HIV disease	2073
5	Diabetes mellitus	1514	Cerebrovascular disease	643	Diabetes mellitus	903
6	Cerebrovascular disease	1359	Diabetes mellitus	611	Cerebrovascular disease	716
7	Chronic liver disease	1049	Congenital anomalies	393	Chronic liver disease	685
8	Congenital anomalies	920	Chronic liver disease	364	Congenital anomalies	527

Abbreviation: HIV, human immunodeficiency virus.

It has been shown that certain types of cancer have a different biology when they affect young adults, as compared with other ages, an observation that is also supported by the higher expression of rare histological subtypes and the more frequent occurrence of hereditary cancers. In children, carcinogenesis is largely related to genetic factors, in the elderly to environmental factors and, in young adults, it is most likely attributed to a mix of these. For example, lymphomas, sarcomas and thyroid cancers, as well as breast, liver and colorectal cancers, may affect AYAs with higher incidences due to the potential coexistence of hereditary cancer syndromes, such as neurofibromatosis, ataxia-telangiectasia syndrome, Li-Fraumeni syndrome, Fanconi pancytopenia, congenital nevi

syndrome, multiple endocrine neoplasia (MEN) syndromes and Turner syndrome. On the other hand, cancers of the uterine cervix, vagina, vulva, anus and oropharynx attributed to human papillomavirus (HPV) infection and melanoma attributed to ultraviolet (UV) sun radiation are very illustrative examples of neoplasms possibly related to specific environmental risk factors.

These unique biological properties may also account for the different sensitivities of these malignancies to standard treatments, as compared with patients in other age groups. For example, breast and colorectal cancers, as well as soft tissue sarcomas, bear a more dismal prognosis when diagnosed in AYAs, as compared with their younger or older counterparts, despite the use of identical therapeutic strategies. Moreover, Ewing sarcoma, nephroblastoma, neuroblastoma, cancer of the uterine cervix, ovarian cancer, liver cancer and brain tumours often have a poorer prognosis in AYAs than in younger patients.

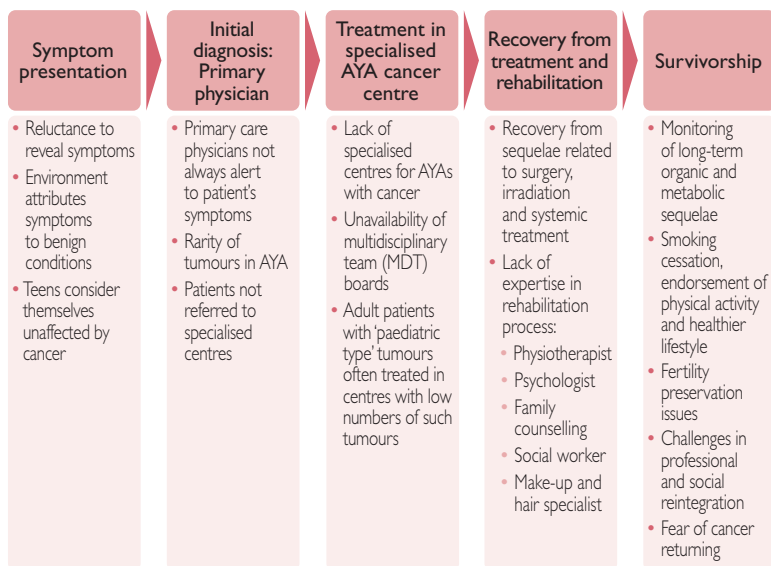
One last, but fundamental, aspect of the care of younger patients with cancer is the adherence to treatment. It is generally considered that younger patients are less likely to adhere to treatment instructions, a follow-up plan or a clinical trial protocol. Potential contributing factors to this suboptimal compliance are lack of surveillance from parents, family or spouse/companion, a sense of hyper-optimism and hyper-self-confidence (characteristic of this age group), the demands of school, studies or work, potential financial issues and problems in patient transportation to and from the hospital.

## The Pathway of Care for AYAs with Cancer

Who Does the Young Patient Initially Address with His/Her Symptoms?

Quite often, diagnosis of cancer in AYAs is delayed and many parameters may account for this, e.g. the reluctance of patients to reveal their symptoms to their families or doctors. A number of studies indicate that both the time from symptom onset to the first contact with a doctor (the so-called ‘patient delay’) and referral to the oncologist (‘referral delay’) are increased in AYAs. A pilot study in the field (Veneroni et al, 2013), showed that the main contributing factor to symptom interval in adolescents

**Figure 1** The pathway of care for AYAs diagnosed with cancer, along with the potential drawbacks, pitfalls and challenges at each step



Abbreviation: AYA, adolescent and young adult.

appeared to be due to the time from symptom onset to the first contact with a doctor; however, the time taken by the physician to refer the patient to a specialist (oncologist or surgeon) able to define the diagnosis of cancer was also longer. Does delay in diagnosis have an impact on patient outcomes? Results from a recent study (Ferrari et al, 2016) suggest that at least a subset of patients can benefit from an earlier diagnosis in terms of survival, while in other cases the intrinsic aggressiveness of the disease may mask the potential effect of diagnostic delays.

AYAs tend to consider themselves unaffected by serious illnesses, such as cancer; they are usually more preoccupied with their studies or developing a career and tend to neglect otherwise alerting symptoms, attributing them to excessive fatigue or stress. Moreover, symptoms relating to the reproductive system (e.g. amenorrhoea, testicular or breast mass, etc.) are less likely to be reported by teenagers or young adults. Usually,

it may be a parent or a sibling or a very good friend that the teenager will reveal his or her symptom to. A pilot study in the field (Magni et al, 2016) showed that inadequate awareness of cancer risk among adolescents is a substantial contributing factor to delayed diagnosis. It is imperative that once the problem is revealed, the young patient is referred to a physician and not to underestimate or neglect the symptom. Sometimes AYAs with cancer complain of persisting symptoms such as weight loss, night sweats, soft tissue masses, lymph node enlargement, dizziness, cough or fatigue, yet their symptoms tend to be neglected, underestimated or attributed to benign conditions. AYAs should feel free to disclose their symptoms, and their entourage must be keen to discuss them.

### Who Makes the Initial Diagnosis?

Usually, the first healthcare professional to see a young patient with suspected malignancy is the primary care physician, general practitioner or paediatrician. This is another very decisive step in the young patients' pathway of care. Due to the rarity of serious illness in these age groups, primary care physicians are not always alert to patients' persisting symptoms. Gradual weight loss may be attributed to anorexia nervosa, stress or depression, a persisting cough to an upper respiratory tract infection, and dizziness and persistent headaches to stress migraine and too much studying.

The spectrum of malignancies in AYAs is rare but serious and every symptom that is worrisome should prompt the appropriate investigation. Physical examination, as well as targeted laboratory and imaging tests to confirm or reject a diagnostic hypothesis, should always be implemented in the diagnostic algorithm. A positive finding on a computed tomography (CT) or magnetic resonance imaging (MRI) scan, sudden onset of persistent anaemia, or any other alarming findings should result in referral of the patient to a specialised centre with the appropriate infrastructure and experience in diagnosing and treating cancer in AYAs.

### To Whom is the Patient Referred?

The pathway of referral to a specialised centre can be very long and sometimes extremely complicated in various healthcare systems. A pilot study in the field (Smith et al, 2018) revealed substantial variation

in pathways to cancer diagnosis and delivery of optimal care; varying regulatory requirements and professional willingness to contribute data were key barriers for the interpretation of the results of this study.

Once the patient is referred to a specialised centre, a complete work-up and diagnostic procedure should be performed, including histological confirmation and staging of the tumour burden at the time of diagnosis. A multidisciplinary team led by an experienced oncologist should oversee this procedure. At all steps of the process, continuous contact with the patient and his/her family should be maintained, including the appropriate psychological support during the difficult first days following diagnosis. The diagnostic process may include some stressful and sometimes painful procedures such as biopsies, lumbar puncture, surgical interventions and repeated blood tests. The final diagnosis might be shocking for the patient and his/her family, who may be completely unaware of the disease entity. The treating physician should devote the appropriate time to carefully and comprehensively explain the meaning of the diagnosis, the immediate consequences and the prognosis. He/she should also provide a robust treatment plan, explaining in detail the treatment modalities, the time schedule and sequence and possible side effects related to treatment. Ideally, at this point and if medically indicated, the treating physician should also offer the possibility of entering an appropriate clinical trial, if such is available at the centre, and especially trials dedicated to AYAs with cancer or those bridging the 18-year age barrier. One of the most crucial aspects of management at this point is that all the caregivers work together as a team, to provide the optimal care for the patient, including the family, the boyfriend or girlfriend and close relatives and friends.

### **Which People Form the Support Team?**

The role of the multidisciplinary team is imperative as well. Depending on the case, the support team might include (but is not restricted to) medical or paediatric oncologists, surgeons, radiotherapists, cancer nurses, research associates, psychologists, physiotherapists, social workers, plastic surgeons, dentists and even make-up and hair specialists. All the aforementioned healthcare providers form the support team and their roles can be imperative and indispensable. The physical and psychosocial wellbeing

of the young patient and the maintenance of an acceptable quality of life for the duration of the therapeutic procedure should be the ongoing aim of the team, until complete resolution of treatment.

### Who Follows Patients After Cancer Diagnosis and Treatment?

The excellent prognosis of many of the tumours in AYAs as well as the curative intent of the treatment modalities underline the role survivorship plays in this age group. A large majority of these patients will hopefully be cured of their cancer and will have a life expectancy similar to that of friends and colleagues who had not been diagnosed with cancer. This notion renders issues of life after cancer and of quality of life after cancer of imperative importance. In recent decades, the scientific community has come to recognise the importance of maintaining an excellent quality of life in cancer survivors. Efforts have been made to minimise the late complications of cancer treatment, including cardiotoxicity, neurotoxicity, renal toxicity, cognitive impairment and metabolic sequelae; they also focus on adopting a healthier lifestyle, including avoiding smoking and excessive alcohol consumption, implementing daily physical exercise, eating healthily and maintaining a normal body weight. This is why AYA cancer survivors should be closely monitored after the end of their treatment and throughout the recovery and rehabilitation period.

Finally, perhaps the most difficult aspect of a young patient's 'journey' through cancer is his/her professional and psychosocial reintegration. Going back to school or university or returning to work can be a challenging experience following a long period of absence and the emotional detachment of the patient can pose serious challenges when he/she decides to return to his/her daily activities. Problems with going back to work and obtaining the same position, and relationships with colleagues, peers, the spouse/companion and family and friends may be overwhelming to the patient who has fought hard for his/her life and is still struggling to cope with professional and financial obligations, the pursuit of a career and the fear of cancer returning. In all the steps of this long and stressful process the help of social workers and, most importantly, of the family and friends can really serve as the catalyst for the smooth reintegration of the young cancer survivor into society.



## Declaration of Interest:

Dr Mountzios has reported no potential conflicts of interest.

Professor Douillard has reported no potential conflicts of interest.

## Further Reading

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