

Psychosocial Challenges and Health-Related Quality of Life of Adolescents and Young Adults with Hematologic Malignancies

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Abstract

Adolescents and young adults (AYA) occupy a unique place within the hematologic malignancy community due to the challenges they face related to their disease biology, physical, psychosocial and economic circumstances, and issues related to access to care and long-term follow-up. Efforts to define age-specific (supportive) care needs and targets for intervention in these areas are evolving. This review discusses the psychosocial issues AYA with hematologic malignancies are dealing with, how these might affect their health-related quality of life (HRQoL), and the challenges in delivering high quality supportive care to this underserved population.

INTRODUCTION

Adolescents and young adults (AYA) are recognized as a distinct population within the oncology/hematology community due to the unique challenges they face. When compared to pediatric and older adult oncology patients, those aged 15-39 years at cancer diagnosis encounter differences in tumor biology, psychosocial challenges, issues related to access-to-care and long-term follow-up.^{1,2}

AYA typically present with hematologic malignancies (HM) that span the spectrum from pediatric cancers (e.g. acute lymphoblastic leukemia; ALL) to adult tumors (non-Hodgkin lymphoma; NHL), as well as tumors that are most common among their age group (Hodgkin lymphoma; HL).³ HM form 34% of cancers diagnosed among AYA aged 15-19 year (15% HL; 7% NHL; 7% ALL; 5% acute myeloid leukemia (AML)), 21% among those aged 20-29 years (10% HL; 6% NHL; 2% ALL; 3% AML) and 11% among 30-39 year olds (3% HL; 6% NHL; 1% ALL; 1% AML) in the Western world.^{1,3-5} For these patients, the 5-year overall survival varies between 50 and 95%.⁶ Although survival in AYA has improved over time, progress made in treatments and survival of specific tumors (e.g. ALL and AML) lags behind that of children and older adults.^{5,6} Potential reasons for the lack of progress in survival are the diverse and incompletely understood tumor biology,⁷ insufficient awareness of cancer risk and symptoms among patients and healthcare professionals (HCP) resulting in diagnostic delays,⁸⁻¹⁰ unequal access to and low participation rates in clinical trials,¹ treatment non-adherence rates of 27-60%¹¹ and limited knowledge among HCP regarding AYA treatment protocols.¹²

PSYCHOSOCIAL CHALLENGES AND NEEDS

Adolescence, emerging and young adulthood are complex phases of life due to the many developmental, emotional and social transitions.¹³ AYA aim to achieve several developmental milestones such as completing education, creating their own identity, establishing autonomy, forming (romantic) relationships, pursuing gainful employment, becoming financially independent and having children.¹⁴ A cancer diagnosis and treatment challenges AYAs' abilities to achieve these milestones.¹⁵ Although AYA patients with a HM face challenges similar to those of older and younger patients, including short-term (e.g. hair loss,¹⁶ pain¹⁷) and long-term effects of cancer treatment (e.g. fatigue¹⁸ and cognitive problems¹⁹), the consequences are different in this phase of life and more pronounced. In the AYA population specifically, treatment decisions should include considerations of impact of long-term and late-effects of treatments.²⁰⁻²⁵

Education, employment and financial challenges

Employment and education provide AYA with a sense of identity, income, and frequently health insurance for needed treatment and follow-up care.^{26,27}

Education

Cancer treatment can lead to serious disruption in educational trajectories,^{28,29} with AYA often missing coursework/exams at a time that is crucial to future career development.¹⁰ Educational settings are an important place for AYA to develop supportive social networks³⁰ and develop a stable sense of self-worth.¹⁰ AYA describe cancer as a major disruption in the pursuit of educational opportunities due to absenteeism, inability to complete exams, and the feeling of being "left behind".²⁸ A recent Dutch study showed that AYA lymphoma (45% HL; 55% NHL) survivors more often had a lower educational level compared to a normative population (27% vs. 3%).³¹ AYA often receive inadequate educational support during treatment (help with coursework, postponing exams),

and indicate a need for assistance with returning to school.³² Close liaison between schools and hospitals is needed.

Employment

Employment problems are common among AYA with cancer.³³ One study conducted in USA showed that 33% of AYA (unspecified % HM) versus 27% of healthy controls were not working,³⁴ whereas in another American study (9% HM), 24% of AYA patients versus 14% of controls reported unemployment due to health issues.³³ A more recent American study (4% leukemia, 26% HL, 24% NHL) showed that 28% of AYA cancer survivors had not returned to work 15-35 months after diagnosis and around 50% reported problems with returning.²⁷ AYA who reported their cancer treatment was “very intensive” and those who had to quit work after being diagnosed were more likely to report that cancer negatively affected their work, with more than half reporting problems with memory and attention.²⁷ AYA with ALL more strongly believed that cancer negatively impacted their work plans compared with AYA with other cancers.²⁷ In an English interview study, AYA reported feeling “left behind” in their job trajectories compared with their peers and those who had previously pursued careers involving physical abilities believed that they needed to adjust their goals as a result of their cancer. In addition, some AYA reported discrimination from employers and job insecurity due to cancer.²⁸

Considering that AYA are at a stage in life when entering the workforce successfully will greatly influence their future earning and career potential, patients may benefit from the incorporation of resources into AYA programs that aid the transition from treatment to occupational pursuits.²⁷ Future research might focus on effective communication strategies between workers and employers to identify appropriate work modifications to help balance the demand of work with adverse treatment-related effects, preventing patients from quitting work altogether.

Financial challenges

Financial toxicity of cancer treatment is especially relevant to AYA with a HM, many of whom undergo long, costly therapies such as allogeneic hematopoietic cell transplantation, with side-effects that may prevent patients from completing education and returning to work.³⁵ An American study showed that AYA (72% lymphoma; 28% leukemia) tend to have less productivity, greater healthcare expenditures, and increased likelihood of financial problems than patients diagnosed at older ages.³⁶ An American study (4% leukemia, 27% HL, 25% NHL) showed that 65-70% of AYA aged 21-39 years and 51% of AYA aged 15-20 years reported a negative financial impact,²⁹ while another American study (unspecified % HM) showed that AYA had lower household incomes compared with healthy peers.³⁴ In the same study, AYA reported higher annual medical costs (\$7417 vs. \$4247 for controls) and annual average lost productivity costs due to illness/disability of \$2200/year. Some AYA with cancer in UK indicated that they need to rely on their parents or other significant others for financial support, which can result in feelings of dependency and loss of control.²⁸ In interviews, AYA with cancer (59% HM) also describe issues with competing responsibilities and experience a lack of financial support for childcare, transportation and elderly care,³⁷ which may also result in lower treatment compliance levels among AYA.³⁸

In interviews, one third of American AYA (59% HM) mentioned difficulties in acquiring or maintaining health insurance.³⁷ Some lacked insurance before their diagnosis because they could not afford coverage and/or felt that they did not need coverage. Others had insurance at the time of diagnosis but worried about future insurability (because of losing employment due to treatment). Access and affordability of insurance is sometimes also a problem for AYA who are working but do not receive coverage through their employers. This can force AYA to seek treatment in an emergency room, a suboptimal strategy given crowding, wait times and lack of continuity of care.³⁹ Lack of insurance may lead to missed care opportunities and subsequent economic burden including tradeoffs with

education and career, using up savings, delinquency on loans, credit card debt, delay in moving out from their parents' home, increased cohabitation, delaying marriage and sometimes difficulty paying for basic necessities like rent and food.⁴⁰

Social relationships and functioning

Engaging in social and romantic relationships are healthy developmental milestones of any AYA, wherein sexuality is explored and future plans to marry and have children are considered.⁴¹ A cancer diagnosis can disrupt social maturation, the process by which young people develop identity, self-esteem and self-worth, social cognition, emotional regulation and communication skills that guide them throughout the remainder of their lives.^{10,30,42,43} Several studies showed that AYA with cancer report greater challenges in social functioning compared with the general population.⁴⁴⁻⁴⁶

Peer and family relationships

Cancer often forces AYA to move home and become dependent on parents or significant others, usually after periods of time living independently. For AYA who are married or in committed relationships when diagnosed, they are similarly forced into dependence on a spouse or partner unexpectedly. In interviews, AYA (59% HM) described the benefits of being cared for and supported, but also the challenges of feeling infantilized by their parents, significant others or partner.³⁷ Emotional development may be negatively affected by learned decisional passivity caused by overprotective parenting.⁴⁷

Furthermore, as AYA with cancer try to deal with or discuss their illness with their parents, partner, or significant others they may discover they have quite different coping strategies. Informal caregivers may want or need to discuss issues with the AYA that he/she does not wish to discuss, or vice versa. Some AYA desire to protect their family members by shielding things they themselves worry about, possibly out of guilt for what their parents, significant others, or partner are going through, or because they can see how upset family members are.⁴⁸ Moreover, in qualitative research AYA patients with dependents experience the drive to keep pushing forward as a function of the need to take care of others (e.g. children), even when they feel sick.³⁷ This reflects the intertwined experiences of fighting cancer and being a parent/caregiver, a non-normative challenge for an AYA. Also, children of AYA cancer patients may go through a distressing time, behavioral problems and restrictive cognitive and physical functioning are reported.⁴⁹

For many AYA, having cancer is catalytic in changing social relationships, either enhancing closeness or creating distance. From the perspective of friends, a cancer diagnosis can be a source discomfort, responding to ill friends by avoiding them. Isolation and alienation are commonly reported among AYA with cancer, particularly as they miss life experiences being shared by their healthy peers.⁵⁰ Disruptions in the socialization process can result in impaired social skills, which may lead to diminished participation, social anxiety and loneliness.⁴⁷ In other qualitative studies, AYA frequently report difficulties maintaining or making new relationships as they feel anxious about 'fitting into' their peer group again.^{37,51,52} Changes in body image often lead to feelings of insecurity and make AYA feel different from peers.⁵³⁻⁵⁹ An American study showed that AYA (27% HL, 25% NHL, 4% ALL) who reported that cancer had an impact on their close relationships were more likely to desire information on how to talk about their cancer with others.⁶⁰ Respectively, 27%, 29% and 5% of the HL, NHL and ALL patients had an information need on how to talk about their cancer experience with family and friends.⁶⁰

Marital relationships

Marriage is another important social milestone for many AYA. An American study found that fewer AYA (6% HM) with cancer were currently married (58 vs. 64%) and more had been divorced or separated (18 vs. 10%) compared with age-matched controls.⁶¹ Twenty-five percent of AYA reported that cancer negatively impacted their relationship with their spouse/significant other. It could be hypothesized that the emotional and financial burden of a cancer diagnosis could lead to marital distress. In a qualitative study (59% HM), divorced AYA patients indicated that their cancer experience catalyzed the breakups because their partners were not willing or able to support them through their disease.³⁷ AYA also discussed challenges initiating new romantic relationships. Negative body image, low self-esteem, infertility concerns, or feelings of “abnormality” as a result of cancer and its treatment might negatively influence AYAs’ readiness and ability to engage in romantic relationships.^{37,62,63}

Future research is needed to examine the complex and nuanced ways that cancer experiences affect relationships between AYA and their significant others, this will ultimately help to develop (digital) social support interventions which will support AYA in developing new social and maintaining existing contacts.³⁰

Starting a family

Around 75% of AYA who have not had children at cancer diagnosis express a wish for future biological offspring.⁶⁴⁻⁶⁷ Cancer treatments have the potential to destroy reproductive cells and can place women at risk for acute ovarian failure/premature menopause and men for temporary/permanent azoospermia.^{68,69} There are several fertility preservation options available,^{70,71} however counseling hematologic AYA patients about fertility threats is challenging due to the undefined risk and variable timing of gonadal failure, indeterminate likelihood and timing of gonadal recovery, and the unknown risks and efficacy of nonstandard but immediately available fertility preservation options.⁷⁰

Despite the available fertility preservation options, discussion, referrals and treatment are inconsistent, and many AYA initiate treatment without discussion or opportunity for fertility preservation.^{72,73-76} For example, an American study showed that, depending on tumor type and sex, 17-83% of AYA patients with HM discussed fertility preservation with their HCP.⁷⁶ In qualitative research, AYA reported false beliefs, unrealistic expectations and uncertainty regarding their reproductive potential and options.^{77,78} Reproductive concerns in AYA cancer survivors have been associated with grief, low self-esteem, an altered sense of identity⁷⁹ and can negatively affect dating, social relationships, and life planning.^{80,81} AYA with confirmed infertility reported regret for not questioning infertility risks, guilt for their current partner or fear of never finding a partner⁷⁹, and long-term distress.⁶⁴

These results emphasize that HCP should be better educated about fertility risks and should inform AYA patients about their risks and fast evolving opportunities for fertility preservation.⁷²

Sexual functioning and intimacy

AYA may experience cancer- and treatment-related sexual dysfunctions.⁸² Treatment can cause problems with erection, premature ejaculation, early menopause, vaginal dryness, shrinking, loss of elasticity, which can all result in discomfort during intercourse and interfere with the patients’ ability to be interested in or enjoy sex.⁸³

An American study showed that 49% of AYAs (28% HL, 24% NHL, 4% ALL) reported negative effects on sexual function 1-year post-cancer diagnosis and 70% of those persisted in their negative perceptions 2-years after diagnosis. Those reporting a negative impact were more likely to report that their diagnosis had a negative effect on physical appearance.⁵³ A Finnish study showed that female leukemia survivors (mean age at study 20.1 years) had more restrictive images of sexuality,

and their attitudes, especially those concerning sexual pleasure, were more negative than those of healthy controls.⁸⁴

In addition, short- and long-term effects of treatment (e.g. fatigue, graft versus host disease, nausea, neuropathy) may hinder intimacy and interest in sexual activity⁸⁵. Patients may feel embarrassed that others see them differently because of physical changes, such as weight gain/loss, hair loss, swelling, scars or the presence of a central line/port. All these treatment-related effects and sexual dysfunctions accompanied by changes in self-esteem (different sense of self-worth and self-confidence) may have (enduring) negative effects patients' and their partners' sex life.^{84,90,86} One study showed that when sexual problems were not discussed, patients were likely to believe that sexual dysfunction and treatment-related damages could not be treated⁸⁶. These results emphasize the need to inform about and improve post-cancer treatments addressing sexuality for AYA and their partners.⁸⁷

Psychological issues

Several studies have shown that rates of psychological distress are significantly greater among AYA when compared with older patients.⁵⁵ Older age and previous life experiences have been recognized as protective factors as they are related to highly developed coping skills.⁸⁸ More so than childhood cancer patients, AYA have the cognitive capacity to understand the severity of their illness and frequently demonstrate persistent distress. A recent American study among AYA treated for ALL, NHL or HL showed that 23% met the criteria for anxiety, 28% for depression, and 13% for post-traumatic stress, respectively, while 46% overall demonstrated post-traumatic stress symptomatology.⁸⁹ Thirty-nine percent were impaired in one or more psychological domain. No differences in psychological morbidity were observed between patients on-treatment compared to early survivors. A Dutch study showed that 69% of AYA cancer patients aged 18-35 years (14% HM) reported fear of recurrence/progression.⁹⁰

Alterations in physical appearance, e.g. scars of biopsies and central lines, weight changes and hair loss, not only make AYA feel different from peers but may also adversely affect maturational processes including development of self-esteem and identity.^{58,91} Fear the body will never return to its original appearance, of not being recognized by others, or of being mistaken for an individual of the opposite sex often lead to shame, social isolation, and regressive behaviors.^{15,63}

Interestingly, HCPs' perceptions of their AYA patients' psychological morbidity is not related to AYA patients' own perceptions,⁸⁹ suggesting HCP are not consistently assessing distress in AYA patients during clinic visits. AYA themselves may delay reporting distress-related symptoms to providers because of a passive-avoidant coping style, individual patient's effort to cope with the disease alone or a fear of stigmatization following acceptance of being diagnosed with a psychological illness. Several American studies show AYA repeatedly report that their psychosocial needs are not met throughout the cancer experience,^{78,92-94} e.g. 41% of AYA reported an unmet need for psychological counseling 12 months after diagnosis.⁹²

Psychological interventions targeting adults or children are not adequate to reduce distress among AYA.⁹⁵ Interventions for AYA must manage competing demands for time such as school, work, and family.⁹⁶ Novel AYA-focused psychosocial interventions delivered in AYA-friendly platforms (e.g. social media) are currently being evaluated.⁹⁷

End-of-life challenges

The diagnosis of advanced cancer may be particularly distressing for AYA. Young people have had less time to learn from other adverse life experiences to help manage the consequences of advanced

disease. They face many complex decisions but may lack the fully developed executive functioning and abstract thinking necessary for medical decision making and coping with uncertainty.⁹⁸ During young adulthood, when new parenthood is common, fears about the welfare of children and significant others and about leaving them behind may add to distress in patients facing end of life.^{99,100}

A Canadian interview study among AYA with advanced cancer aged 18-35 years, showed that patients experience their diagnosis as isolating (e.g. feeling misunderstood or alienated) and unexpected (e.g. cancer is a disease of older adults) and feel forcefully removed from the normal life trajectory.¹⁰¹ In an American interview study AYA (20-40 years) reported anticipatory grief over their life that has not yet been lived,¹⁰² a psychological state that may be difficult for AYA to process, and may be reluctant to face the irreversibility and progression of their disease.¹⁰² This may lead to delays in the receipt of appropriate palliative and end-of-life care. An American study showed that AYA (26% HM) who die in the hospital tend to utilize palliative care services very late in the disease trajectory and often undergo aggressive treatment until death is near.¹⁰³ Early use of palliative care would have great utility in providing physical, psychosocial and spiritual support.

HEALTH-RELATED QUALITY OF LIFE

The combination of trying to achieve developmental milestones while coping with a life-threatening disease may have a negative impact on the HRQoL of AYA.¹⁰⁴ Two recent review papers show that AYA with cancer experience worse HRQoL compared with a normative population.^{105,106} Studies conducted among AYA with HM support these findings.^{31,107-109} Risk factors for poor HRQoL were low socio-economic status, female sex, unemployment, high levels of distress and physical symptoms.^{31,107,109} A recent longitudinal study conducted in USA showed that most improvements in HRQoL (n=141; 11% HL, 8% NHL, 26% leukemia) take place in the first year after diagnosis,¹¹⁰ presumably once AYA have acknowledged and adapted to new life routines that revolve around treatments and visits to clinics, hospitals, and doctors' offices. In the second year after cancer diagnosis no significant HRQoL improvements were found. The transition from cancer patient to off-treatment survivor is often fraught with new challenges as AYA cancer survivors are confronted with survivorship concerns about their future lives.²⁹ AYA patients may therefore benefit from supportive care interventions administered during the second year following diagnosis to help AYA near completion of therapy [re]-normalize their lives.

HRQoL assessment in clinical practice throughout the disease trajectory is important as it can facilitate communication, improve symptom control and patient satisfaction and reduce hospital admissions.¹¹¹ In order to integrate HRQoL assessments in routine clinical care, it is essential to have measures available that capture the full range of issues relevant to AYA with hematologic malignancies. Generic HRQoL instruments (e.g. EORTC-QLQ-C30,¹¹² FACT-G¹¹³) do not efficiently capture the unique experiences of this group. Tumor-specific questionnaires (e.g. EORTC modules for lymphoma and leukemia,¹¹⁴ FACT-Lym¹¹⁵/FACT-Leu¹¹⁶) accompanied by age-specific questionnaires (e.g. EORTC-AYA)¹¹⁷ should be administered to assess the impact of treatments, provide optimal supportive care and ultimately translate into meaningful outcomes for AYA with HM.

Up to now, most studies are limited by heterogeneous study samples of AYA patients with different tumor types and sub-analyses were rarely performed. Future research should explore the specific challenges of AYA with hematologic malignancies in more detail.

DELIVERING QUALITY SUPPORTIVE CARE

AYA have often be identified as the "lost tribe".¹¹⁸ Neither pediatric nor adult oncology/hematology departments are able to provide age-appropriate care single-handedly to this group. In general, there

is strong potential benefit from closer collaboration between pediatric and adult hematologists to improve long-term outcomes.^{119,120} Studies show that AYA with cancer report high levels of unmet supportive care needs,^{35,121} especially with regard to receiving age-specific information and psychosocial supportive care.⁹² In recent years, several AYA programs were formed in an attempt to bridge the gap and address unmet supportive care needs.^{2,122-124,123,125}

Multidisciplinary supportive care

As a result of the complexity of their care, the lack of experience navigating medical systems and the variety of age-specific challenges, AYA will likely benefit from an AYA multidisciplinary team approach. In addition to routine medical professionals, this may include specialized nurses, fertility and sexual experts, dietitians, physical therapists, psychologists, and social workers.¹²⁶ Early intervention by the multidisciplinary care team is essential to provide effective (psychosocial) support to AYA including fertility and sexuality counseling, programs to maximize education and vocational functioning, concrete financial and housing support, and access to age-specific information.¹⁴ Addressing physical, psychosocial and economic challenges early in the disease trajectory will help reduce the impact of long-term effects. Supportive care for family members should also be discussed.

Given the relatively small number of AYA as part of the whole cancer population diagnosed each year, it is not realistic to expect every hospital to possess all the personnel, facilities, and components needed for the best treatment of AYA; or to create own AYA programs.¹²⁷ For community hospitals, an oncology clinical nurse could specialize as AYA nurse specialist. Nurses spend ongoing and dedicated time with patients and are therefore well positioned to support and educate them. AYA specialist nurses can provide patients with developmentally appropriate educational resources and support, are critical for managing care transitions and engaging experts from other disciplines, and could function as a resource for colleagues who are less familiar with AYA age-specific needs.¹²⁸ In complex cases, an AYA can be referred to a center with a specialized AYA program. In larger centers, an AYA clinical nurse specialist could be introduced to improve awareness of clinical trials, assist in enrolling AYA in these trials, promote multidisciplinary discussions and care, and provide access or referrals to age-appropriate psychosocial care or health-promoting interventions, altogether providing patients with a sense of continuity of care.¹²⁷

Inpatient and outpatient facilities

One of the most commonly expressed feelings by AYA cancer patients is that they do not belong to any specific group or place.¹²³ The healthcare environment can support the maintenance of a sense of normalcy by having accessible visiting hours¹⁴ and availability of dedicated, social space facilities (e.g. to play games) to suit the age-specific needs. Studies have also shown that support received from other AYA cancer patients is incredibly important.¹²⁹ Inpatient wards and social space facilities within the hospital provide AYA the opportunity to connect, share experiences, learn from each other, and feel genuinely understood.¹³⁰ This is particularly important for AYA who have to undergo extensive in-patient treatments like stem cell transplantation. For the large proportion of AYA also receiving out-patient treatment, AYA support interventions, such as face-to-face weekly meetings, online communities and retreats, have been shown to significantly reduce feelings of social isolation and improve knowledge and problem-solving skills.¹³⁰⁻¹³²

Training and education of HCP

HCP and treating institutions can reasonably be expected to have knowledge of medical and supportive care opportunities for AYA with cancer and to provide referrals to appropriate expert centers when necessary.¹²⁷ Currently, most HCP training programs do not address AYA-specific

issues, resulting in poor recognition of AYA cancer risk and an inadequate response to their physical and psychosocial needs.² An AYA module should be required for HCP of different disciplines.⁴²

Until now, several countries have made recommendations about what AYA cancer care should look like.^{2,133,134} The current AYA programs need to be evaluated in terms of improvements in patient satisfaction, HRQoL, survival and clinical outcomes (e.g. trial participation). Studies need to provide objective evidence demonstrating the efficacy of critical components of the AYA care programs in order to create evidence-based guidelines, referral pathways and education.^{127,135} In addition, the AYA oncology agenda should be moved beyond high-income countries to support those in less privileged circumstances.¹³⁶

AUTHORSHIP

O.H. performed research, analyzed data and wrote the paper. P.C.H. and W.T.A.vdG. wrote the paper

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CONFLICT OF INTEREST

None of the authors has a conflict of interest to declare

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