Palliative Care for Adolescents and Young Adults (AYAs)

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Epidemiology of Hematologic Cancers and Serious Blood Disorders in AYAs

Adolescents and young adults (AYAs) are an important population with age-related challenges that make their illness experience distinct from their younger and older counterparts. Various definitions have been used to define AYAs, although 15–39 years of age is now the standard accepted by the National Cancer Institute [1].

The three most common types of cancers in AYAs are thyroid, breast, and lymphoma [2] (Fig. 21.1). However, the incidence of hematologic cancers varies substantially within AYA cohorts. For example, leukemia and lymphomas account for 36% of cancer diagnoses in younger AYAs (aged 15–19), compared to approximately 11% in older AYAs (aged 30–39) [2]. Importantly, hematologic malignancies are also a major cause of death in AYAs, accounting for over 18% of cancer deaths in males and approximately 11% in females [2] (Fig. 21.2).

For non-malignant, serious blood disorders, exact prevalence in AYAs has not been well defined. Serious blood disorders represent a diverse diagnostic group including bone marrow failure syndromes, aplastic anemias, and sickle cell disease. Bone marrow failure peaks in young childhood due to inherited conditions, and again in early adulthood, typically due to acquired causes [3]. Sickle cell disease is estimated to affect 100,000 Americans across age groups [4] and with improvements in care, most children with sickle cell disease now survive into young adulthood [5]. This heterogenous group therefore represents an increasingly important population of AYAs with distinct needs.

It is well established that AYAs have not benefited from the same improvements in survival over the past few decades compared to children and adults [6]. Over the last 40 years, pediatric mortality rates in sickle cell anemia have declined, while AYA mortality has increased [7]. In hematologic malignancies, despite treatment advances, survival rates for AYAs have not reached the levels achieved by children [8]. These differences are partially related to unique biology, as AYAs are more likely to have unfavorable biologic features than children with the same diagnoses [9]. Additional barriers to achieving optimal outcomes include a delayed presentation [10], difficulties with treatment adherence, and limited or lack of healthcare insurance [8]. Inferior outcomes in AYAs also reflect the historical evolution of separate healthcare sectors devoted to pediatric and adult care [8]. For AYAs with sickle cell disease, the time of transition to adult care in particular is associated with increased mortality [5]. As AYAs exist on the periphery of both pediatric and adult populations, they have not represented the "typical" patient on which research efforts have focused [8]. As a result, they are also less likely to be referred to or participate in clinical trials [11]. Furthermore, AYAs, by definition, live in a period of developmental transition, which leads to countless psychosocial vulnerabilities that can impact treatment success [12].

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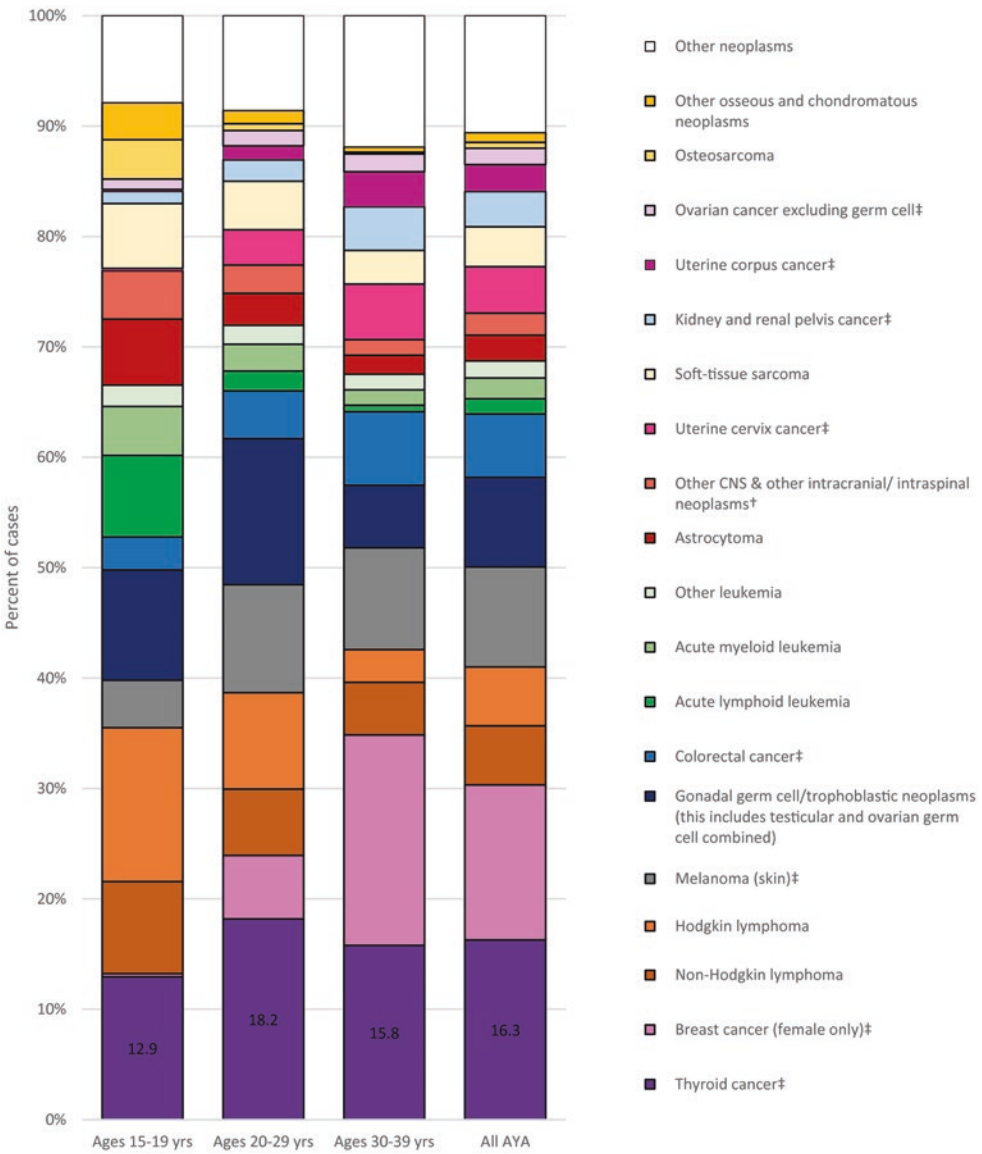

Fig. 21.1 Case distribution (%) of selected AYA cancer types by age group, 2011 to 2015 [2]. †Excludes benign and borderline brain cancers. ‡Coding for these cancers is based on Surveillance, Epidemiology, and End Results site recode International Classification of Diseases for Oncology, third edition/World Health Organization 2008 definitions. Kidney includes renal pelvis. CNS indicates the central nervous system. Source: Case distribution, North American Association of Central Cancer Registries public use database, 2018, as cited in Close A. Adolescent and young adult oncology—past, present, and future. *CA* cancer journal for clinicians 69 (6):2019

CANCER TYPE	CANCER DEATHS 2012-2016, %		AAPC 2007-2016, %[a]	
	MALES	FEMALES	MALES	FEMALES
Leukemia				
Acute lymphocytic	5.0	2.4	−0.8[b]	−2.0[b]
Acute myeloid	5.1	4.2	−0.7[b]	−1.7[b]
Brain and CNS	13.8	8.4	0.6	1.0
Colorectal	11.0	8.1	1.1[b]	0.6[b]
Lymphoma				
Non-Hodgkin lymphoma	6.0	3.2	−4.1[b]	−4.9[b]
Hodgkin lymphoma	2.0	1.3	−5.1[b]	−10.0[b]
Soft tissue	6.1	4.1	−0.3[b]	−0.7[b]
Bone and joints	5.3	2.6	0.6[b]	0.5[b]
Melanoma of the skin	4.3	2.9	−3.4[b]	−2.8[b]
Thyroid	0.3	0.3	−0.6	−1.0[b]
Kidney and renal pelvis	2.4	—[c]	2.2	−1.4[b]
Testis	4.1	—[c]	0.2	
Breast	—[c]	22.2		−0.2
Ovary	—[c]	4.6		−1.5[b]
Uterine cervix	—[c]	9.5		−0.1
Uterine corpus	—[c]	2.3		2.8[b]

Fig. 21.2 Percent of AYA cancer deaths (2012–2016) for patients ages 15–39 years [2]. Reproduced with permission of Close et al. (2019). Abbreviations: AAPC, average annual percent change; CNS, central nervous system. [a]AAPCs are based on joinpoint models using 1970 to 2016 mortality data, allowing for up to 5 joinpoints. [b]Percentages are not shown because of sparse data (<10 deaths during 2012–2016). [c]The AAPC is statistically different from zero ($P < 0.05$)

Challenges Facing AYAs with Hematologic Cancer and Serious Blood Disorders

The AYA life stage is one of transition and personal growth; it often includes finishing school, pursuing a career, and starting a family. It is typically a time of increasing independence, where youth progressively form their individual adult identities [13] and personal social networks [14]. AYAs living with chronic serious blood disorders must adapt to the challenges of emerging adulthood while simultaneously navigating the transition from pediatric to adult care. These challenges include shifting parental-AYA healthcare responsibilities, finding a new adult healthcare provider, learning the nuances of emergency care, and understanding medications and symptoms [15]. In contrast, AYAs newly diagnosed with cancer experience an unexpected disruption to their future plans [16]. These implications are far-reaching, impacting many aspects of life, such as peer relations, family dynamics, fertility, and educational plans [16] (Fig. 21.3). Rather than increasing independence, AYAs facing an oncologic diagnosis may find themselves unable to study or work, which can have long-term career implications [17]. AYAs with cancer may find themselves unexpectedly financially and physically reliant on others for their day-to-day necessities. This regressive dependency on parents or loved ones can have a significant impact on one's sense of identity [17] and lead to increased distress and decreased treatment adherence [18].

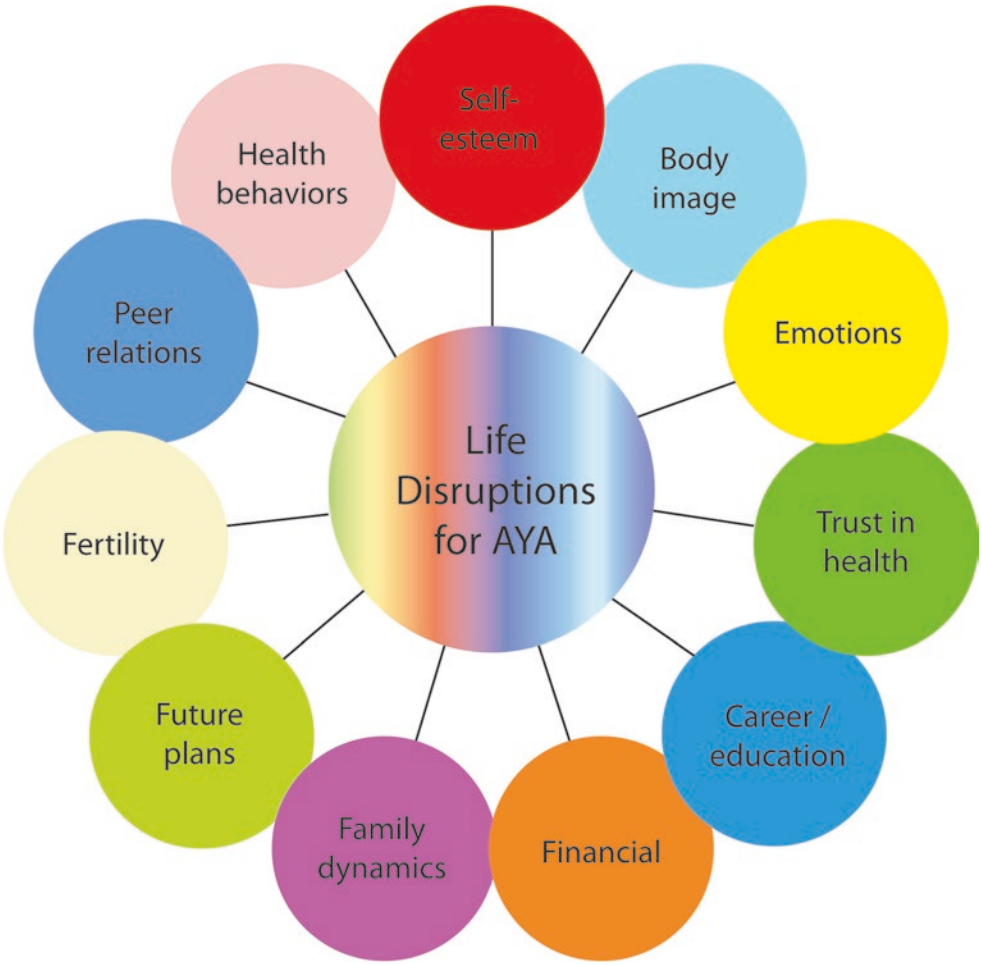

Fig. 21.3 Possible life disruptions for AYA patients with cancer [54]. Reproduced with permission from Nass et al. (2015)

Late teenage and early adult years often involve developing intimate and romantic relationships. While typical AYAs establish their own sexual identity, AYAs may face disease or treatment-related physical changes that can impact self-esteem [18]. These physical differences may impact AYAs' interest in engaging in sexual relationships and their ability to form romantic connections. Approximately half of AYAs endorse their cancer diagnosis has harmed sexual function [19]. Sexual dysfunction remains an unmet concern for many AYAs up to 2 years after diagnosis [20]. Rather than forming or building on existing relationships, AYAs may feel unable to form new romantic relationships and experience strain on existing relationships [17]. In long-term relationships, youth may question their partners' motivations to stay together and wonder if their partner is experiencing feelings of guilt and obligation [10].

Due to the transitional life stage of AYAs and challenges developing and maintaining romantic relationships, youth may reside with their parents, their spouse, or a combination. This situation can lead to various preferences for individual or shared decision-making when it comes to treatment choices [21]. Decision-making preferences are often a process, and do not abruptly change when an adolescent turns 18. Many AYAs want to make medical decisions after reflection on their parents' opinions, and others prefer shared decision-making with their spouse [21]. Some patients may bring both their spouse and parent to medical appointments with them for support. These preferences may evolve over one's illness journey, and it is important for clinicians to continually check-in with AYAs about their wishes.

The AYA life stage is also a time where healthy youth engage in experimentation and substance use. Preconceptions about substance use and misuse in AYAs can negatively impact care. Specifically, healthcare providers' assumptions about drug-seeking behavior in AYAs with sickle cell disease can lead to inadequate pain management and avoidance of emergency care [15]. There are often concerns that AYAs with cancer are at increased risk for substance abuse due to access to legitimate opioid prescriptions [22]. However,

AYAs with cancer have reported similar substance and illicit drug use as age-matched peers [22]. Furthermore, rates of opioid misuse are similar in AYAs with cancer to adult oncology patients [23].

There are also differences in how AYAs routinely interact with the healthcare system. Compared to pediatric patients, AYAs are more likely to delay seeking medical care following symptom development [10]. This delay may be related to feelings of invincibility, embarrassment, or denial [24]. AYAs also less often identify with a clear primary care clinician, leading to less frequent routine health checks [10]. In the sickle cell population, this leads to increased reliance on emergency room care during the adolescent and young adult years [25]. Furthermore, AYAs face significant challenges complying with treatment recommendations [26, 27]. As many as half of AYAs may not adhere to outpatient therapy plans [26]. Cognitive-emotional factors, lack of peer and family support, and the youth's relationship with their clinician have all been shown to impact treatment adherence [27].

Symptom Distress in AYAs with Hematologic Cancer and Serious Blood Disorders

Advanced illness in AYAs leads to symptoms of physical, psychological, and existential distress. Many physical symptoms may be similar to those experienced by younger and older populations; however, unique psychosocial factors may influence the symptom burden experienced by AYAs.

In AYAs with cancer referred for palliative care, pain is the most commonly reported physical symptom (endorsed by 91% of patients) [28]. As a result, most adolescents with cancer reportedly use pain medication at the end of life (EOL) [29]. Diminished well-being, fatigue, and anorexia are also frequently experienced (endorsed by 76%, 75%, and 67% of patients, respectively) [28]. Pain, fatigue, and edema are the most common physical symptoms reported in AYAs post-hematopoietic cell transplantation (HCT), documented in over 80% of patients in the last month of life [30] (Fig. 21.4). Compared to patients with central nervous sys-

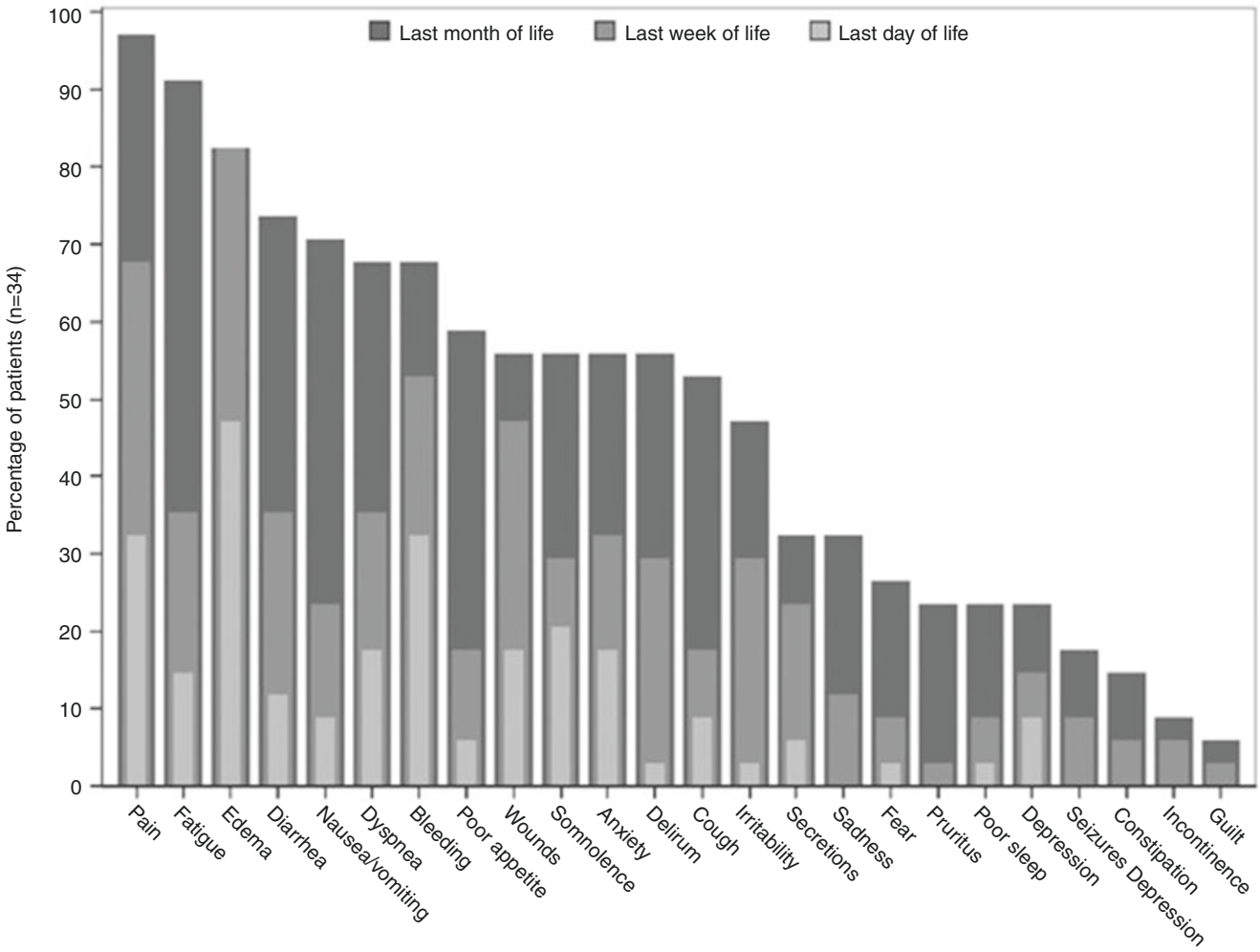

Fig. 21.4 Symptoms present during the last month, last week, and last day of life for AYA patients who received allogeneic hematopoietic cell transplant and died while inpatient at St Jude ($n = 34$) [30]. Reproduced with permission from Snaman (2017)

tem (CNS) tumors, adolescents diagnosed with leukemia or lymphoma are more likely to use oxygen at EOL [29].

In AYAs with sickle cell disease, death is often due to a sudden deterioration such as an acute pulmonary or cardiovascular event [31]. The experience of physical symptoms is therefore specific to the presenting event, such as dyspnea in acute chest syndrome, or neurological symptoms associated with stroke. Moreover, the real possibility of sudden death can lead to significant fear [32]. Psychological suffering, such as symptoms of depression and anxiety, is common in adolescents with sickle cell disease [33]. AYAs with cancer also report higher mental health concerns than age-matched peers [19]. Although feelings of anxiety, fear, and sadness are common across all ages at the EOL, AYAs experience more anxiety and depression than their younger counterparts [34]. At EOL, the use of anti-anxiety medications has been reported as significantly higher in late adolescents (aged 18–21) compared to early adolescents (aged 10–13) [29]. Anxiety and delirium were the most commonly experienced psychological symptoms in AYAs post-HCT, occurring in over 50% of patients admitted to hospital in the last month of life [30]. This pattern of increased psychological symptoms may reflect higher rates of intensive medical interventions when compared to non-HCT AYA oncology patients. Frequent assessments and prompt management of psychological symptoms in this high-risk population is essential.

Grappling with advanced illness and EOL, many AYAs also face existential distress. Rather than feelings of invincibility enjoyed by their healthy peers, premature awareness of mortality confronts AYAs with life-limiting illnesses [35]. Many adolescents also worry about being a burden to their loved ones [36]. Compared to older adults, what is important to AYAs at EOL is undoubtedly different [37]. Facing death while parenting young children, rather than adult offspring, brings a unique distress level [37]. Young adults facing EOL, who are parents themselves, often worry about being a strain on their children [38]. Processing some of these complex emotions during the experience of illness can lead to inward reflection and a search for purpose. For some AYAs who identify as religious, faith can remain a source of support and meaning, whereas others question their beliefs and faith in God [39]. Regardless of religiosity, most AYAs endorse spiritual concerns such as quests for purpose and legacy creation [39]. At the EOL, having adequate pain control, feeling physically comfortable, and finding spiritual peace, has been reported as most important for adolescents [36].

Given the transitional period of the AYA life stage, the importance of social support is paramount. AYAs with chronic hematologic conditions such as sickle cell disease, often lean on existing peer support to navigate transition [15]. Unfortunately, AYAs facing cancer frequently experience isolation from healthy peers due to their increased medical needs [40]. With advancing disease, AYAs may experience further isolation from those AYAs with cancer still pursuing curative treatment [40]. Interestingly, a study by Geue et al. (2019) found that AYAs with hematologic malignancies reported similar positive social supports to older oncology patients [14]. However, AYAs were more likely to report detrimental social interactions (e.g., people in their lives made suggestions that they found unhelpful or upsetting) than older counterparts [14]. These interactions may be related to larger social networks or less well-established social relationships in AYAs. Alternatively, it may reflect younger peer supports who are less familiar with advanced illness and uncertain about how to support their friend. Recognizing the unique social networks of AYAs and offering to help AYAs navigate those relationships is essential in providing appropriate care. Clinicians with psychosocial expertise (such as social workers) can be an excellent resource.

In terms of the care received, most AYAs are high users of medically intensive care towards EOL [13]. In the sickle cell population, compared to children and older adults, young adults (aged 22–40 years) had the highest rates of emergency room deaths, with 20% dying in the emergency room [32]. In a cross-sectional study using cancer registry data, Mack et al. (2015) explored EOL care in AYA oncology patients [13]. They found that the majority of AYAs received at least one form of high-intensity medical care in the last month of life (22% were admitted to the intensive care unit (ICU); 22% had >1 emergency room visit, and 62% were hospitalized) [13]. In their cohort, AYAs with leukemia were higher users of medically intensive EOL care than patients with soft tissue or gastrointestinal cancers [13]. Snaman et al. (2018) similarly found that nearly 80% of AYA after HCT died in hospital, and many received high-intensity care such as mechanical ventilation and dialysis in the last month of life [30]. Bell et al. (2010) looked at the EOL experience of younger adolescents aged 10–21 years [29]. They found that in adolescents who continued to receive aggressive life-sustaining measures at EOL, most were patients with leukemia or lymphoma [29]. Furthermore, more adolescents with leukemia or lymphoma died in the ICU than patients with solid tumors or CNS cancers [29]. This finding in part may be due to higher rates of treatment related mortality in AYAs with hematologic cancers. Additionally, AYAs with hematologic malignancies or serious blood disorders may have unique disease specific needs that can be challenging to manage as an outpatient. For example, AYAs with refractory leukemia may derive symptomatic benefit from frequent transfusion support that practically may not be feasible in certain community settings.

Although the use of high-intensity care has consistently been demonstrated in AYAs, it remains unclear if continued

hospitalization or medical intensive care is aligned with the goals of care of those patients that receive it. These findings emphasize the need to explore further the wishes of AYAs and optimal strategies to ease suffering.

Easing Suffering in AYAs with Hematologic Malignancies and Serious Blood Disorders

Exploring the goals of care of AYAs with advanced illness is essential to ease suffering and deliver optimal care. Numerous practice guidelines highlight the importance of the early introduction of a palliative care team to an AYA before symptom escalation or the discontinuation of curative treatment [41]. This early introduction allows for exploration of goals of care and rapport building while decreasing time pressure on challenging EOL conversations. Early introduction of palliative care is also essential for AYAs with serious blood disorders who are at risk for premature death [32]. Many patients and clinicians may want to avoid the early introduction of palliative care due to perceptions that palliative care means "giving up" or discontinuing active therapy [40]. Educating patients, families, and caregivers on an expanded definition of palliative care can help increase comfort and normalize palliative care involvement. Clinicians should highlight that palliative care focuses on quality of life, not only for the patient but the entire family [42]. The focus on quality of life is often beneficial independent of prognosis and/or treatment goals. Symptom management and EOL care are important although only partial, parts of delivering optimal palliative care.

For the alleviation of EOL pain and dyspnea in AYAs, similar to children and adults, opioids remain the mainstay of treatment [43]. Studies to date have not demonstrated differences in pharmacodynamics in AYAs compared to older adults [43]. Methadone has also been shown to provide effective analgesia of both nociceptive and neuropathic pain in adolescents with leukemia and lymphoma [44]. Consider gabapentin/pregabalin and duloxetine for neuropathic pain management, such as vincristine-related neuropathy [45, 46]. Of note, gabapentinoids require titration and time to reach therapeutic levels [47], and therefore should be introduced before the last weeks of life. In AYAs with leukemia and lymphoma, other EOL symptoms, such as bleeding, can be treated with similar strategies for younger and older patients.

To address psychological symptoms in AYAs, providing professional support through social workers, music therapists, and psychologists is invaluable [40]. Asking about an AYA's spiritual beliefs can be a helpful starting point to explore hopes and worries and to determine how to best provide support [39] (Fig. 21.5). Flexible scheduling that accommodates late awakenings in AYAs can promote connection and continuity of care [48]. Using virtual care where possible, may also decrease travel time and minimize disruption to an AYA's school or work commitments. Clinicians must also recognize the unique social networks of AYAs and find creative solutions to combat feelings of social isolation. To facilitate connection, hospice facilities should include shared spaces that promote interaction [40]. Furthermore, the innovative use of technology for video conferencing and social networking can provide an alternative medium to

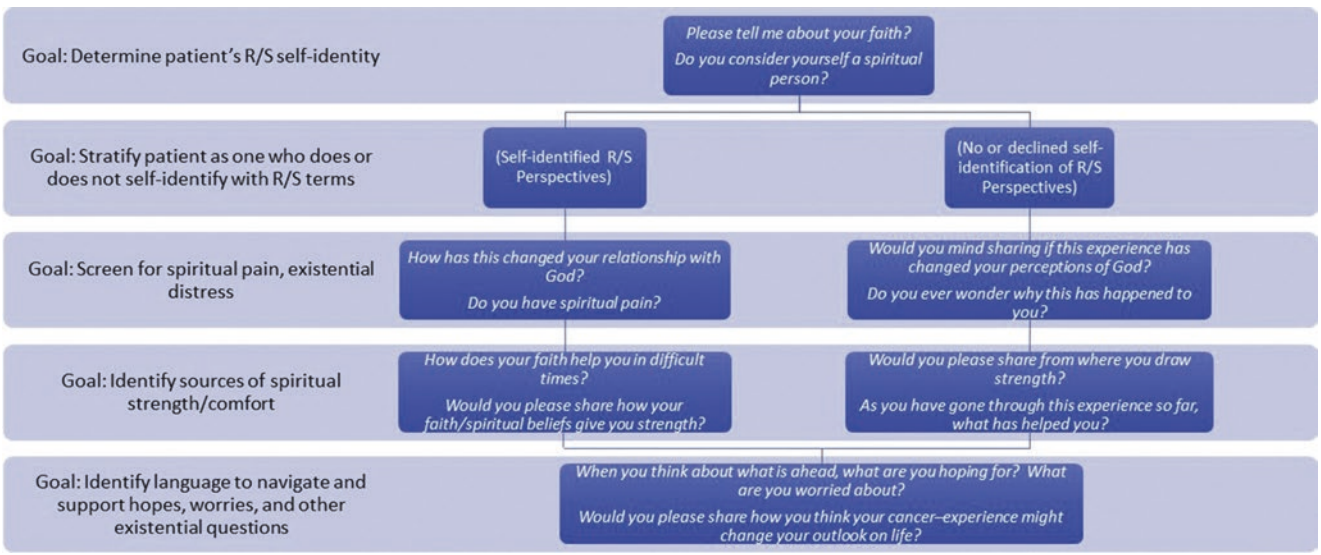

Fig. 21.5 A conceptual framework for navigating discussions of religion, spirituality, and hope with AYA who do/do not immediately endorse religious/spiritual (R/S) beliefs [39]. Italicized phrases are sample questions to use in conversation. This framework does not necessarily reflect a single discussion; rather, clinicians may use it to navigate ongoing discussions spanning screening, spiritual history taking, and assessments of religious/spiritual supportive needs. Reproduced with permission from Barton (2018)

maintain relationships between AYAs [40]. For AYAs who are parents themselves, supporting AYAs in communication with their own children is essential. Parents want assistance and resources from care providers to help explain their illness to their children [49]. Connecting families with child life and grief support specialists can help parents navigate these difficult conversations.

In addition to addressing physical and psychological symptoms, clear communication and planning around EOL are essential for AYAs. Adolescents report that honesty from their healthcare team is important [36]. However, many clinicians find EOL conversations with AYAs challenging. As experts in communication, palliative care clinicians have unique expertise in navigating difficult discussions. Involving a palliative care team also provides an opportunity for AYAs to share fears or worries that they may not wish to share with their primary treating team. Effective communication with AYAs requires recognition of the complex interaction of their social context and developmental stage [41]. First asking about an AYA's understanding of their illness and specific worries or wishes they have may provide a starting place for more difficult EOL discussions. AYAs may still be developing their cognitive capacities to reflect on EOL issues and may have limited or no experience with death and dying [41]. Recognizing a youth's developmental stage and adjusting language and concepts to their cognitive abilities is essential. Providing examples of questions other patients have asked about death and dying, and acknowledging feelings of distress in others can also normalize the experience and create a space for further discussion [48]. For example, clinicians may ask, "Other patients in a similar situation have asked me what will happen if there is progression on their next scan. Is that something you have been wondering about?" Importantly, cultural or family beliefs in protective paternalism may influence openness to involve AYAs in EOL discussions [41]. It is essential to give teens and young adults permission to be involved as much or as little as they want. Over half of AYAs express a desire to engage in shared decision-making with their healthcare team; however, some still prefer to defer to their parents [21]. Using phrases such as, "Are there things you would rather I talk to your parents about first?" can help introduce difficult conversations and honor individual preferences [50]. Recognizing the range of decision-making preferences is imperative to deliver personalized care for AYAs.

Early palliative care involvement facilitates the early introduction of advance care planning (ACP). ACP should ideally take place at diagnosis, throughout treatment, at relapse, and again at EOL [42]. Transitions in the treatment plan, such as stem cell transplant, can create a natural opportunity to discuss uncertainty and EOL [29]. Gentle but recurring ACP discussions create numerous opportunities to explore AYAs' wishes [50]. To assess AYAs' readiness to engage in ACP, clinicians can utilize the Advance Care Planning Readiness Assessment (2008) developed by Pao and Wiener [51]. The measure asks three questions:

1. "Whether talking about what would happen if treatments were no longer effective would be helpful
2. Whether talking about medical care plans ahead of time would be upsetting
3. Whether they would be comfortable writing down/discussing what would happen if treatments were no longer effective" [51].

An adolescent's answers to these questions can be a practical starting point for conversation. If adolescents report such conversations would be upsetting, allowing space and time before revisiting these topics is important. For some patients, talking in advance is unhelpful, and following the lead of each individual AYA is essential. Additional strategies to introduce and normalize discussions about EOL include the concept of parallel planning. It can help to explain that we continue to hope for the best while simultaneously plan for the rest [29]. This explanation promotes discussion without eliminating hope. This can be particularly important for AYAs who continue to discuss future plans, such as school or career goals. Remaining future oriented does not necessarily indicate a lack of illness understanding or denial. Rather, it may highlight holding hope and worry simultaneously. Again, sharing experiences of other patients can be helpful when exploring goals of care. For instance, when discussing disease progression, consider stating, "Some people say they want to be home with their family and others say it is important to keep trying new medications. There is no wrong answer here, and we will support you no matter what you decide" [50].

Initiating early EOL conversations may help ensure the wishes of AYAs at EOL are met [41]. However, evidence suggests EOL conversations are often had late in AYAs [41]. Bell et al. (2010) found that compared to those with solid and CNS tumors, adolescents with leukemia and lymphoma were more likely to have initial EOL conversations within the last 7 days of life [29]. Discussions about resuscitation also often occur late in disease progression. The authors found that in 50% of their population, donot-resuscitate orders were signed within 7 days of death [29]. Importantly, similar findings have also been shown in children [52] and older adults [53] with hematologic cancers. Compared to solid tumors, children and adolescents with hematologic cancers are less likely to receive specialized palliative care support [52]. The reasons underlying these findings in AYAs are multifold and include provider inexperience with advanced care planning discussions, clinician desire to protect the AYA and pressure from caregivers to focus on anti-cancer treatments when facing the loss of a young person.

Table 21.1 AYA Advance Care Planning Tools

Resource	Description	Link
Voicing my choices	An AYA focused advance care planning document	https://store.fivewishes.org/ShopLocal/en/p/VC-MASTER-000/voicing-my-choices [55]
Five wishes	A legal document that designates a healthcare decision-maker for EOL and medical care	https://www.fivewishes.org/for-myself/ [55]
Living out loud	An online Canadian resource with significant patient contributions and a comprehensive resource section for discussing EOL and advance care planning with AYAs	https://livingoutloud.life [56]
Together for short lives	A UK website that contains helpful resources to guide difficult discussions with AYAs	https://www.togetherforshortlives.org.uk/get-support/supporting-you/family-resources/difficult-conversations-young-adults/ [57]

The majority of AYAs express a wish to discuss EOL care in advance; however, many AYAs had never heard of an advance directive [36]. The use of ACP tools can help facilitate and structure EOL conversations with AYAs and their families [41]. Multiple tools exist and are outlined in Table 21.1.

Location of care is also a critical discussion to initiate with AYAs and their families. In a study conducted by Jacobs et al. (2015), 88% of AYAs did not know that hospice care was available or what it entailed [36]. Individual factors such as having children or elderly parents in the home may influence preferred location of care. Most adolescents discuss a preference for dying at home [36]. However, this preference contrasts findings that many AYAs receive medically intensive care in the ICU or inpatient ward in their final weeks of life [13]. This fact highlights the importance of educating patients and their families on available care options and exploring patients' wishes in advance. Only then can clinicians facilitate the care plan that most closely reflects the AYA and their family's values.

Summary

AYAs represent an important group of patients facing serious hematologic disease. Their unique position, bridging pediatric and adult populations, is associated with unfavorable outcomes and complex psychosocial challenges. Recognizing the impact of an existing serious blood disorder or a cancer diagnosis during this pivotal time of identity formation and establishing relationships is essential. Early exploration of communication preferences and goals of care can improve the care team's ability to provide personalized EOL care aligned with patient values. Many tools exist to aid the clinician in ACP and EOL discussions. Early involvement of palliative care teams can assist primary teams in navigating these difficult discussions, aid in symptom management and ensure focus on quality of life. AYAs with cancer and serious blood disorders are not simply big children or small adults; they are a distinctive group that requires customized expert care.

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