We Don't Know What We Don't Know About Adolescent and Young Adult Patients with Familial Adenomatous Polyposis-Related Colorectal Cancer

Jessica Grubman, MD,¹ and Afsaneh Barzi, MD, PhD²

SINCE THE 1970s, CANCER OUTCOMES in pediatric and adult populations have improved dramatically, while those in the adolescent and young adult (AYA) group, defined as those 15–39 years old,¹ have remained stagnant.²

AYAs face unique issues and a growing body of research advocates care tailored to this population.¹ Though a pediatric model of care is promising for AYAs with pediatric type cancers, there are no data on how to treat those with adult-type cancers such as breast and colorectal cancer, which become more common after the age of 25 years. A significant proportion of young adults with these types of cancers suffer from genetic cancer syndromes and therefore have additional stressors and care needs.

The focus here is on AYAs with colorectal cancer secondary to the rare genetic disease familial adenomatous polyposis (FAP). Much research has explored the genetics, clinical manifestations, and unique psychosocial issues of FAP patients. Although comprehensive polyposis registries exist in many countries, the authors know of no collective data examining survival and quality of life outcomes of FAP patients with colorectal cancer. Lack of data about genetic colorectal cancer in registries limits the ability to compare the outcomes of these patients with those with sporadic cancers.

Familial Adenomatous Polyposis

FAP is an autosomal dominant disease whose primary manifestation is the development of colon adenomas, which invariably lead to colorectal cancer at a mean age of 39 years.³ The incidence of FAP is estimated at 1 in 10,000, with men and women affected at equal rates.^{4,5} FAP is caused by mutations in the tumor suppressor gene APC, located on chromosome 5q21. Known FAP cases account for a small percent of colorectal cancers.

Screening of FAP kindred through polyposis registries has decreased the average age of diagnosis, cancer rates, and overall mortality in FAP patients.^{5,6} However, many young FAP patients still present with cancer. Those with *de novo* mutations or inherited germline mosaicism may not be

identified by FAP registries^{7,8}; others are lost to follow-up and miss screenings and prophylactic surgical care. Rarely, cancer may present after prophylactic colectomy.⁹

FAP as a Special AYA Cancer

Common concerns in cancer patients include changed interpersonal relationships, body image and sexuality, achievement of life goals, and existential issues.¹⁰ AYAs experience more disruption from cancer than their older counterparts.¹¹ AYAs with genetic cancer syndromes face the general issues, as well as the challenges of a rare genetic disease.

AYAs have more difficulty accepting cancer and maintaining a positive attitude, coping with side effects of treatment, and seeking support than older patients.¹² They also tend to be more self-conscious and appearance-focused, and low body image after cancer treatment hampers adjustment and contributes to social anxiety.¹³ The radical prophylactic colectomies that are a standard of care for FAP may further challenge mental health, body image, and overall quality of life.¹⁴

Although imperative to proper care, genetic testing and knowledge of having FAP may cause increased psychosocial distress. Worry about affected relatives, experience of the loss or illness of a family member with FAP, increased anxiety in relatives, and anger toward an affected parent are potential psychosocial stressors in AYAs with FAP.¹⁵ More psychiatric issues have been found in children and AYAs with FAP than in the general population.¹⁶

Cancer-related infertility and sexual dysfunction can also be detrimental to mental health and adjustment of AYAs, and family planning is an especially salient issue for patients with genetic cancer syndromes. Anxiety about passing a mutation to children is a major source of long-term distress in many individuals with FAP.¹⁷

AYAs also have more difficulty dealing with the impact of cancer on work life than older patients,¹¹ who generally have fewer time commitments and stresses on their resources.¹⁸ Staying involved in work and school decreases social isolation, and improves self-esteem and quality of life. However, a

¹Department of Obstetrics/Gynecology, University of Texas Southwestern Medical Center/Parkland Memorial Hospital, Dallas, TX.

²Department of Hematology/Medical Oncology, Keck School of Medicine of the University of Southern California, Los Angeles, California.

majority of AYAs report that cancer negatively impacts their career and education plans.¹⁹

Health insurance is another major concern for AYAs. Lack of insurance is a detriment to overall health and a determinant in cancer course. The Affordable Care Act will allow previously uninsured young adults to pursue healthcare. However, young adults still have low rates of health insurance, tend to have lower compliance and be lost to follow up, and remain vulnerable to illness-related losses of income and education.

Pitfalls and Proposals for Better Care

AYAs represent a unique patient population that deserves age-appropriate medical and psychosocial care. AYAs tend to be treated in different centers by pediatric, adult, or surgical oncologists with no standard treatment protocols and few age-specific resources.² Lack of clinical trial enrollment is one of the largest obstacles in AYA cancer care. Reasons for low AYA participation on clinical trials include insurance barriers, treatment at community versus academic centers, and lack of AYA-focused trials.²⁰ Less than 10% of 20–30 year olds participate in trials,²¹ likely a lower proportion of patients with rare cancer syndromes. In contrast, up to 70% of pediatric cancer patients enroll in clinical trials, and survival advances have paralleled the outcome improvements reported by trials.²²

Hereditary cancer syndromes in AYAs have been especially overlooked. Evidence suggests younger colon cancer patients tend to present with higher stage and have a lower 5-year survival.²³ Despite these differences, treatment regimens are the same for colon cancer patients of all ages, and the difference between sporadic and FAP-related cases is not clear.

Care for AYAs with cancer should be implemented on a broad scale, encompassing education of primary care physicians and adult and pediatric oncologists and broader modes of communication between these physicians and AYA cancer specialists. Many barriers have prevented extensive AYA-focused care in the United States, including funding deficits, organizational issues, and resistance to a new specialty,²⁴ but several major academic institutions have recently launched AYA programs. These programs focus on AYA cancer research as well as specialized AYA clinical care and support, for instance “AYA@USC,” a partnership between the Norris Cancer Center at USC and Children’s Hospital Los Angeles.

Although the academic AYA cancer programs are focused on innovative and collaborative research, the academic model reaches a limited patient and physician population, and developing protocols is not currently feasible given the low number of cases in each center.

Since the distinction between sporadic and FAP-related colon cancer is not made in cancer registries, long-term cohort studies on FAP cancer survivors have not been conducted. Collaboration with other research institutions is proposed to create a database of colon cancer patients with FAP. Establishing a database of FAP-related colon cancer cases would bring attention to this disease, and could increase physician referral of patients to FAP-specific resources. Likewise, cross-referrals between the FAP registry and the existing FAP kindred registries would facilitate better patient care and participation in studies. Creating a database of FAP

patients with colorectal cancer would allow research on tumor biology, as well as psychosocial needs of this specific AYA population. Conducting such studies would potentially be of great benefit to young FAP patients with colon cancer. For example, the interaction between treatment and Lynch syndrome in response to chemotherapy and targeted agents is well established.²⁵ Such knowledge for FAP patients is unknown. In the proposed database, patients with colorectal cancer who receive chemotherapy could be captured, and it could be determined if the response rate or duration of response to chemotherapy in FAP patients is different from that in non-FAP patients.

These FAP-focused studies should come as part of a broader focus on AYA cancer care with greater attention to the issues discussed above. Ideally, FAP patients will benefit from a more age-appropriate, tailored care model, which includes research and resources for AYAs with rare hereditary cancers.

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Address corresponding to:

Jessica Grubman, MD

University of Texas Southwestern Medical Center/

Parkland Memorial Hospital

Department of Obstetrics – Gynecology

5323 Harry Hines Boulevard

Dallas, TX 75390-9032

Email: jessica.grubman@phhs.org