REVIEW

Cancer centers of excellence for the multidisciplinary management of urologic cancers

The intersection between education, research, and healthcare

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ABSTRACT

Urologic cancers are among the leading causes of morbidity and mortality in the world, representing more than 10% of the total number of new cancer cases worldwide. These complex diseases are linked to several issues related to their diagnosis, management, monitoring, and treatment — issues that require multidisciplinary solutions that encompass and manage patients as complex entities. In response to this, the so-called cancer centers of excellence (CCEs) emerged, defined as multidisciplinary institutions specialized in the diagnosis, management, monitoring, and treatment of specific diseases, including cancer. Different institutions, such as the European Association of Urology (EAU), have proposed and encouraged its consolidation, especially for the management of prostate cancer. These institutions must be composed of three areas: healthcare, education, and research, which have complementary interactions and relationships, stimulating research and problem-solving from a multidisciplinary approach and also covering elements of basic science and mental health. The implementation of these CCEs has generated positive results; therefore, it is necessary to stimulate their implementation with a uro-oncologic approach.

INTRODUCTION

Cancer is a chronic, non-communicable disease characterized by uncontrolled cell proliferation and the lack of an efficient immune response.[1] It is a multifactorial disease, physically and emotionally impacting patients, family members, and/or caregivers.[2] Urologic cancers involve organs of the genitourinary system, such as the bladder, prostate, kidney, testicles, penis, and urethra, affecting both men and women.[3] The International Agency for Research on Cancer (IARC) estimated a high incidence of urologic cancer cases worldwide; therefore, these diseases have among the most significant economic impact and strain on healthcare systems, especially in high- and middle-income countries.[4]

Urologic cancer is a complex disease that can be studied in four stages: prevention, diagnosis, prognosis, and treatment. These four phases are complementary and transversal in the life of a patient. Each phase has limitations or problems that have been discussed over time and require a solution that has a multidisciplinary approach. In prostate cancer prevention, for example, several risk factors have been identified, increasing the chance of developing the disease: genetic predisposition,[5] an unbalanced diet,[6] and excessive consumption of alcohol and tobacco.[7] Being a multifactorial problem, its solution must be multidisciplinary since the individual must be addressed

in each one of its facets, using different disciplines.[8] Only a multidisciplinary approach, which may involve nursing, psychology, social work, genetics, nutrition, epidemiology, and/or general medicine, would make it possible to change the modifiable risk factors that reduce the yearly number of cases.

In the case of prostate cancer diagnosis and prognosis, there is currently a low rate of early diagnosis. In most cases, this leads to disease identification when it is advanced, making it difficult to establish a timely treatment plan that prevents complications.[7] This problem demands the formation of a multidisciplinary team that encompasses both basic and clinical science and allows the identification of new biomarkers that work for early diagnosis and establishment of risk, allowing the specialist to estimate a patient's prognosis.[9] In such cases, the urology specialist's field of action and knowledge is limited to covering specific elements, such as bioavailability, formation, and excretion cycles of measurable molecules, and applying techniques that allow their identification and quantification with high sensitivity and specificity.[10] Furthermore, this type of research will reduce the routine use of invasive standardized tests[11] for diagnosing various urologic cancers, reducing the psychological burden of patients with suspected urologic cancer.

A multidisciplinary team would allow the creation and standardization of new therapies or pharmacological treatments that combine basic and clinical science and help formulate new alternatives for patients with atypical cases or who are resistant to routine treatments.[11] Because these problems require a multidisciplinary intervention for an efficient solution, the approach and construction of a cancer center of excellence (CCE) takes strength; this is a specialized and multidisciplinary space that provides comprehensive care, supporting research, and educational instruments for solving problems related to cancer.[12]

Therefore, and based on the need for multidisciplinary teams that provide comprehensive care to a patient with urologic cancer, we aimed to review the multidisciplinary management of patients in uro-oncology, taking as an example the usefulness of CCEs in covering three main areas: education, care, and research.

EPIDEMIOLOGY OF UROLOGIC CANCERS

Urologic cancers represent 12.6% of the total cancer cases reported worldwide, with an estimated 2.5 million cases; exceeding the annual number of breast cancer cases (2.2 million) annually.[13] Prostate cancer is the most common urologic cancer and the fourth most common type of cancer in the world, with an average of 1.4 million cases and 375 000 deaths reported each year, mainly in Europe (473 344) and North America (239 574).[14] Bladder cancer follows, with an average of 573 000 cases and 212 536 associated deaths reported per year.[15] In third place is kidney cancer and renal pelvis carcinoma with 431 288 cases and 179 368 deaths,[16] and in fourth place is testicular cancer with 74 458 and 9934 deaths.[17] The least frequent is penile cancer, with 36 068 cases and 13 211 deaths.[18]

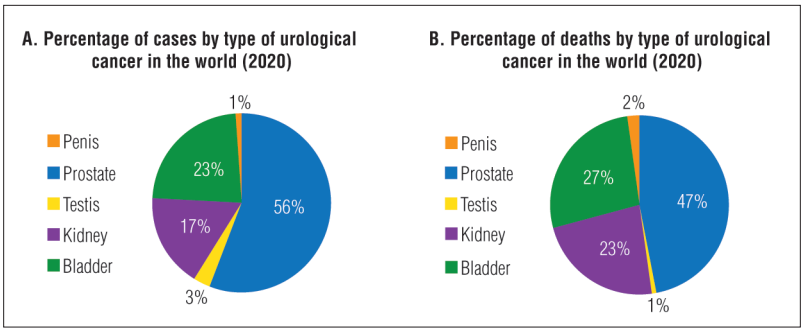

Figure 1. Epidemiology of urologic cancers in the world 2020. (A) Percentage of reported cases, in both sexes, of primary urologic cancers. (B) Percentage of associated deaths by type of urologic cancers in both sexes.

The highest fatality rate for 2020 is kidney cancer at 42%, followed by penile and bladder cancer at 37% each. Prostate cancer has a fatality rate of 27% and testicular cancer of 13%; these fatality percentages must be considered because each type of urologic cancer has a different percentage of adverse outcomes, and therefore, multidisciplinary interventions must be directed accordingly. The following figure summarizes the percentage of reported cases and deaths by type of urologic cancer, according to the IARC (Figure 1).

Latin America is considered an emerging region due to the increase in the reported number of cases of urologic cancers;[19] by 2020, almost 302 992 cases and 90 112 deaths were reported, with an overall fatality rate of 27.7%.[13] The magnitude of these cancers places urologic cancers among the leading causes of consultation, morbidity, and mortality in the world, generating an increase in the cost of health services and a decrease in life expectancy, especially in low- and middle-income countries.[4] This problem must be considered to stimulate the formation of multidisciplinary teams, which cover a complete panorama and allow the generation of valuable proposals to improve the lives of people with urologic cancer.

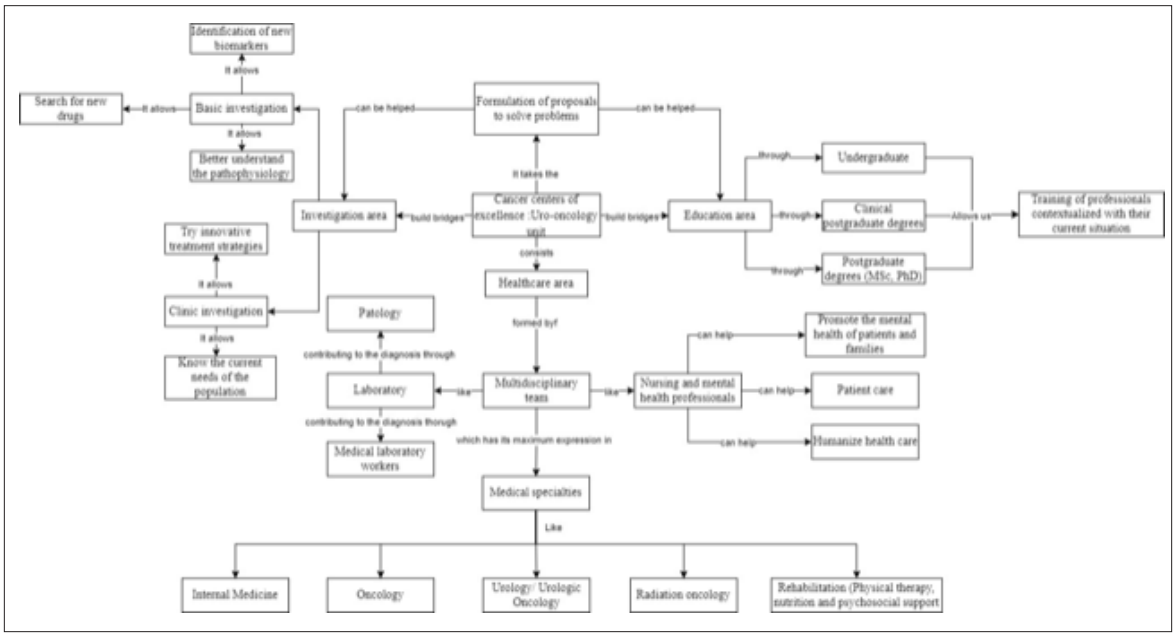

Figure 2. Mind map of the working relationship between the uro-oncology units of the cancer centers of excellence and the healthcare, educational, and research areas.

A MULTIDISCIPLINARY TEAM: THE ROLE OF CANCER CENTERS OF EXCELLENCE

The multidisciplinary approach to cancer diagnosis, prognosis, and treatment is not new, but its systematic implementation and functionality are still lacking in many countries.[20] Currently, a multidisciplinary approach has been widely implemented in hospital centers of level 3 and above, including a so-called "tumor committee," which is a team composed of different medical-surgical and nursing specialties that discuss and evaluate cases of cancer with or without a definitive diagnosis to establish a clear path of care and appropriate intervention. Traditionally, this committee may be composed of two committee representatives (physicians), one representative from each medical-surgical specialty associated with the cancer case to be evaluated, two oncologists, a mental health professional, nursing staff, and two cancer researchers (epidemiologists or basic science), among others.[21] Implementing these committees has brought many benefits to patients' health since each patient's case is analyzed with a broader view, allowing more precise and efficient interventions.[20] Despite this, the tumor committees only cover the care area (hospital) and leave out educational and basic research, which are exclusive and, therefore, not genuinely interdisciplinary.

A Cancer Center of Excellence (CCE) is defined as a highly specialized and multidisciplinary space that provides quality and humanized care to patients suffering from an oncological process. It should be clarified that the centers of excellence are not exclusive to oncological treatment and can include surgical specialties, such as orthopedics, thus becoming reference centers.[8,22] These centers do not function as regular hospitals, but as centers specialized in the diagnosis, treatment, and management of patients withoncological diseases. Centers have tumor committees made up of representatives from different surgical specialties,[12] oncologists, and nursing specialist, unlike those who have more interaction with academia, to propose both basic and clinical research to improve some of the areas of cancer care. The CCEs function as specialized units for the comprehensive management of patients with urologic cancers and build bridges allowing integration with academia and research. The following figure represents CCEs' interactions for managing uro-oncology patients (Figure 2).

As can be seen, CCEs are the center of the multidisciplinary team and are related to its three main components: education, research, and healthcare. This approach is much more complete because it not only stimulates comprehensive patient care; it also allows healthcare professionals to analyze and refer to the situation to stimulate research that allows them to better understand the illness and propose alternatives that improve the situation. This is done under the strict rules of ethical approval of research and work with humans,[23] respecting the integrity, will, and life of the people whom the CCEs treat.

The implementation of CCEs is not new for the comprehensive management of patients with urologic cancers; the European Association of Urology (EAU) has proposed their creation and implementation for the comprehensive management of patients with prostate cancer, as it is the most prevalent urologic cancer in the world. The EAU has even published a list of minimum functionality and quality requirements for its operation. For a CCE to function, it must be composed of three elements or areas: a clinical or healthcare area, an education or educational area, and a research area; each with a series of requirements and minimum quality standards that allow its authorization and accreditation.[8] We will explain these elements in detail below.

Table 1. Minimum characteristics necessary for constructing a CCE for urologic cancer according to the EAU

	Healthcare area	Educational area	Research area
Main features by area in a CCE for uro-oncology	Medical specialties: Urologist, radiation oncologist, medical oncologist, pathologist, and radiologist	Programs for training specialists such as urologists and oncologists	Projects that allow the publication of at least 1 scientific article per year
	Associated services: Nursing, psychology and mental health, physiotherapy, sex therapists, physical therapists, and palliative care specialists	MSc and PhD programs, either at the center or in alliance with local universities	Ethics committee that guarantees the integrity of the participants and allows their active participation in research projects
	Diagnostic routes: Standard tests for diagnosis, monitoring, and prognosis	Undergraduate student bonding	Projects led by a principal investigator who follows up and encourages the involvement of others
	Clear treatment route: Options, alternatives, and treatments certified by national or international regulatory bodies	Research projects that link students in training	Support integration and multidisciplinary work

CCE: cancer center of excellence; EAU: European Association of Urology.

THE HEALTHCARE AREA

The main characteristic of a CCE is that it must have a multidisciplinary team that allows the disease to be covered from a physiological, psychological, and social point of view.[24] The EAU recommends inclusion of the following professionals: a minimum number of different specialist physicians, including a urologist, radiation oncologist, medical oncologist, pathologist, and radiologist; associated services such as nursing, psychology and mental health, physiotherapy, sex therapists, physical therapists, and palliative care specialists; diagnostic routes that include standard tests for diagnosis, monitoring, and prognosis; and a clear treatment route offering options that are certified by national or international regulatory bodies.[8] In addition, the CCE's healthcare area must include facilities that comply with all the regulations of to the country where it is located; and have a space that allows patients to gather, be listened to, and actively participate in all the activities carried out by the hospital center. The patient's comfort must be prioritized in the architecture of the space, also incorporating stimulating spaces for recreation and leisure.[22] There must also be spaces for academic discussion that allow interaction between professionals to formulate ideas, projects, and strategies for comprehensive care for patients with oncological diseases.[22]

Among the countries that have approved the formation of CCEs is the United States. Since 2017, the construction of these centers has been regulated, which has increased the focus of resources and efforts for testing new oncological therapies. This allows cost reduction and increases the number of clinical trials, since it is easier to identify individuals.[25] The interdisciplinary conversation between professionals that characterizes CCEs has had positive effects in social contexts, increasing and focusing efforts to identify cases of cancer in ethnic groups and/or minorities that, due to structural conditions of society, have been underdiagnosed or not treated in traditional hospitals. Thanks to CCEs, the rate of participation of African Americans in cancer studies in the U.S. has increased from 5% to 13.3%, guaranteeing better representation of the disease in this population and consideration of specific variables that may influence treatment decisions.[26] It has also contributed to reducing economic inequalities in accessing cancer treatment, especially in low-income countries such as Rwanda and disadvantaged populations such as children, focusing resources more efficiently and reducing the final cost to the patient, increasing accessibility to a larger population.[27]

Despite all the benefits CCEs have brought, several limitations have also been identified. For example, in emergencies such as the SAR-COV2 pandemic in 2020, many CCEs in Germany were not prepared to face a new form of care, generating a 21% decrease in the provision of care and treatment of different oncological processes.[28] It also led to flare-ups and recrudescence of the disease in patients, with severe consequences. However, the pandemic generated problems and altered patient care worldwide. It is nonetheless essential to mention it, since CCEs must reformulate their strategies for monitoring and providing care if a similar situation is repeated. Another of the main limitations of CCEs is that, like a traditional clinic or hospital, they only

offer treatment for widespread situations, ignoring treatment for people with rare diseases or uncommon variations in developing countries. Developing a few centers of excellence would further limit care coverage and the marginalization of cases.[29] The following table summarizes the main characteristics that a CCE must have, focusing on the comprehensive management of patients with urologic cancers in keeping with the recommendations of the EAU (Table 1).

THE EDUCATIONAL AREA

The EAU proposes that CCEs focused on the comprehensive management of urologic cancers should help train young doctors and researchers, stimulating their research interests. A minimum of one year of training should be proposed, entailing either exclusively clinical management for one year, or two phases: six months of comprehensive and clinical management of patients with urologic cancers, and six months of basic research. One year of basic research must be stipulated for the other members of the interdisciplinary team who are not doctors or health professionals caring for patients. For urologists being trained at a CCE, the EAU establishes that they must receive training in basic urology, oncological medicine, and oncological radiology.[8] To do this, principal researchers must have active research projects once the students enter, and function as mentors or guides for doctors or researchers in training. These projects may have a clinical or primary focus and must be linked to some activity. This is what CCEs do in the comprehensive management of patients with urologic cancers.

The CCEs become training institutions for professionals in various fields, allowing training at almost all levels of university education from undergraduate to clinical graduate degrees, such as specialties in urology, urologic oncology, oncology, or radiation oncology, including MSc and PhD degrees. This training can be focused on different areas, such as palliative care, mental health promotion, and basic and/or clinical investigation.[30] The CCEs offer comprehensive training to urologists and oncologists through internships. For example, in the U.S., different institutes offer training in managing urologic cancers through developing surgical skills, treatment alternatives, and the study and management of rare variations of urologic diseases or sporadic cancers.[31] For example, among urologic cancers, the rarest of all are penile and urethral cancer; it is estimated that only 17% of urologists manage to treat at least one case in their first five years of professional practice. Therefore, CCEs specialized in the comprehensive management of penile cancer have become an excellent option to train urologists capable of treating any patient with uro-oncological problems.[30,32] It also stimulates residents and professionals to enter the area of research by linking their academic training with problems that require a solution.

Nursing is the cornerstone of intensive care, palliative care, and mental health in patients, companions, and family members. The linking of undergraduate and graduate students in nursing has yielded positive results,[33] as it stimulates their education in primary and secondary disease prevention and provides training for specialists in oncological and other areas or care. For MSc and PhD students, the alliance with universities can be critical in the initial stages; however, it is possible to complete these types of graduate courses in the same centers. For example, research centers in the U.K. offer their master's programs in oncology with both clinical and basic science approaches,[32] having advantages in locating patients with particular characteristics around which projects can be developed.

Little is known about the advantages and learning that undergraduate students would have; however, it is known that institutions such as Florida Atlantic University invite their undergraduate students in health sciences to participate in the center's activities to learn about the management of patients with complicated diseases, stimulating their interest in research in basic or clinical sciences.[34]

Because CCEs are centers for comprehensive patient care and management, all their care protocols must be based on the most recent clinical guidelines for urologic care and endorsed by urology/oncology societies recognized by state organizations. These guidelines must be discussed with the personnel and ratified by experts that guarantee compliance with the highest quality standards.[8,35] One of the main limitations of CCEs with regard to education is the lack of communication between the various actors involved in education, especially if the entry of university institutions into multidisciplinary work is proposed. While communications between educational health professionals and universities have improved, there is still much to work on.[36]

THE RESEARCH AREA

Although education and research go hand in hand, they are different. On the contrary, they are complementary, further explaining interdisciplinarity's importance. The EAU also establishes a series of considerations that must be considered for the opening and functioning

of the research area; among them the collection of information on treated individuals, discriminated by type of cancer, evolution, treatment, followup, interventions, and outcomes, to provide important information that allows decisions to be made based on collected evidence.[8] As in the educational area, universities have an essential role in countries like Colombia, since they are the leading research centers and those that produce most of the country's knowledge. In addition, they have overseen the appropriation of social knowledge and its dissemination to different communities.[37]

Research in CCEs can have three main focuses: basic, translational, and clinical investigation.[8] On the one hand, basic research focuses mainly on the search for valuable elements that allow support for the diagnosis and treatment of different urologic cancers, either through the identification of new biomarkers that help identify early cases of different types of urologic cancers, improving the prognosis of patients and reducing the possibilities of complications associated with the oncological process. Several studies have been developed to support the diagnosis of different urologic cancers, such as the implementation of CRISPR as a screening test for the detection of prostate cancer,[38] and the use of microRNAs as potential markers for prognosis and diagnosis of prostate[39,40] and bladder cancer.[41] All these elements include tools provided by the basic sciences. Therefore, forming multidisciplinary teams that allow the participation of biologists and basic science researchers is essential.

On the other hand, we have clinical research, which allows the application and evaluation of different elements related to the oncological process, mainly the evaluation of treatment efficiency and effectiveness; this branch of research, although it is also multidisciplinary, must be headed by medical specialists and can serve as a complement to the basic one by functioning as an applicator of its proposals. The CCEs become specialized centers for applying randomized clinical trials since they allow for identifying, characterizing, managing, and monitoring patients with oncological diseases. This would help us better understand their disease and propose solutions that improve their quality of life.[29] These projects can focus on different types of urologic cancer. They could allow the evaluation of the safety of certain medications or compounds that would serve as pharmacological[42] therapies, all under the strict supervision and approval of an ethics committee.

Globalization and the connection of people have led to the globalization of research and the exchange of ideas and resources between researchers. Thanks to this, the exchange of research in public health has been allowed, allowing us to improve the conditions of life of patients with urologic cancers in countries that do not have the resources to implement such complex clinical trials.[43] Translational research has had positive effects, especially in countries with little human capital, since it allows the mobilization of researchers for collective learning and the building of support networks that improve the living conditions of patients suffering from similar situations and, therefore, stimulating interdisciplinary research.[44]

Publications are a mandatory criterion to guarantee quality in the educational and research area in a CCE; it is mandatory to produce at least one publication per student during their period.[8] To achieve this objective, there must be monitoring by the mentors and a commitment by the students to begin proposing ideas, writing articles and projects, and publishing them. Universities are the main, or in some cases only, centers of research; both clinical and basic; especially in low- and middle-income countries, which do not have significant industrial progress.[45] Therefore, the alliance between CCEs and universities in Colombia seems to an ideal option to stimulate and promote comprehensive research.[12] For example, the alliance between public universities and university hospitals has allowed the comprehensive training of multiple professionals in the health area, and stimulates both clinical and basic research for the understanding of different diseases; they play and would play a fundamental role in the consolidation of CCEs,[46] strengthening their competencies in basic and clinical research and providing experience, facilities, equipment, and personnel.

CONCLUSIONS

Urologic cancers are complex to diagnose, manage, and treat; therefore, they require comprehensive multidisciplinary management that guarantees the highest possible quality standards of care. In addition, CCEs become an attractive alternative that allows not only a multidisciplinary approach, but also stimulates the entry of academics and research into the discussion, allowing to solve problems seen while treating patients with urologic cancers.

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