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Palliative Care in Colorectal Cancer

Ricardo Caponero

Abstract

Approximately 25% of patients present with liver metastases at the time of the first diagnosis and up to 50% will further develop recurrence in the liver during their disease course. Traditionally approached surgically, by resection of the primitive tumor or stoma, the management to incurable stage IV colorectal cancer patients has significantly changed over the last three decades and is nowadays multidisciplinary, with a pivotal role played by chemotherapy. Most patients with stage IV colorectal cancer have a poor prognosis, but numerous palliative modalities are available today. When a cure is no longer possible, treatment is directed toward providing symptomatic relief. Good symptom management in oncology is associated with improved patient and family quality of life, greater treatment compliance, and may even offer survival advantages.

Keywords: palliative care, supportive measures, symptom control

1. Introduction

Cancer is a major public health problem worldwide, and colorectal cancer is the third most diagnosed cancer among both men and women in the United States [1], Brazil [2] and, overall, it is the third more frequent malignant disease around the world (1.85 million of new cases/years; 10.2% of total malignancies), with a 2.27% cumulative risk of onset between 0 and 74 years [3].

The mortality from colorectal cancer varies with several factors from the genetic variations of disease to the developmental status of a nation. Tumor staging remains the main prognostic factor.

The last two decades have seen substantial progress in the treatments to metastatic disease offering significant improvements in survival. According to SEER, the 5-year relative survival rate for patients diagnosed from 2008 to 2012 was about 64% for all stages taken together, and it was 14% for patients with metastatic disease [4].

At the time of first diagnosis, approximately 25% of patients present stage IV, with liver metastases, and up to 50% will develop recurrence in the liver during the disease course [5]. Most of these patients have liver metastasis considered unresectable at presentation [6], but about 20–30% of patients have a resectable disease that is confined to the liver [3], and despite a metastatic diagnosis, a half these of patients may benefit from the surgical resection of liver metastasis with curative intent, with improvements in a 5-year survival [7].

Colorectal cancer survival disparities are largely driven by socioeconomic inequalities that result in differences in access to early detection tests, refinements in molecular diagnosis, and the receipt of timely, high-quality treatment [8].

Today, the median overall survival for patients with metastatic colorectal cancer being treated both in phase III trials and in large observational series or registries is about 30 months and is more than double that of 20 years ago [9]. These patients with unresectable disease remain incurable and the treatments are mainly palliative.

We performed a non-systematic literature review of the results of a search in PubMed® with terms “palliative care” and “colorectal cancer” published in the last 5 years without restrictions of language. We found 304 articles that were manually selected for reading and synthesis of this work.

2. Palliative care

Palliative care has appropriately been receiving increased attention in recent years, due to better comprehension of this field of action and due to incremental costs of antineoplastic therapy disproportionated with clinical results.

From practical standpoint, therapy is considered palliative when resection of all known tumor sites is no longer possible or advisable and chemotherapy have limited benefit rate. Since a cure, as commonly defined, is not possible, the goal of treatment and eventually the success of therapy become judged by the control of symptoms and alleviation of suffering, not more by survival advantages or longer disease-free intervals [10].

Providing optimal palliative care for the patient with advanced colorectal cancer is a complex and challenging process. The success rate depends on proactive multidisciplinary interventions, taken early in metastatic disease [11].

Palliative care can improve all phases of the disease, it allows better decisions in the end-of-life care and potentially reduces health-care expenditures, but the exact understanding of commonly used terms such as “supportive care,” “symptom control” “palliative care,” and “hospice care” was rarely and inconsistently defined in the palliative oncology literature [12].

The roots of palliative medicine may be traced since Hippocrates through medieval medicine until a more recent approach of Cicely Saunders and to a new concept of modern palliative care. It has evolved from a philosophy of care for the dying to an interprofessional discipline that addresses mainly the quality of life for patients and their families throughout the disease trajectory [13].

The best palliative care will ever require a multidisciplinary approach where treatment plans will be made in accordance with the wishes of the patient and his family with a goal of decreasing morbidity and focus on improving quality of life by addressing their physical, emotional, and spiritual needs, and on supporting their families [14].

The provision of optimal palliative care for these patients is a compound and demanding process and becomes more challenging when an incurable and asymptomatic primary progress to advanced metastatic colorectal disease [15].

Surgical resection may provide good palliation of symptoms and prevent future tumor-related complications as we saw before [15].

Better than dividing patients into strict treatment protocols and different models of care, this new concept supports the provision of patient care by a single discipline comprised of a team of health-care professionals with expertise in symptom management, psychosocial care, spiritual support, caregiver care, communication, complex decision-making skills, and end-of-life care [16].

The need for incorporating palliative care into routine oncology practice is still enormous, but the benefits of doing so are even more significant. Outside United States and some places in Europe, financially strained health systems will need cost-effective models of palliative care delivery. As the aging population increases, the

number of people diagnosed with cancer, and degenerative disease will increase, raising the need for this kind of approach.

As we see in the United States, as the cancer population grows, an already limited oncology workforce will be further strained. Cost- and resource-effective models of palliative care delivery will be required.

Volunteer work fills a large part of these gaps and can be the way out to overcome difficulties in access and funding [17], but adequate training of volunteers is essential to obtain the appropriate level of performance [16].

Community involvement needs to go beyond resource mobilization. In the current context of health systems, reaching higher levels of participation, involving the community as a partner in the implementation and support of these projects is something more complex and more difficult to achieve. Common barriers include the lack of mandatory preparatory work to understand the community's social and political dynamics, the facilitators' values and agenda [18].

Public expectations will rise and require that expectations will rise and require that palliative care be well integrated into all oncology care settings. All these factors will serve to promote the integration of expectations of a new way of oncology care.

The most important goals of palliative care are establishing a good communication and offer an outstanding symptom control. Without adequate symptom control, no psycho-emotional measures can be adequately developed.

3. Symptoms of advanced disease

Initial symptoms vary from mild anemia to bowel obstruction. In extremis, two main situations are considered, asymptomatic (or minimally symptomatic) and severely symptomatic patients needing aggressive management, including emergency cases [9].

For a significantly part of symptoms or complications, the main treatment approach is surgery, by resection of the primitive tumor or stoma, eventually resection of liver metastasis, combined with radiotherapy (for rectal cancer) and chemotherapy (adjuvant or for metastatic disease).

Beyond surgery, the management of metastatic disease has significantly changed over the last three decades with the incorporation of antiangiogenics (bevacizumab and panitumumab) and anti EGFR1 agent (cetuximab), and more recently, immunomodulation with anti-PD1 and Anti PD-L1 agents. Nowadays the multidisciplinary approach is essential [19].

Emergency management of colorectal cancer patients still represents a major issue and is associated to high morbidity/mortality, and where there was often no time for patient directives to be established. The two major situations are obstruction and massive bleeding. Perforation is a rare presentation [20]. For these situations, palliative surgery may be the most appropriate approach.

Obstruction is traditionally approached surgically by colonic resection, stoma, or internal by-pass or a stenting [21].

Bleeding may be managed by surgery or less invasive approaches, including radiotherapy, laser therapy and other transanal procedures [12].

Perforation is associated with the highest mortality and remains mostly matter for surgeons, by abdominal lavage/drainage, colonic resection and/or stoma [11].

In cases of more advanced disease, patients may present with jaundice (due to liver metastasis or biliary tract obstruction) or malignant ascites. As the number of patients with malignant distal biliary obstruction who will undergo curative surgery is limited, endoscopy has a crucial role in palliation [22].

Biliary obstruction was most common cause of jaundice, and standard techniques of biliary cannulation by endoscopic retrograde cholangio-pancreatography are the main treatment option. When it fails, endoscopic ultrasound-guided biliary drainage is a better option compared to percutaneous drainage [23].

Biliary obstruction can be the presentation of an advanced stage of disease. Median overall survival after onset of jaundice was 1.5 months but may improved to 9.6 months in patients submitted to a biliary decompression who were able to receive further chemotherapy. Jaundice due to metastatic colorectal cancer is often an ominous finding, representing aggressive tumor biology or exhaustion of therapies [14].

Jaundice represents a major concern for patients, from the unpleasant feeling of itching and to the limitations of social interaction because the change in color of the skin.

Malignant ascites accompanies a variety of abdominal and extra-abdominal metastasis and mainly peritoneal dissemination of disease. It is a cause of high morbidity, major discomfort, and several other symptoms, leading to a significant reduction in the patient's quality of life. This situation raises several treatment challenges where treatment options include a multitude of different procedures but with limited efficacy, new clinical problems as loss of proteins and electrolyte disorders that may cause diffuse edema, and some degree of risk [24].

Patients with anasarca usually present with great discomfort, with cold, thin skin and with skin transudate. These are situations that may require palliative sedation and suspension of parenteral hydration since excess of fluids worsens symptoms [25].

The treatment of malignant ascites primarily includes paracentesis and diuretics, as first-line treatments. Diuretic therapy is effective at the very beginning of the disease but efficacy declines with tumor progression and was associated with dry mouth and orthostatic hypotension [15].

Paracentesis is widely adopted but it is associated with significant patient discomfort, risks of bleeding or bowel perforation, and loss of significant amount of albumin, with worsening of peripheral edema.

Intraperitoneal chemotherapy, targeted therapy, immunotherapy, and radioisotopes are rarely an option in this situation [13].

Some symptoms of advanced disease may be less specific for colorectal carcinoma and represent a systemic impairment by neoplastic disease, like cachexia/sarcopenia.

Cachexia is a multifactorial syndrome characterized by loss of appetite, weight, and skeletal muscle (sarcopenia) [26], leading to a cluster of symptoms like fatigue, functional impairment, increased treatment-related toxicity, poor quality of life, and reduced survival. Across malignancies, cachexia becomes more prevalent as the disease progresses, impacting approximately half of patients with advanced cancer [27].

Cachexia is a situation where preventive treatment is the most efficient. Once severe sarcopenia is established, the condition is rarely reversible. The nutritional approach should start with the development of anorexia, before weight loss begins [28].

Dietary counseling and physical activities must be offered with the goals of providing patients some advice for the preemptive management of cachexia. Enteral feeding tubes and parenteral nutrition should not be used routinely due to the discomfort, increment of costs and social life limitations.

No specific pharmacological intervention can be recommended as the standard of care, but progesterone analogs and short-term corticosteroids. It may be choose wisely because is associated with thromboembolic risk and gain of more fat gain than muscle mass [16].

Among other nonspecific symptoms of colorectal carcinoma, but often associated with advanced neoplasia, 35–96% of patients experience pain, 32–90% experience fatigue, and 10–70% experience breathlessness [25]. The broad ranges of incidence arise from the forms and time of assessment.

Symptom assessment in patients with advanced disease shows a progressive clustering of cascading events. Patients typically experience more than one symptom at any one time [29]. Grond et al. [16] found that 94% of those referred to a cancer pain clinic experienced additional symptoms, with 15% reporting at least five.

Symptoms may be a result of the interactions of conditions not only caused by the cancer itself, but as indirect consequences of the cancer, early or late adverse effects of treatment, and/or comorbid conditions [30].

Most patients with stage IV colorectal cancer have a poor prognosis, but numerous palliative modalities, as seem, are available today. When a cure is no longer possible, treatment is directed toward providing symptomatic relief, and a better quality of life [31].

It is difficult to draw the line between the usefulness of chemotherapy and therapeutic futility. As more drug options become available, the greater the tendency to prolong antineoplastic treatment.

Functional activity indexes can correctly evaluate disability but need to be combined and integrated with other parameters to assess prognosis.¹⁵ Poor performance status values are the main point to assess the possibility of the usefulness of chemotherapy.

Chemotherapy administration near death, showed that this approach did not improve quality of life for patients with poor performance status, and can be detrimental also for patients with good performance status [13]. Third line and beyond treatments prolonged overall survival versus palliative care, in high selected [32].

Aggressive care near the end of life as a sign of poor-quality cancer services [33] but, although numerous studies have measured these indicators, different criteria were used to define populations of interest make a comparison of results difficult [34].

Despite the frequency of symptoms and the limitations of antineoplastic therapy, oncologists did not systematically refer patients to a palliative care specialist, but only requested their intervention for pain and symptom management [35].

We need to change reality and dispel myths and prejudices in relation to palliative care to improve the quality of life between cancer diagnosis and death. It is necessary to change the role of the physician in navigating this course [36], or create referral programs regardless of the physician.

4. Time of palliative care in colorectal cancer

When a cure is no longer possible, treatment is directed toward providing symptomatic relief. The data available today leave little doubt that surgical resection, when feasible, may provide good palliation for some patients with metastatic disease. Although palliative surgery has been the mainstay of palliative care, an individualized multidisciplinary approach, which may involve both surgical and nonsurgical modalities, is probably the best current option [31].

In the last decade major changes in health-care delivery, changing demographics, and new treatment options have significantly changed the cancer patients' trajectory [37]. Now is the time to adapt the current models of palliative care to achieve the strongest dissemination to all cancer care settings. Implementation of palliative care can be achieved through recognition of emerging best practices and financial support to afford this model of care [38].

The difference between curative and palliative care lies in defining the main goal of treatment, since palliative treatments can extend life [39]. Palliative care is incorrectly associated with the suspension of all forms of antineoplastic therapy, but the persistence of inappropriate antitumor treatments in non-responding patients and overly aggressive care often affects a patient's quality of life [40].

A report from a retrospective cohort study including all patients who died of colorectal cancer between 2004 and 2012 in Manitoba, Canada, provides the better evidence that early palliative care involvement is associated with decreased odds of dying in hospital and lower health-care utilization and costs in patients with colorectal cancer [41].

5. Expected results

The goal of palliative care is improvement of quality of life. Good communication skills and flawless symptom control is associated with improved patient and family quality of life, greater treatment compliance, and may even offer survival advantages [42].

A 2016 meta-analysis evaluated 40 palliative care trials and concluded that this care was associated with improved patient quality of life and control of symptom burden [43].

The American Society of Clinical Oncology (ASCO) recommends the integration of palliative care into oncology practice [23], but despite the increasing evidence of the benefits of palliative care there is little consensus regarding strategies for integrating palliative care into the routine practice of oncology [44]. The lack of qualified professionals, the difficulties of access and the remuneration of professionals are still the biggest obstacles, especially in underdeveloped countries.

Palliative care has emphasized support for family caregivers. Although the family caregiver literature is even more limited than patient-focused studies, there is growing evidence of the benefits of palliative for family caregivers [15], but our current models of remuneration are insufficient to cover the care of the patient's family members, and especially in the assistance to bereavement.

For palliative care to be truly integrated into oncology care, it will need to take on new forms, expanding for greater use in outpatient and community settings, survivorship clinics, and the most important, primary practice of oncology [45].

In an era of limited resources and incremental costs of health care, expanding palliative care capacity to meet clinical guidelines and population health needs seems to save costs. The major problem is a significant variance in estimates of the effects of treatment on costs, depending on the timing of intervention, the primary diagnosis, and the overall illness burden.

Because ASCO guidelines state that palliative care should be provided concurrently with other treatment from the point of diagnosis onward for all metastatic cancer, a broad evaluation is required to evaluate the cost effects of palliative care across the entire disease trajectory [46].

6. Conclusion

Colorectal carcinoma is a frequent entity, with many patients being diagnosed with metastatic disease "de novo" or having recurrences of the disease after primary treatment.

Although a fraction of patients may undergo resection of metastases with curative intent, the vast majority will remain eligible only for palliative treatment modalities, which may include surgery or systemic antineoplastic therapy.

Fundamentally, the practice of palliative care includes an impeccable control of symptoms, good communication, and psycho-emotional support for patients and their families.

The demand for palliative care to be integrated throughout the cancer trajectory, combined with a limited palliative care workforce, means that new models of care are needed.

Palliative care began in academic centers with specialty consultation services, and its value to patients, families, and health systems has been evident.

Volunteering can help fill most of the gaps in palliative care, but its implementation is still difficult and restricted to some more developed centers.

This chapter discusses evidence regarding the need for integration of palliative care into routine oncology care and describes the best practices recognized for dissemination of palliative care. The available evidence suggests that palliative care be widely adopted by clinicians in all oncology settings to benefit the patients with cancer and their families. Efforts are needed to adapt and integrate palliative care into community practice.

The benefits of palliative care can only be realized through effective dissemination of these principles of care, with more primary palliative care delivered by oncology clinicians.

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