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# Why Young Patients are Having Colorectal Cancer?

**Erika Ruiz-Garcia***

*GI Oncology Department & Translational Medicine Laboratory, Mexico*

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***Corresponding author:** Erika Ruiz-Garcia, GI Oncology Department & Translational Medicine Laboratory, Instituto Nacional de Cancerologia, Av San Fernando N.22, ZC 14080, Mexico

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## Opinion

Colorectal cancer (CRC) rates are still expected to increase to more than 2.2 million new cases and 1.1 million deaths by 2030 worldwide suggesting that CRC remains a major global health burden [1].

Traditionally, CRC is considered a cancer of older people, taking into account that around 90% of CRC patients are over 55 years old. However, while overall incidence rates have been declining since the mid-1980s, the incidence of early onset colorectal cancer, defined as arising before 50 years of age has increased over the last 10 years [2].

Starting around 1990, incidence increased in this age group (20–49 years) from 8.6 per 100,000 to 12.5 per 100,000. The largest absolute increases in incidence have occurred among 40–49-year-olds, from 18.2 per 100,000 in 1992 to 26.5 per 100,000 in 2015. Similar increases have been reported across the world [3]. Asian studies (institutional reports) showed similar trends in patients less than 40 years of age, with a prevalence of 19.5-28.6%, which is clearly higher than that in the USA [4-6] meanwhile in Mexico at the National Cancer Institute, we reported an incidence of 22.8% [7].

It is important to remark the propensity in young patients towards to present an advanced stage (stage III and IV), thus influencing overall prognosis. One survey of the SEER database between 1991 and 1999 demonstrated that the overall five-year cancer-specific survival was significantly worse for the young adults compared to an older group (61.5 vs. 64.9%; p = 0.015) [8]. However, when adjusted for stage at presentation, outcomes were similar.

## But why Young Patients are having Colorectal Cancer?

One possible explication is the increasing epidemic of obesity, which is a major risk factor for CRC. We noted that in the past three decades, the prevalence of obesity has increased markedly among individuals of all ages and racial/ethnic groups in the USA, which may have contributed to the overall increase in CRC incidence rates among young adults. On the other hand, chronic diseases as Diabetes Mellitus has been increasing dramatically, especially in young people and could also explain the increasing incidence considering that DM has been established as a factor for developing colon neoplasms [9]. Another possible explanation for the increasing incidence of CRC among young patients could be the change in alimentary habits. In some Asian countries, the increasing incidence of CRC in young patients has been attributed to “Westernized” diet or lifestyle.

Trying to understand the genetic of early onset colorectal cancer disease, Memorial Sloan Kettering Cancer Center performed Next Generation Sequencing panel (> 300 genes, MSK IMPACT) in 384 young patients and compared with a cohort of average onset colorectal cancer (n=543). They found similar histology and few molecular differences when compared average onset CRC: TP53 mutations (87 vs. 78%, p = 0.001) and 20q amplifications 5 vs 1% p = 0.006), respectively. Even more, the metastatic young cohort was associated with better survival (73 vs 69months, p = 0.022) [10].

It is believed that not just genetic factors, chronic inflammation, contribute to the pathogenesis of colorectal cancer but also intestinal microbiota dysbiosis. Pathways used by pathogens to establish infections (quorum sensing, invasion, biofilm formation) are able to derail mechanisms controlling cellular proliferation and pre-clinical and clinical research are producing mounting evidence that the gut microbiota is strongly associated with CRC carcinogenesis [11].

Perturbations of the microbiota may effectively change the course of carcinogenesis directly as well as indirectly as microbial actions seem to impact both genetic and epigenetic alterations

promoting dysplasia, clonal expansion, tumor growth and invasive cancer [12,13]. Although the microbiota is stable over long periods of time, a variety of factors such as aging, obesity, western diet, lack of exercise, diseases and antibiotics shifts the microbiota towards a less diverse and pro-inflammatory profile [14].

With all this information we can only say that colorectal cancer is more complex that we once thought.

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