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Comment on: Clinicopathological features and oncological outcomes of patients with young-onset rectal cancer

Editor

We read with interest the article by Zaborowski *et al.*[1], analysing clinicopathological features, long-term survival and disease recurrence patterns among patients aged less than 50 years (young-onset) diagnosed with rectal cancer, compared with those aged 50 years or more. Young-onset cases were more likely to have microsatellite instability and therefore Lynch syndrome, and received more neoadjuvant and adjuvant therapies, although they showed disease-specific outcomes comparable to the elder subset[1].

Recently, we looked at young-onset colorectal cancers (CRC) as they may differ from late-onset CRCs, especially those showing microsatellite stability[2]. Regarding tumour location, we compared rectal cancer with other colon locations (right and left) within a young population[3], and more recently, we compared each particular location between the two different subsets of age at onset[4]. Rectal tumours in the young-onset population showed microsatellite stability, CpG island methylator phenotype-low-0 (CIMP-low-0) and low chromosomal instability, with recurrent altered chromosomal regions in common with left-sided young-onset colon cancer, possibly in relation with microsatellite and chromosomal stable tumours, but with an unexpected familial component and the worst prognosis between the three locations[3]. Comparison of rectal cancer between the two different age-of-onset populations showed remarkable differences, with young-onset rectal cancers being diagnosed at more advanced stages, associated with fewer polyps during follow-up, and more than half associated with familial history of Lynch syndrome-related neoplasms, without a reliable microsatellite instability component[4].

Other groups have also shown the existence of key differences between young-onset colon and rectal cancers but with disparities in age-of-onset cut-offs. We also carried out our previous studies in a young-onset population with a cut-off of 45 years, but it seems more appropriate to definitively set the cut-off at younger than 50, and therefore we agree with Zaborowski *et al.*[1] that a consensus cut-off is needed for future work. The apparent uniqueness of young-onset rectal cancers from a phenotypical and molecular point of view, together with their marked increase in incidence, apparent overtreatment on many occasions or diagnosis in more advanced stages, highlights the need to carry out prospective multicentre studies that allow design of effective strategies for their management.

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