Early-onset colorectal cancer: Never too young

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Colorectal cancer (CRC) is the second most common cancer in Aotearoa New Zealand, second only behind prostate cancer in men and breast cancer in women. It is the second highest cause of cancer death behind lung cancer, with approximately the same death rate as prostate and breast cancer combined. In 2019, there were 3,318 colorectal cancers diagnosed in New Zealand and, while the overall rate is slowly declining, early-onset colorectal cancer (EOCRC), defined as CRC in adults under the age of 50, is on the rise. From 1995 to 2012, early-onset rectal cancer in New Zealand men increased by 18%, and by 13% in New Zealand women. This pattern is not confined to New Zealand, with increases reported in at least 18 other countries; however, New Zealand is seeing the second fastest increase in incidence in the world. Moreover, the increase in EOCRC is occurring independently of late-onset CRC (LOCRC) and, if current trends continue, it has been estimated that by 2030 1 in 4 rectal cancers diagnosed will be in patients under 50.

Clinical characteristics

EOCRC usually presents in the distal colon (sigmoid) or rectum and, compared to LOCRC, it has several distinct clinical and pathological characteristics. The vast majority (up to 95%) of EOCRC cases present with symptoms, the most common being rectal bleeding, change in bowel habit and abdominal pain. These cancers are thought to show more aggressive histopathological characteristics with higher rates of mucinous or signet ring histology and poorly differentiated cancers. EOCRC patients are more likely to present with advanced (stage 3 or 4) disease.

Delays to diagnosis are reportedly more common in younger patients, ranging from a median time of 217 to 239 days in USA and New Zealand studies, respectively. In contrast, these studies also report a median time from symptom onset to diagnosis in older patients as 29 and 122 days, respectively. Moreover, this effect is likely to be larger if under 50s are subdivided out from the under 60s. That young people tend to not seek help when symptoms arise likely contributes to this delay, but another factor is when healthcare professionals do not adequately investigate symptoms in younger patients because they believe they are “too young” to have cancer. This can result in general practitioners (GPs) not referring young patients who are symptomatic, or in those referrals not been accepted by public hospitals despite evidence of rectal bleeding. Delays to CRC diagnosis made up the highest proportion of cancer-related complaints in a Health and Disability Commissioner (HDC) review in 2015, comprising nearly a third of delayed cancer diagnosis complaints.

Optimal treatment for EOCRC remains unclear, and current major guidelines do not recommend any different management based on age alone. However, studies show EOCRC patients receive
more aggressive chemotherapy and radiation treatment regimes at every stage of disease, often without any matched survival benefit. This, in turn, raises concerns that some may be being overtreated, and at risk of harm from unnecessary treatment.\textsuperscript{13,14,16,17}

The psychosocial impact of EOCRC is also different compared to that of LOCRC. Younger patients are at a different stage of their lives and have different concerns to older patients. This leads to a greater impact on quality of life and concerns around career, financial problems, sexual functioning, family functioning and emotional distress.\textsuperscript{18–22} This needs to be considered when clinicians are looking after EOCRC patients, routinely enquiring about these issues, with early referral for supports when needed.

What could be driving the increasing incidence of EOCRC?

The exact reason behind the increasing incidence is not known, and it is likely multifactorial. While EOCRC patients do have a higher proportion of germline mutations than commonly seen in older patients, the majority (75–84\%) of EOCRC are sporadic.\textsuperscript{23} A recent study from the Memorial Sloan Kettering Cancer Center found no differences in survival, concluding that “while EOCRC are more commonly left sided...[they] are otherwise clinically and genomically indistinguishable from LOCRC”.\textsuperscript{24}

The risk factors for LOCRC such as obesity, alcohol, processed meat, sugary drinks, and the “Western diet” (high fat, high meat, and low fibre) may or may not contribute to EOCRC.\textsuperscript{15,30–35} An individual’s gut microbiome may also play a role. Several bacterial species have already been implicated in adenoma or CRC development.\textsuperscript{25,26} While data specific to EOCRC are lacking, recent studies suggest the microbiome in patients with EOCRC is different compared that found in patients with LOCRC and healthy controls.\textsuperscript{27,28} These differences may reflect early-life events and/or ongoing environmental factors, many of which emerged over the past several decades. These include caesarean delivery,\textsuperscript{29} formula feeding,\textsuperscript{36} antibiotic use,\textsuperscript{37} changing diet, synthetic food dyes, MSG high-fructose corn syrup, or perhaps even microplastics.\textsuperscript{38}

What should be done?

The biggest predictor of survival is the stage of disease at diagnosis; therefore, early detection of EOCRC is crucial.\textsuperscript{8} The first step to reducing delays to diagnosis is to increase public awareness of symptoms, as exemplified by a recent study where one third of men were unable to name a single symptom of bowel cancer.\textsuperscript{39} However, while the “Never Too Young” campaign recently run by Bowel Cancer New Zealand (https://bowelcancernz.org.nz/never-too-young) is helping to increase public awareness of significance of symptoms of this disease, there also needs to be timely and adequate investigation once patients present to their GPs seeking help.

New Zealand recently introduced the national bowel cancer screening programme (NBSP), but the 25-year delay to establish this program is considered by many as an embarrassment rather than a success. This program currently only includes individuals over the age of 60, although this is being lowered to 50 for Māori patients to address the inequity caused with a higher proportion of Māori patients with bowel cancer presenting before the age of 60.\textsuperscript{40} While this is a very welcome move, New Zealand is still behind many other Organisation for Economic Co-operation and Development (OECD) countries with the British National Health Service (NHS),\textsuperscript{41} Australia,\textsuperscript{42} Canada\textsuperscript{43} and Germany,\textsuperscript{44} all offering bowel screening from the age of 50. Germany has been doing this for the past 20 years.\textsuperscript{44} The USA preventative task force guidelines for bowel cancer screening have recently recommended to reduce screening age to 45.\textsuperscript{45,46}

Alongside lowering the screening age, timely access to colonoscopy for symptomatic young patients needs to be improved. In the future, as our technology and knowledge of drivers for EOCRC improves, we may be able to selectively screen high-risk patients based on faecal testing, polygenic risk scores and presence of known risk factors.

There is concern that our already struggling health system cannot accommodate increasing demand for colonoscopy and New Zealand has a shortage of colonoscopists, gastroenterologists\textsuperscript{47,48} and surgeons. However, failure to recognise the changing epidemiology of the disease, the impact this will have on changing our clinical behaviour, and the need to incorporate this impact into health planning will only make matters worse.
COMPETING INTERESTS
Nil.

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