

## Trends in early onset colorectal cancer (EOCRC) in a South Asian cohort: data from a specialized tertiary care center in western Sri Lanka

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### Abstract

#### Introduction

Early onset colorectal cancer [EOCRC] has significantly increased during the past decade globally. It is defined as cancers diagnosed in those aged 50 years or less. Most research on EORC are from western populations where the tumour biology and risk factors may differ from other regions. Evidence on EOCRC from the South Asian region is particularly scarce. This study presents the basic trends in presentation and overall survival [OS] pattern of EOCRC using data from a single specialized tertiary care institution over two decades.

#### Methods

A total of 723 patients treated at the University surgical unit of the North Colombo teaching hospital from 1995 to 2020 were included in the analysis. Overall survival of the EOCRC was compared with that of the older population using Kaplan-Meier survival curves. Survival patterns over two time periods [pre-2010 vs post-2010] were also compared between the two populations. The stage at presentation, family history of colorectal or related cancers, tumour site, and tumour stage were also compared.

#### Results

The proportion of EOCRC in this cohort has not shown a significant increase over the past two decades [2001-2010: 24% vs 2011-2020: 21%]. The advanced tumour stage at presentation and the presence of significant family history are also comparable. EOCRC cohort demonstrates a better OS for the entire study period [Median survival: < 50 years – not reached; >50 years – 91 months; 95%CI – 72-132; P<0.001]. However, this survival advantage is only observed during the pre-2010 period [Median survival: < 50 years – 160 months; 95%CI – 120 – not reached; >50 years – 84 months; 95%CI – 62-132; P=0.01] and becomes comparable in the 2010-2020 period [P=0.16]. OS of the EORC has not also improved over the two decades from 2001 to 2020 [P=0.51].

#### Conclusion

There is no significant increase in the EOCRC rates in this population over time although the rate has remained high throughout. The OS of the EOCRC population is better compared to the older population. A significantly better OS is observed during the pre-2010 period in the EOCRC but is not present in the post-2010 period. Advancement in therapy may have improved the survival of the older population during the latter part but not that in the EOCRC due to its inherently aggressive nature. This paper provides preliminary data on EOCRC from Sri Lanka. The South Asian population may have a different disease pattern with younger age at onset compared to the western populations and needs to be further explored.

#### Introduction

Colorectal cancer [CRC] is the fourth most commonest cancer globally accounting for 1.9 million new cases in 2020 representing close to 10% of all cancers [1]. It has the third highest mortality rate from cancer with over 900,000 deaths annually. Bowel cancer screening programmes worldwide have been able to achieve a reduction in incidence and mortality [2]. Identification of premalignant lesions through screening has helped in reducing the incidence while early identification of cancer has improved overall survival from CRC [2].

A recent rise in the incidence of early-onset colorectal cancers [EOCRC] has been reported globally. CRC in adults up to the age of 50 years is classified as EOCRC. Studies from Europe, the USA, Australia and other high-income earning countries have reported a significant increase in the incidence of EOCRC during the past couple of decades [3-5]. Some authors have linked the increase to the obesity pandemic given the causal relationship between the two [6]. The EOCRC are detected at a higher stage compared to the older

**Table 1.** Demographics of the study population

|                       | ≤50   | >50   | Pvalue |
|-----------------------|-------|-------|--------|
| <b>Number</b>         | 153   | 466   |        |
| <b>Age</b>            |       |       |        |
| Median                | 47    | 73    |        |
| Range                 | 17-50 | 51-85 |        |
| <b>Sex</b>            |       |       |        |
| Female                | 54%   | 49%   | 0.28   |
| <b>Stage</b>          |       |       |        |
| >T3/T4                | 77%   | 72%   | 0.22   |
| <b>Family history</b> | 17%   | 17%   | 1      |

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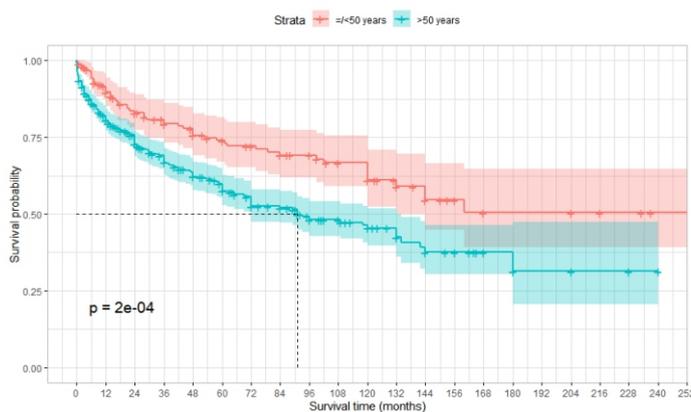
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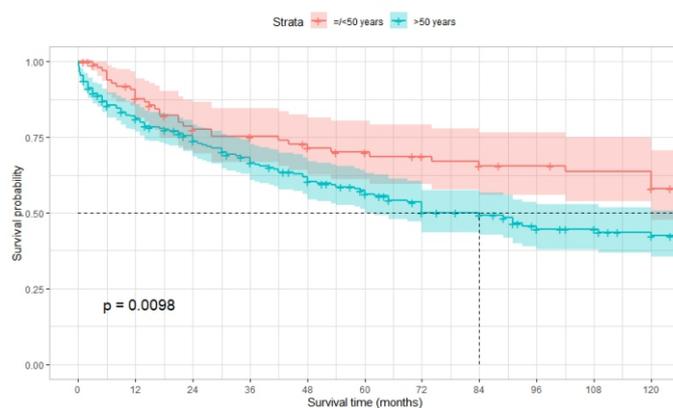
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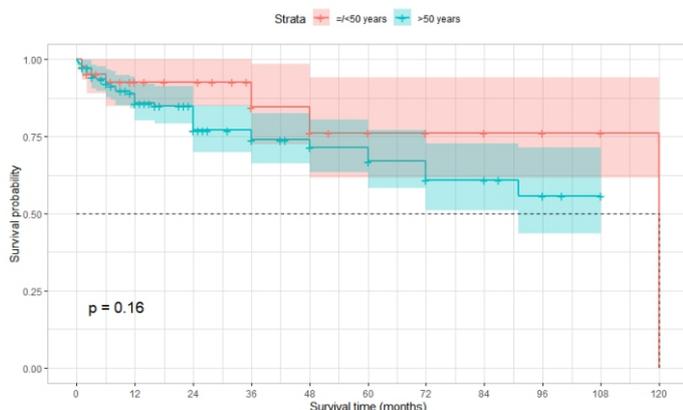




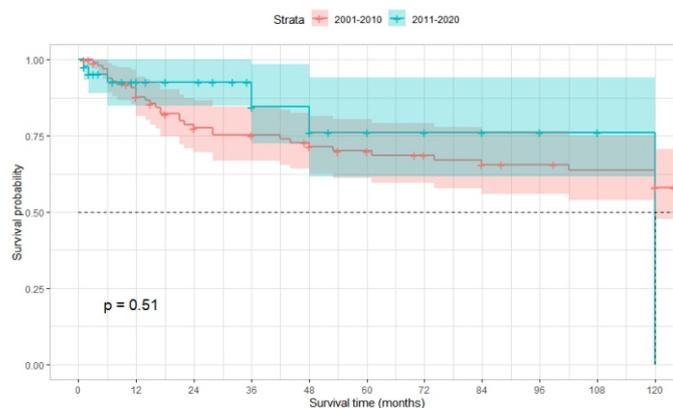
**Figure 1.** Kaplan-Meier survival curves comparing overall survival between EOCRC and older patients  $>50$  years following surgery for colorectal cancer from 1995 to 2020.



**Figure 2.** Kaplan-Meier survival curves comparing the overall survival of EOCRC versus older patients between 2001 and 2010.



**Figure 3.** Kaplan-Meier survival curves comparing the overall survival of EOCRC versus older patients between 2011 and 2020.



**Figure 4.** Kaplan-Meier survival curves comparing the overall survival of the EOCRC patients during time periods 2001 – 2010 and 2011–2020.

populations although they haven't reported a worse outcome [4, 5]. Data on EOCRC from the South Asian region is scarce. In this article, we present the trends in EOCRC over 25 years to the University Surgical Unit of the North Colombo Teaching Hospital [NCTH] in Sri Lanka. The unit is a tertiary care speciality centre for colorectal surgery and the NCTH is the only tertiary care centre located in the Gampaha district. The district has a population of over 2.5 million and has a fair representation of all socio-economic fractions in the country [7].

### Methodology

All patients presented to the University Surgical Unit of the North Colombo Teaching Hospital between 1995 and 2020 were included in the analysis. All patients were treated as per the unit protocol. Following preoperative staging locally advanced rectal cancers diagnosed after the year, 1999 were subjected to neo-adjuvant chemo-radiation [NCRT]. All receiving NCRT followed with surgery after an interval of 6 to 8 weeks before 2006 and 8 to 10 weeks from 2007 onwards. All patients were prospectively followed up with 3 monthly intervals for the first 2 years, 6 monthly intervals for the next 3 years and annual intervals thereafter. The survival time was

right censored and where the ten-year periods were compared the censoring was done at 120 months. Those who were lost to follow-up were censored at the last follow-up date. Those who were 50 years or less were considered in the EOCRC group. The stage at presentation, family history of colorectal or related cancers, tumour site, tumour stage and overall survival [OS] were analysed. Kaplan-Meier curves were used to compare the survival between the EOCRC and older counterparts with open source software R Core Team [2021]. Test of proportions and the T-test were used to compare the populations with a P value of 0.05 considered significant.

### Results

Out of 845 patients, a total of 723 CRC patients with completed prospective follow-up records presented between 1995 and 2020 were analysed [drop-out rate - 14%]. Of the total, 184 were aged 50 years or less [Female = 100, Mean age- 43 years, Age range – 17 to 50 years]. Considering the past two decades, EOCRC accounted for 24% of the total CRCs between 2001 and 2010 while it was 21% between 2011 and 2020. There was no statistically significant difference in the proportion of EOCRC detected between the two time periods. The median age of the EOCRC cohort is 34.5

years [range 17-50] compared to 63 years [range 51 to 89] from 1995 to 2010 and 35 years [range 21-50] compared to 63 years [range 51-85] in the period from 2011 to 2020. The median follow-up for the pre-2010 period is 48 months [range 0 - 256] and for the post-2010 is 24 months [range 0 – 120]. A family history with at least one 1st degree family member or two 2nd degree family members with CRC or related cancers was observed in 17% of the study subjects in the EOCRC group and was comparable with the older population [P=1]. The proportion of advanced tumours [ $>T3$ ] at presentation is also comparable between the two groups [Table 1]. The overall survival of patients with EORC who underwent curative surgery from 1995 to 2020, is significantly better than their older counterparts [Median survival:  $< 50$  years – not reached;  $>50$  years – 91 months; 95%CI – 72-132;  $P<0.001$ ] [Figure 1].

### Survival pattern between periods

On subgroup analysis comparing periods from 2001-2010 and 2011 – 2020 [n=619], the EOCRC patients demonstrate a significantly better OS compared to older patients in the period from 2001 to 2010 [Median survival:  $< 50$  years – 160 months; 95%CI – 120 – not reached;  $>50$  years – 84 months; 95%CI – 62-132;  $P=0.01$ ] [Figure 2]. However, the OS between the two groups is comparable during the period from 2011 to 2020 [Median survival:  $< 50$  years – 120 months; 95%CI – both values not reached;  $>50$  years – median survival not reached;  $p=0.16$ ] [Figure 3]. Also, there is no change in the OS at 10 years of the pre and post-2010 EOCRC patient cohorts [Median survival: Pre 2010 – 160 months; 95%CI – 120 – not reached;  $>50$  years – median survival not reached;  $P=0.51$ ] [Figure 4]. Advanced cancer [T3/T4] proportion for the EOCRC were 77% vs 70% and 67% vs 70% for the older age group for the two time periods.

### Discussion

Although there is a significant increase in the incidence of EOCRC globally, this study did not demonstrate an increase in EOCRC as a proportion during the past decade. It is noteworthy that the data is from a single centre, although NCTH is the only tertiary care centre in the district of Gampaha which has a representative Sri Lankan population sample with both urban and rural communities [7]. Over time, the proportion of EORC in this population has remained above 20% of the total CRC incidence, which is higher than that observed in western populations [3-5, 8, 9].

A study on migrant South Asians in the UK has shown a younger age of onset of CRC compared to the Caucasian population indicating a possibility of a different disease pattern in this group [10]. A population-based study from India also reported a young CRC [ $<40$  years] rate of over 34% [11]. The same study and several other authors have also reported a mean age of less than 50 years in Indian patients with CRC [11-13]. The CRC in the younger population is considered to be generally more aggressive and to have a higher chance of recurrence [14, 15]. However, in this cohort,

the EOCRC does not have a worse outcome. Other authors have also observed a similar pattern with better overall outcomes in the young CRC cohort probably owing to their better physiological reserves [9]. Also, the proportion of those having a significant family history is comparable between the two groups. It is worth noting that a recall bias may affect this information since the family history was not confirmed with medical records.

The OS of the populations were compared in the two decades pre and post-2010, as the treatment facilities and resources have changed over time. Use of better imaging, improvement in adjuvant treatment and advancements in surgical technique may all have had an impact on the overall survival of patients. The post-2010 period saw an improvement in the availability of imaging, high-quality radiation and chemotherapy facilities in the local healthcare system. Improvement in infrastructure and services in perioperative care was also observed during this period.

The significant gap in the OS between the two groups observed in the pre-2010 decade narrowed during the following decade. However, the OS of the EOCRC group has not significantly improved post-2010, while that of the elderly counterparts shows a significant improvement.

This improvement in OS can probably be attributed to the improvement in overall care affecting the OS of the elderly population but not so much of the younger population. The discrepancy could be due to the aggressive nature of the EOCRC, which fails to improve even with better oncological care. There is a significant lack of data on EOCRC from the South Asian region. Future studies from this region with robust data are necessary to arrive at definitive conclusions.

### Limitations

This study includes data from a single centre hence may not reflect the entire population and the data may be biased. Detailed analysis of the co-morbidities, different oncological treatment modalities, and histopathological and molecular profiling data if available would have given a better overall picture of the EOCRC. However such information is not historically available. The survival analysis is not a multivariate analysis therefore might not reflect the effect of co-morbidities and disease-related factors on survival.

### Conclusion

There is no significant increase in the EOCRC rates during the past two decades in this cohort over time although the rate has remained high throughout. In the study group, the OS of the EOCRC population is better compared to the older population. A significant difference in the survival pattern is observed during the pre-2010 period but not in the post-2010 period. The improvement in imaging and treatment modalities could be attributed to the better survival observed in the older population in the post-2010 period although not conclusive without considering other confounders. However,

the EORC population may not demonstrate a similar improvement owing to the tumour biology and the aggressive nature of cancer. The South Asian population may have a different disease pattern compared to the western population and needs to be further explored.

#### List of abbreviations

EOCRC – early onset colorectal cancer

CI – Confidence interval

CRC – colorectal cancer

OS – overall survival

NCTH – North Colombo Teaching Hospital

#### Ethics approval and consent to participate

Informed consent from individual patients was not required as the study was a cohort study based on analysing clinical outcome data. Ethical clearance to analyse the database has been obtained from the Ethics Review Committee of the Faculty of Medicine, University of Kelaniya.

#### Authors' contributions

PC and SK were involved in patient management, concept, data analysis, manuscript writing and critical appraisal of the paper. JW and GM were involved in the assessment of pathological specimens and MDT management of the patients. PC and SG were involved in data collection, data analysis, preparation of the manuscript and PC, SK, JH and GM critical appraised the paper.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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