

Colorectal cancer survivorship in a cohort of Sri Lankan patients; the time to widen focus from the care of acute patients to long-term survivors

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Abstract

Background

Survival of patients with colorectal cancer (CRC) has improved the world over and cancer survivorship has placed new demands on the provision of healthcare. Sri Lanka is a low to middle income country with good healthcare outcomes based on WHO regional data. Up to now, studies from Sri Lanka and South Asia focused on achieving a global standard of acute cancer care in the areas of curative and restorative resection for CRC. There is a lack of data from this region that focuses on CRC survivors and their needs. This study compared survival in two cohorts of Sri Lankan patients across two decades to evaluate perceived improvement in the outcome of treatment for CRC and assessed quality of life (QOL) in a subgroup of survivors to better define the needs of future healthcare requirements in the continued treatment of patients with CRC.

Materials and methods

Two groups of patients with CRC were compared: Group A (425), 1996 to 2010 (rectal cancer-RC, 276 [65%] and colon cancer-CC, 149 [35%]) vs. Group B (289), 2010 to 2020 (RC, 165 [57%] and CC, 124 [43%]). Overall survival (OS) for the entire group, and RC and CC separately, was evaluated and compared. Histological characteristics of the resected specimens were compared for the two periods. In a subset of 100 (RC-65, CC-35) QOL in the physical component (PC) and emotional component (EC) domains were evaluated to compare RC with CC.

Results

Overall survival was better for patients post-2010 vs. pre-2010 ($P < 0.001$); one, three and five-year survival for post-2010 were 89% (95%CI: 85.5% - 93.2%), 75% (95%CI: 69.9% - 82.2%) and 68% (95%CI: 61.5% - 76.0%) respectively versus 79% (95%CI: 75.8% - 83.5%), 67% (95%CI: 62.9% - 72.1%) and 59% (95%CI: 54.3% - 64.2%) for pre-2010 time period. This is because of a better OS and DFS for RC but not CC. QOL was similar for those with RC vs. CC in both physical and emotional domains, and for those who survived less than 5 years vs. greater than 5 years. Over two-thirds (69%) reported organ dysfunction, 30% experienced alteration in lifestyle and 7% reported depression.

Conclusion

Improvement in survival of patients with rectal cancer after 2010 contributed to overall improvement in survival for patients with CRC. The improvement in RC, OS and DFS correlates with the improvement in histological specimen quality. This may be attributed to the improvement in preoperative planning and technique post 2010. There is an emerging need for rehabilitation and multi-disciplinary services, outside the realm of acute care, for rectal cancer survivors, specifically, and for CRC patients in general.

Introduction

Globally, the incidence of colorectal cancer (CRC) has risen to be the third-most common cancer. [1-4] Simultaneously, survival rates for CRC and reduced rates of local recurrence have improved owing to early detection, better surgical techniques, improved adjuvant and neoadjuvant treatment.[5-7] The result is that a large population of patients now live with CRC, either receiving or following completion of treatment. An increase in the number of survivors has posed new healthcare challenges with unique requirements for this patient population; quality of life is one. Globally, healthcare systems have adapted to meet the physical and psychological needs of survivors.[6] In the past decade, Sri Lanka, a low to

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middle income country with a free healthcare system, reported improvement in the clinical management of cancer.[7,8] Yet, there is much to be achieved in survivorship. In 2020, the number of recorded new cases of CRC in Sri Lankans for all ages and both genders occupied third spot.[9] While there has been improvement in curative resection rates and survival,[10-12] the global emergence of a new and expanding cohort of CRC survivors has posed healthcare challenges. Also, there is paucity of published data on CRC survivor related outcomes and healthcare requirements from South Asia. This study aims to outline goals of care for future management of those surviving colorectal cancer in Sri Lanka by comparing the result of CRC survival following treatment in a single unit with curative intent over two consecutive decades. In the instance that there was improvement in survival of patients with CRC, we wished to further study if the observed improvement was due to colon cancer, rectal cancer or both. Hence, we compared survival in colon versus rectal cancer. Also, we evaluated quality of life using the SF-36 questionnaire in a sub-set of one hundred patients with 5 to 10-year survival following curative treatment. The objective of the study is to report the survival rates in colon and rectal cancers in a specialised health care setting from the South Asian region which is not widely published compared to data from developed economies, demonstrate the improvement in survival in two sequential time windows and discuss the factors that require focus in the resource scarce health care setting.

Materials and Methods

The study period was between 1996 and 2020. All patients diagnosed with CRC and treated with curative intent at the university surgical unit of the North Colombo teaching hospital were prospectively followed up and data entered in real time on a prospective data base. At regular intervals, we undertook data cleansing, ensuring to fill in blank data spaces and to undertake regular communication with patients to update their status on recurrence and survival. For uniformity of data, surgical operations were performed by trained teams and conformed to a protocol-based standard of care for CRC.[13,14] Surgical specimens were examined by colorectal pathologists according to a proforma that was previously described.[15] Follow-up data were recorded at outpatient clinic visits and by periodic telephone interviews of patients. Those lost to follow-up at any time point were excluded from the study.

Pre-operative work-up and Treatment Strategy

The overall strategy of treatment in all patients was to confirm a histopathological diagnosis and to exclude synchronous

cancer by colonoscopy examination. Also, the latter was useful in excluding polyposis syndromes of the colon. Staging of the disease was done by clinical examination, contrast-enhanced computed tomography (CT) of the abdomen to exclude liver metastasis, metastatic ovarian pathology in women, and to exclude metastatic spread to the greater omentum and peritoneal cavity, and CT of the pulmonary areas. A pre-operative serum carcinoembryonic antigen level was undertaken in all for baseline assessment and for post-operative surveillance. For those who presented with large bowel obstruction, which precluded total colonoscopy, completion colonoscopy was performed within 6 months of initial surgical treatment. From 2015, magnetic resonance imaging (MRI) scan of the pelvis was added in assessment of rectal cancers in the majority, and from 2018, MRI became mandatory for all patients with low rectal cancer. In the case of rectal cancer, after 1999, locally advanced rectal cancers were referred for neo-adjuvant chemo-radiation (NCRT), indicating evolution in treatment with updated treatment strategies. Following neoadjuvant treatment, surgery was offered after an interval of 6 to 8 weeks prior to 2006 and 8 to 10 weeks from 2007 onwards. All patients were managed in a multi-disciplinary setting on a referral basis prior to 2010 and with on-site meetings post-2010.

Treatment indications and operative treatment

The indications for curative surgical treatment were based on the presence of locally invasive cancer confined to the large bowel or rectum. In the case of rectal cancer, if tumour regression had been achieved, treatment was offered either by trans-anal resection or segmental resection and restoration of gut continuity [16]. If there was poor tumour regression or, in the case of poorly differentiated distal third rectal cancer, abdominoperineal resection of the anorectum was offered. In the majority with irradiated rectal cancer, a temporary diverting proximal loop ileostomy was included in the treatment options.

Post-operative follow-up

The unit policy for follow-up after surgery for CRC was streamlined with three-monthly physical exams, carcinoembryonic antigen (CEA) levels and an abdominal ultrasound scan through the outpatients' clinic. Surveillance colonoscopy was performed at 12 months, 36 months and 60 months. A CT scan of the abdomen, pelvis and chest was undertaken at the end of the first year and subsequently determined by clinical evaluation and/or elevation in serum CEA level. Frequency of follow-up was 3-monthly for the first 2 years, 6-monthly from 3 to 5 years and annually thereafter.

Quality of life assessment

A subgroup of 100 patients was selected through convenient sampling for the assessment of quality of life (QOL) and patient concerns. Quality of life was assessed through a self-administered, 36-item short form (SF36) questionnaire, which was also translated in the native language and validated.[17] Main patient concerns were assessed through interviewer-based questions. Eight domains of SF 36 were broadly categorised into a physical component summary (PCS) and emotional component summary (ECS) for comparison. Patient concerns were categorized into organ function, lifestyle and psychosexual problems.

Statistical analysis

The year 2010 was selected as the halfway point in our analysis, representing survival a decade before and a decade after 2010, which enabled the comparison of sufficient patient numbers in each group and provided adequate follow-up time to evaluate long-term survival. Also, it was an appropriate time point to assess the effect of the department's improvement in surgical and allied services on outcomes. Post 2010 in Sri Lanka marks a unique improvement in all sectors following the cessation of the 30-year civil war. The improvement in the Sri Lanka Prosperity Index from a negative value to a positive in the decade following 2010 is confirmed by the published data of the Central Bank of Sri Lanka. [18]

The Mann-Whitney U test was employed to compare continuous variables between before and after 2010 patient groups. The Pearson's Chi-square test was used to compare categorical variables. Survival analysis assessed differences in overall survival (OS) and disease-free survival (DFS) between the two groups. Survival curves for each group were estimated using the Kaplan-Meier method, and the log-rank test was used to compare survival differences between the two groups.

Ethical Consideration

The Ethical Committee of the Faculty of Medicine, University of Kelaniya, approved the North Colombo Colorectal database study (P/39/04/2015 and P/148/11/2024).

Funding

Funding was obtained from The Research Council of the University of Kelaniya to set up and maintain the database. The funding assisted with study design, data collection and analysis. The grant did not cover the manuscript writing/editing or publication decision. There were no

conflicts of interest with regard to the grant and our manuscript.

Results

Eight hundred forty-five patients with CRC were treated with curative intent during the study period. 131 patients were lost to follow up, and 714 were included in the analysis. 425 patients (52% male; median age 58 years, range 17 to 89 years) were treated in the time prior to 2010 and 289 (47% male; median age 59 years, range 21 to 85 years) from 2010 to 2020. Of 425 patients treated before 2010, 276 (65%) had rectal cancer and 149 (35%) had colon cancer (right colon – 68, left colon – 81) compared with 165 (57%) rectal cancer and 124 (43%) colon cancer (right colon – 49, left colon – 76) of a total of 289 patients in the post-2010 group. Further demographics and details of tumour characteristics have been previously reported. [19]

Overall survival in CRC

Overall survival for patients post-2010 was significantly better compared to pre-2010 ($P < 0.001$). The one, three and five-year survival for post-2010 were 89% (95%CI: 85.5% - 93.2%), 75% (95%CI: 69.9% - 82.2%) and 68% (95%CI: 61.5% - 76.0%) respectively versus 79% (95%CI: 75.8% - 83.5%), 67% (95%CI: 62.9% - 72.1%) and 59% (95%CI: 54.3% - 64.2%) for pre-2010 time period (Figure 1).

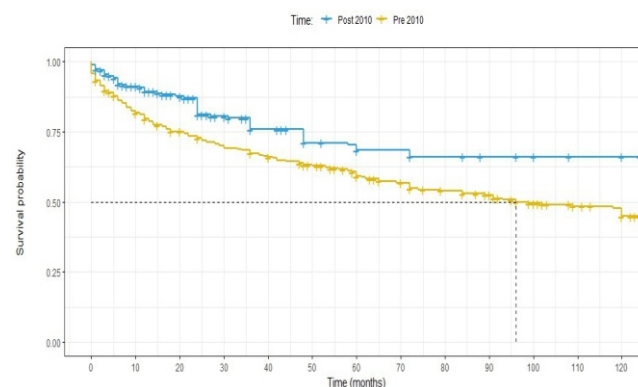


Figure 1: Overall Survival in CRC; Pre- vs. Post 2010 comparison.

Rectal cancer - disease free and overall survival pre-2010 vs post 2010

Patients with rectal cancer demonstrated a significantly better disease-free survival (DFS) during the post-2010 period compared to the pre-2010 period ($P < 0.0001$) (Figure 2).

The five-year disease-free survival for the post-2010 cohort was 91.7% (95%CI: 86.9% - 96.9%) compared to 73% (95%CI: 67% - 79.6%) in the pre-2010 time period. In terms

of overall survival, post-2010 patients fared significantly better compared with pre-2010 rectal cancer patients ($P<0.001$); The overall survival at one, three and five years for post 2010 were 91% (95%CI: 86.6% - 95.9%), 79% (95%CI: 71.6%–86.8%) and 69% (95%CI: 60.3%–79.3%) respectively versus 76% (95%CI: 71.2% – 81.2%), 62% (95%CI: 56.6%–68.4%) and 54% (95%CI: 47.6%–60.1%) for pre 2010 time period (Figure 3).

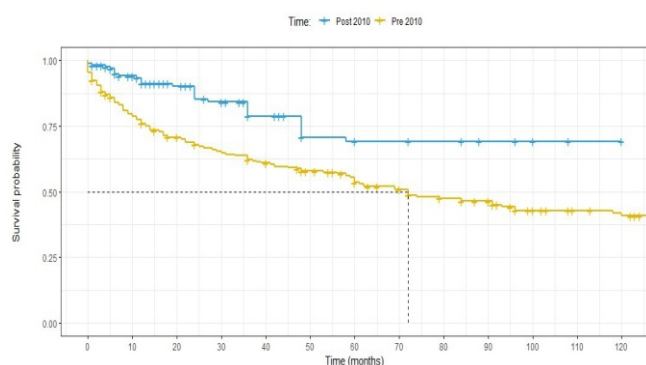


Figure 2: Disease free survival of patients with rectal cancer: Pre- vs. Post-2010

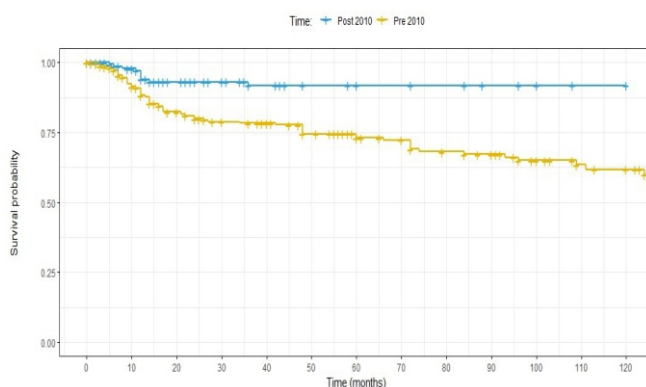


Figure 3: Overall survival of patients with rectal cancer: Pre- vs. Post-2010

Colon cancer - disease free and overall survival pre-2010 vs. post 2010

Disease free survival for colon cancer did not significantly differ between the time periods ($P=0.2$). The five-year DFS for the post-2010 cohort was 87% (95%CI: 79% - 96%) compared to 79% (95%CI: 71.3% – 86.5%) in the pre-2010 time period. (Figure 4).

Similarly, the overall survival between the two time periods were comparable for colon cancer ($P=0.8$); Overall survival at one, three and five years for the post 2010 cohort was 87% (95%CI: 80.4%–93.6%), 72% (95%CI: 62.1%–82.5%) and 67% (95%CI: 56.5% – 79.3%) respectively versus 86.3% (95%CI: 80.9%–92.1%), 77% (95%CI: 70.5%–84.5%) and 70% (95%CI: 62.3%–78%) for the pre 2010 cohort. (Figure 5)

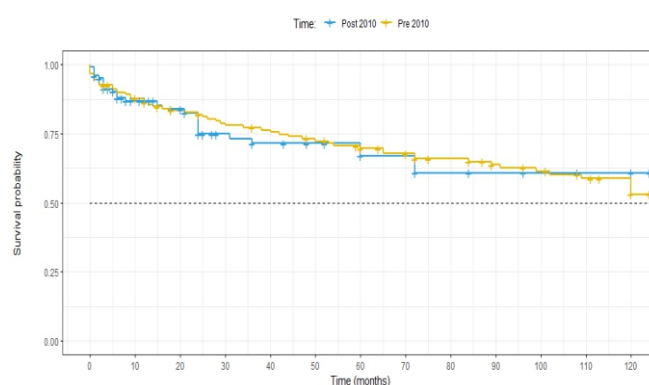


Figure 4: Disease free survival of patients with colon cancer: Pre vs Post-2010

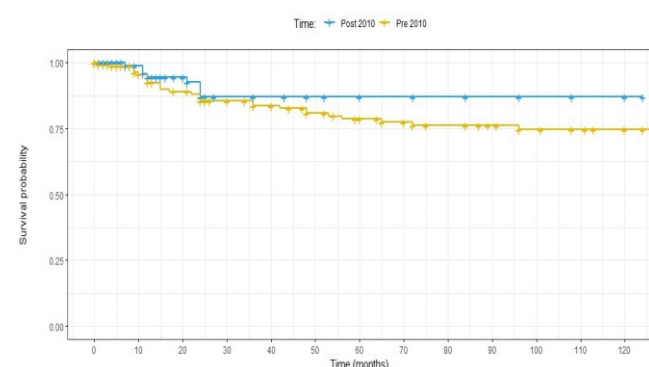


Figure 5: Overall survival of patients with colon cancer: Pre vs. Post-2010

Histological assessment

The histopathological characteristics of the specimens from the two periods that could be implicated in OS and DFS demonstrated significant differences. The median nodal harvest in the post-2010 period was 13 compared to 9 in the pre-2010 period ($P<0.001$). The margin positivity in rectal cancer specimens significantly reduced from 16% to 6% ($P=0.01$). Although the proportions of well and moderately differentiated cancers are different there is no significant difference in the poorly differentiated cancers between the two time periods (Table 1). The other histological tumour characteristics are also comparable between the two groups.

Quality of life assessment

A subgroup of 100 patients completed the QOL survey (44% male, median age 61 years; range 25 to 86 years). Sixty-five per cent of the subgroup was patients with rectal cancer, while 35% were those with colon cancer. Overall, patients who survived curative therapy for CRC reported a PCS of 0.64 and an ECS of 0.67 (Max-1.0) (Figure 6). There was no difference in QOL components between rectal and colon cancers (PCS: rectal – 0.64 vs. colon – 0.63, $p=0.9$; ECS: rectal – 0.65 vs. colon – 0.66, $p>0.05$). Further, when we compared QOL in survivors less than 5 years with QOL in those greater than 5

years, we found that the length of follow-up did not influence the QOL indicators in patients (QOL < 5 years vs. QOL > 5y; $p=0.9$ for PCS and 0.3 for ECS respectively). Organ function-related problems were reported by 69% of the population, of which increased bowel frequency was the main complaint in 27%. Furthermore, 51% of complaints were related to the gastrointestinal system, and 12% were genito-urinary in origin. Lifestyle-related issues were a complaint in 30%, of which easy fatiguability (20%) was foremost. Twenty-four percent had sexual/psychological problems; impotence in 13% and depression in 7%. (Figure 7).

Table 1: Comparison of histopathological characteristics of the tumour specimens between pre and post 2010.

Characteristic	2010-2020 N=289	Pre-2010 N=425	P value
Differentiation			
Well	16 (5.6%)	60 (14%)	<0.001
Moderate	260 (90%)	340 (80%)	<0.001
Poor	13 (4.4%)	25 (6%)	0.2
T stage			0.22
T 3/4	202 (70%)	319 (75%)	
T 1/2	87 (30%)	106 (25%)	
N stage			0.87
0	153 (53%)	225 (53%)	
1	78 (27%)	102 (24%)	
2	58 (20%)	93 (22%)	
3	0 (0%)	4 (1%)	
Nodal harvest			<0.001
Mean (SD)	14 (9)	10 (7)	
Median (IQR)	13 (10)	9 (9)	
Range	0 - 74	0 - 46	
Margin + rectal ca	10 (6%)*	44 (16%)*	0.01
PNI	25 (8.6%)	55 (13%)	0.20
LVI	43 (15%)	51 (12%)	0.31
AI	20 (7%)	55 (13%)	0.11

PNI-perineural invasion; LVI – lymphovascular invasion; AI- angio invasion; * - N=165; † - N=277

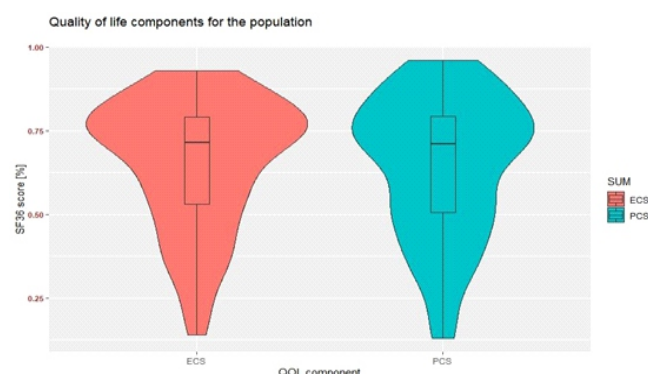


Figure 6: Violin plot demonstrating the distribution of the two components of QOL scores for CRC.

Table 2: Components of patient reported concerns

Organ Function Related	
Increased Bowel Frequency	27
Altered Bowel Habits	9
Urinary Incontinence	7
Urine Urgency	5
Body aches	5
Faecal incontinence	3
Flatus Incontinence	1
Constipation	3
Stoma related problems	6
Incisional Hernia	5
Poor urinary stream	1
Rectal Bleeding	1
Tenesmus	1
Miscellaneous	14
Lifestyle Related	
Easy Fatiguability	20
Travelling Difficulty	8
Diet	2
Psychological/Sexual	
Impotence	13
Depression	7
Fear of Recurrence	2
Not Well Defined	2

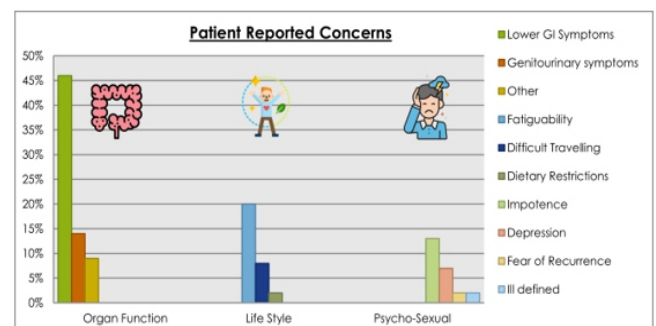


Figure 7: Patient reported concerns in colorectal cancer survivors

Discussion

This study was undertaken to evaluate the process of continued adaptation, evolution in the management of cancer of the colon and rectum upon disease-free and overall survival for colon and rectal cancer, and to assess quality of life in a cohort of survivors at a centre based in the North Colombo region of Sri Lanka. Our results indicate an overall improvement in survival of patients with CRC over two consecutive decades; overall and disease-free survival in patients with rectal cancer made the single-most important difference to improvement in survival. Management of rectal cancer has evolved in a global context during the first decade of the 21st century. Pre versus post-2010 improvements in

disease-free and overall survival of patients with rectal cancer indicated in the Kaplan-Meier curves are reflections of our continuous efforts at evaluating and adopting new evidence-based practice protocols and overall improved compliance to agreed treatment changes across all specialties of the multidisciplinary treatment team. Refinement of surgical techniques, greater use of adjuvant and neo-adjuvant therapies, including biological agents, and improvement of perioperative care in colorectal surgery stand out as some of the significant contributory factors towards improved survival.

A 2022 epidemiological study of over 1500 patients with CRC treated at the National Cancer Institute in Sri Lanka pointed to the variation in concordance to guidelines, chiefly in the use of pre-operative NCRT, in treatment of rectal cancer.[20] However, at the university surgical unit North Colombo teaching hospital, treatment of rectal cancer evolved continually and uniformly from surgical management alone in the nineties to the use of NCRT (initially with a post chemoradiation waiting time of <8 weeks, currently extended to >8 weeks) from 2005 and beyond. Also, the quality of pre-operative irradiation had improved from cobalt-based treatments in earlier times to the use of linear accelerators in irradiation delivery. Adopting total mesorectal excision as the standard of care in surgical training was another contributor to improving care. During this time, structured pathology reporting and training younger pathologists to increase the number of lymph nodes harvested became a matter of routine. Currently, magnetic resonance image features in rectal cancer, such as wall staging, extra-vascular lymphatic involvement and pelvic side-wall involvement, are the standard of care for low rectal cancer in Sri Lanka. We believe that the improvement in survival of patients with colorectal cancer post-2010 was influenced by all the above interventions. The significant improvement in nodal harvest and margin positivity, which are histopathological characteristics that have implications on survival, in the post 2010 cohort further supports this hypothesis.

Consequently, there has been an increased burden of survivorship. Survivors are faced with unique challenges because of treatment. The medium and long-term quality of life in these patients was affected by increased bowel frequency, sexual dysfunction and such conditions as depression, like psychosomatic reports of the low anterior resection syndrome (LARS). [21] As much as neo-adjuvant treatment and TME surgery improved DFS and OS, the downsides are increased rates of radiation enteritis and

genitourinary dysfunction. High ligation of the inferior mesenteric artery, which, on the one hand provides a better lymph node yield, poses a higher risk of pelvic splanchnic nerve injury on the other, leading to sexual dysfunction. Similarly, the low anterior resection syndrome (LARS) following sphincter preservation procedures for rectal cancer, which requires specialized nursing management, is lacking on a wider scale in Sri Lanka. Also, there is concern that most patients with CRC feel abandoned because of the lack of supportive care to manage these conditions following treatment.[22] In a systematic review of specific needs of CRC survivors, in which the authors evaluated a total of 54 studies, the greatest call in 51% of survivors was for emotional support and reassurance irrespective of the clinical stage of disease.[23] Furthermore in a Danish Cancer Registry study of over 9000 survivors of both colon and rectal cancer, the authors revealed that survivors compared with matched controls displayed reduced work participation for up to 10 years post-treatment. Rectal cancer survivors fared worse than those of colon cancer. Specifically, these data indicated that individuals' return to work was mostly affected between 1- and 4-years post-completion of treatment [24], which differed from the present study that showed no significant difference in overall quality of life before and 5 years after completion of treatment. This may be explained by the specific nature of the question sought in the Danish series compared with ours, which was an overall quality of life assessment. Nonetheless, in many ways, this translates to a cured acute state of ill-health transitioning to chronic illness. In Sri Lanka, except for stoma care services that are available nationwide, allied health care services in the forms of pelvic floor nursing, sexual dysfunction clinics, cognitive therapies and psychological support have not developed in par with mainstream clinical practice. This may be attributed to a lack of awareness of the needs of survivors and, consequently, failure to allocate funds for such services. This study demonstrates that the commonest patient reported QOL concern amongst this population is organ function related issues. To address this, a strong health support network is essential.

A comprehensive cancer screening programme would be the ultimate solution for the early detection of CRC thus improving the outcomes. However, being a developing economy, a community screening programme in CRC is far beyond the capacity of most countries in the South Asian region. While we envisage such developments, the focus needs to be on improving the survivorship through therapeutic interventions and supportive care.

Thus, the next phase of development in care of CRC in Sri Lanka and perhaps most countries in South Asia should be to develop patient care support services preferably in patients homes and in the community. We propose a post-surgical care multi-disciplinary team comprising of surgeon and oncologist, psychologist and counsellor, colorectal nurse/enterostomal therapist, nutritionist, social worker and a member of the survivor's family to help support and guide colorectal cancer survivors, similar to some upper and middle-income countries of the world. [25] The limitation of this study is the part-retrospective nature of data evaluation although data were entered in a prospective manner that was frequently audited.

In conclusion, we have demonstrated an improvement in disease-free and overall survival in patients with CRC, mainly due to better survival of patients with rectal cancer. Whilst hospital-based care of CRC patients, over time, had developed in multiple ways, there is a need for improvement in extended communication and support services for CRC survivors in Sri Lanka and South Asia. With the rising trend in the incidence of CRC, a community-based screening programme aimed at prevention and early detection should be the long-term vision in this region which is currently hindered by scarcity of resources.

Ethical Approval and Consent to participate

This is a retrospective analysis of the colorectal cancer database maintained under the approval of the ethics review committee (P/39/04/2015 and P/148/11/2024) of the Faculty of Medicine of the University of Kelaniya.

Human Ethics

No biological samples were collected for research purposes and no interventions were carried out or deviations from the standard practice was taken up for research purposes.

Consent for publication

Individual consent for publication is not required due to the nature of the study. Identifiable data are not published.

Availability of supporting data

The data will be available on reasonable request from the authors.

Competing interests

None of the authors have conflicts of interests to declare.

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Author contributions

PC and SK were involved in conceptual design, patient management, data collection, analysis, manuscript writing and critical appraisal of the manuscript. RD and SG were involved in data collection, analysis, manuscript writing and critical appraisal of the manuscript. DE was involved in statistical analysis, manuscript writing and critical article appraisal. BG was involved in patient care, data collection, data analysis and critical appraisal. GM and JH were involved in pathological assessment of the specimens, manuscript writing and critical appraisal of the manuscript.

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