

The Cost of Survival: An Exploration of Colorectal Cancer Survivors Experiences of Pain

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Abstract:

Background:

The Institute of Medicine report *From Cancer Patient to Cancer Survivor* has drawn widespread attention to the experiences of cancer survivors. Research examining the symptom experiences of survivors are proliferative within the literature but limited by samples which include multiple tumour groups and varying inclusion criteria. This cross-sectional quantitative study seeks to examine pain and quality of life (QoL) in the context of colorectal cancer (CRC) survivorship, as defined by the Institute of Medicine.

Materials and Methods:

A purposive sample of CRC survivors ($n=252$) attending hospitals and cancer support centres in the Republic of Ireland were recruited between September 2014 and January 2016. Self-rated health (SRH), QoL and pain were assessed in the sample using the EuroQOL questionnaire, the Functional Assessment of Therapy–Colorectal (FACT-C) questionnaire, and symptom experience items.

Results:

One hundred participants (39.7%) indicated they had pain on the day of the survey or in the past week. Of those with pain, many also experienced a lack of energy (94.9%), bowel dysfunction (74%), sleep disturbance (76.3%) or interference with their ability to enjoy life (74.5%). Pain was associated with younger age, female gender, current chemotherapy treatment, and previous radiotherapy treatment. Although participants reported positive QoL scores, statistical analysis revealed pain was linked to significantly poorer SRH and overall QoL, and poorer physical, emotional, functional, social/family and CRC-specific well-being, compared to those who did not indicate pain.

Discussion:

Pain was experienced by almost two-fifths of CRC survivors up to five years after treatment and was associated with poorer SRH and QOL. In light of these findings, healthcare professionals must endeavour to manage cancer survivors' symptom needs in a holistic manner, remaining cognisant of the burden of pain and other symptoms in long-term cancer survivors.

Manuscript:

Introduction:

Pain is a complex, multifactorial phenomenon which impacts physical, psychological and social domains of living [1]. Modern evolution of cancer treatments means many cancer patients may look forward to long-term cancer survivorship, as cancer is managed as a chronic illness. However, growing rates of cancer survivorship bring new concerns, as chronic effects of cancer treatment gain prominence. A growing discourse surrounding the unmet needs of cancer survivors' has emerged since the publication of *From Cancer Patient to Cancer Survivor: Lost in Transition* [2] a decade ago.

Previous studies concluded that CRC survivors regain quality of life (QoL) of similar or greater levels than those reported by normative populations [3-5]. The positive reframing of QoL in the presence of chronic symptoms is a widely discussed and accepted concept within the chronic illness literature [3, 6]. However, it is estimated one-third of cancer survivors experience pain following curative cancer treatment [5, 7-11], compared to almost two-thirds of those receiving anticancer treatment, or living with advanced metastatic or terminal cancer [7]. Pain is ranked as a one of the most common symptoms experienced by cancer survivors [4, 9, 10], and has been associated with poorer physical [12] functional [11-14], psychological [14, 15] and overall [16] QoL, and may contribute to social isolation in survivorship [17].

Several factors have demonstrated an influence on the presence and intensity of pain including age [9, 13, 18], female gender [10, 11, 13, 14, 16, 18], ethnicity [13, 14], symptom clusters [13], previous chemotherapy treatment [13, 18], previous radiotherapy treatment [18], time since treatment [13, 16], stage of disease [19], and income [11]. Furthermore, pain has been shown to occur in clusters with fatigue, insomnia [19], depression [8, 11] and

anxiety [11]. The influence of age on pain is the subject of debate. Although almost one-third cancer survivors report pain [5, 7-11], approximately one-tenth of older CRC survivors attribute pain to cancer-related factors [9], compared to almost two-fifths of general CRC survivor samples [11]. Studies have revealed older cancer survivors are reluctant to attribute symptoms of pain, fatigue or cognitive dysfunction to cancer [17], while age-related factors have greater predictive ability than cancer-related factors for symptoms of pain, low energy levels and weakness [13]. Previous research suggests that ageing does not influence increased risk for pain, fatigue or insomnia in elderly cancer survivors [19]; however, no consensus has been reached regarding the intensity or frequency of pain flares [15, 18].

Although under-treatment of pain during cancer treatment has reduced over the past decade [20], the prevalence of pain and its impact on CRC survivors' QoL in the survivorship period remains poorly evaluated. Many studies of cancer survivors' pain focus on samples which include multiple tumour groups and varying inclusion criteria [8, 9, 13-15], resulting in small samples of each tumour group or a lack of analysis of data pertaining to particular tumour groups. Meanwhile studies which evaluate the pain of colorectal cancer (CRC) survivors' have limited generalisability and scope due to small samples sizes [11, 16], lack of clear definition of cancer survivorship [15], or sampling of older [12, 19], early stage (<2 years) [18, 19] or long-term cancer survivors (>5 years) [12]. Therefore the present study sought to explore the prevalence and experience of pain in a sample of CRC survivors up to five years following diagnosis.

Material and Methods:

Participant Selection:

The current study is part of a larger mixed-methods study to examine CRC survivors' QoL and healthcare experiences. This report details the results of the cross-sectional survey of CRC survivors attending three hospitals and twenty-one cancer support centres for routine follow-up care in the Republic of Ireland. All adult CRC survivors who were between 6 months and five years post-diagnosis, over the age of eighteen years, resident in the Republic of Ireland, able to speak, read and comprehend English and able to provide informed consent were eligible to participate in the study. In keeping with the Institute of Medicine [2] definition of cancer survivorship, CRC survivors were considered eligible for participation in the study regardless of their disease status. To minimise the effect of acute toxicities on the study findings, CRC survivors were excluded if they were receiving primary cancer treatment, or less than six months post-diagnosis. Ethical approval for this study was granted by the Research Ethics Committees of the participating hospitals and university.

Data Collection

Cancer-related QoL in the seven days preceding the study was measured using the 36-item Functional Assessment of Cancer Therapy-Colorectal Cancer (FACT-C) questionnaire [21]. The questionnaire contains four subscales of the core FACT-General (FACT-G) questionnaire, physical well-being, social well-being, emotional well-being, and functional well-being, and colorectal cancer subscale. FACT-C items are assessed using a Likert-scale format, with item scores ranging from 0, "not at all" to 4, "very much", higher scores on each subscale reflect better QoL.

Cancer survivors' self-rated health (SRH) was assessed using the five-item EuroQOL EQ-5D-5L questionnaire and visual analogue scale which measures SRH on the day of the survey on a scale of 0-100 [22]. Each health dimension of the EuroQOL questionnaire (Mobility, Self-Care, Usual Activities, Pain/Discomfort, and Anxiety/Depression) is measured on a five level Likert scale, ranging from 0, "no problem," to 4, "extreme problems". Both the EuroQOL and the FACT-C questionnaires are widely used and have demonstrated validity and reliability with CRC populations.

The presence and intensity of pain was assessed 1) on the day of the survey using the EuroQOL item "Pain/Discomfort," and 2) in the week prior to the survey using the FACT-C item "in the past 7 days, I have pain". Each item was rated on a five-point Likert scale, with higher scores reflecting greater pain. Clinical and demographics characteristics assessed in the questionnaire included diagnosis, previous and current treatments, time since diagnosis, age, gender, living arrangements, employment status, ethnicity and healthcare insurance status.

All eligible CRC survivors identified by gatekeepers during the study period between October 2014 and January 2016 were offered written study information and invited to participate. Consenting participants were invited to complete an online or paper-based survey. Reminder letters were sent to those who had not returned a completed questionnaire after four weeks.

Data Analysis

For the purpose of analysis, participants who had missing responses to the EuroQOL and FACT-C pain items were excluded. Incomplete data from the FACT-C and EuroQOL questionnaires were recorded as missing and excluded from relevant analysis. Responses to

the EuroQOL and FACT-C pain items were collapsed into binary items, a pain score of 0 was coded as “no pain”, while scores ranging between 1-4 were coded as “any pain” in the corresponding binary items “pain today” (EuroQOL) or “pain in the past week” (FACT-C).

Data was analysed using SPSS v21. Cronbach’s α was used to assess the internal consistency of the FACT-C scale and subscales. Descriptive statistics were used to characterise the demographic and cancer-related attributes of the sample. The prevalence of pain within the sample are reported using proportions. QoL and pain intensity scores are reported using descriptive measures of centre and spread. Interval estimates of the proportion of the population experiencing pain and population mean scores for QoL and SRH are reported using 95% confidence intervals.

The relationship between pain and demographic and medical characteristics were examined using Chi-square analysis. Where significant values were recorded, odds ratios were calculated using a standardised formula (Table 3). The results of t-tests to examine differences in SRH and QoL between groups with and without pain on the day of the survey are reported, and Spearman’s Rank Order Correlations were calculated to estimate the relationship between pain and QoL. All analysis were undertaken at the level $\alpha \leq 0.05$ level of significance unless otherwise stated.

Results:

Sample Characteristics

Of the four hundred and four CRC survivors screened and eligible for the study, three hundred and four provided informed consent and returned a completed questionnaire (raw response rate: 75.2%). Fifty-two participants failed to complete one or both of the EuroQOL and FACT-C pain items and were therefore excluded. A final sample of two hundred and

fifty-two CRC survivors were included (response rate: 62.3%). Cronbach alpha results for the FACT-C subscales were acceptable at $\alpha \geq 0.743$, and for the FACT-G and FACT-C scales at $\alpha = 0.94$.

The demographic characteristics and the clinical characteristics of the sample are presented in Table 1. The mean age of participants was 66.4 years ($SD=11.4$). The average time since diagnosis for the sample was 3.0 years ($SD=1.4$). Fifty-five percent were male, eighty percent lived with family or friends and more than half had private health insurance (50.2%) or a medical card (57.1%), which allows the holder to receive healthcare free of charge or at a discounted rate in the public healthcare system. Almost half of participants were retired (47.7%).

Pain

Frequencies and mean pain ratings reported by the participants' are reported in Table 2. On the day of the survey, ninety participants (35.7%, CI: 29.8%-41.6%) reported pain, while seventy-seven participants had experienced pain in the seven days prior to the study (30.6%, CI: 24.9%-36.3%). The low mean pain scores reported by the sample on the day of the survey ($\bar{x}=0.47$, $SD=0.72$) and in the week prior to the survey ($\bar{x}=0.46$, $SD=0.81$) are reflective of the large proportions reporting no pain or low-moderate levels of pain.

Overall, 39.7% ($n=100$) reported pain at one or both time points. Figure 1 presents the frequency of the most commonly reported symptoms experienced by CRC survivors who had any pain. Compared to participants who did not experience pain, those with pain were more likely to report a lack of energy ($p \leq 0.0005$, $OR=17.84$), body image disturbance ($p=0.002$, $OR=2.76$), or an inability to work ($p \leq 0.0005$, $OR=5.58$). High proportions of those with pain indicated challenges with enjoyment of hobbies (78.8%, $n=78$), ability to work

(79.4%, $n=77$) and enjoyment of life (74.5%, $n=73$). 74.5% of participants with pain were discontent with their QoL, compared to 32% of those with no pain. A greater proportion of CRC survivors with pain were more likely to indicate problems with all FACT-C and symptom items ($p \leq 0.05$) with six exceptions; feeling close to one's partner ($p=0.236$), satisfaction with one's sex life ($p=0.178$), difficulty urinating ($p=0.068$), urinary frequency ($p=0.118$), fear of cancer recurrence ($p=0.269$) and fear of cancer spread ($p=0.078$).

Table 3 presents the results of Chi-square analysis to determine differences between CRC survivors' based on demographic and medical characteristics. Younger age ($p=0.003$, $OR=2.271$), receipt of current anti-cancer treatment ($p=0.002$, $OR=3.494$), previous chemotherapy treatment ($p \leq 0.0005$, $OR=3.639$) and previous radiotherapy treatment ($p=0.006$, $OR=2.241$) were each significantly associated with cancer survivors experience of pain on the day of the survey. Likewise, younger age ($p=0.027$, $OR=1.822$), receipt of current anti-cancer treatment ($p=0.001$, $OR=3.969$) and previous chemotherapy treatment ($p=0.001$, $OR=2.806$) were significantly associated with cancer survivors experience of pain during the week prior to the survey.

Quality of Life

Table 4 presents results of descriptive and inferential analysis of QoL and SRH for the sample based on pain experience. The sample reported positive perceptions of their health ($\bar{x}=81.4$, $SD=16.2$) and CRC-related QoL (FACT-C: $\bar{x}=111.9$, $SD=18.9$). CRC survivors who reported pain on the day of the survey and in the week preceding the survey reported significantly poorer SRH and QoL scores on all scales ($p \leq 0.05$). The results of correlation analysis between pain and QoL indicators are presented in Table 5. Increasing pain today or in the past week was negatively associated with SRH and QoL on all subscales ($p \leq 0.05$). The relationships between pain today or in the past week and QoL were moderate for all

subscales with two exceptions. Physical well-being had a strong correlation with pain on the day of the survey ($r_s=-0.653$) and in the past week ($r_s=-0.691$). Social well-being had a weak correlation with pain on the day of the survey ($r_s=-0.281$) and in the past week ($r_s=-0.293$).

Discussion:

This study sought to explore the prevalence and experience of pain in a sample of CRC survivors up to five years following diagnosis and the effect of pain on CRC survivors' QoL. Two-fifths of the sample reported pain on the day of the survey or in the past week. When the groups were compared based on the demographic and medical variables under study, CRC survivors who reported pain today and pain in the last week were more likely to be younger, receiving current anti-cancer treatment and have previous chemotherapy treatment. Previous radiotherapy treatment was associated with experience of pain on the day of the survey only. CRC survivors who reported pain on the day of the survey or the week preceding participation in the survey indicated significantly poorer SRH, lower overall QoL scores, worse physical, social, emotional and functional well-being and a greater degree of CRC-specific QoL concerns compared to CRC survivors who did not report pain.

The prevalence of pain in this sample of CRC survivors mirror the findings of previous research of cancer survivors which include multiple tumour groups [5, 7-11], albeit slightly higher than the prevalence reported in CRC survivor samples of other studies [5, 9].

However, the finding that gender and time since diagnosis are not associated with CRC survivors' experience of pain refutes the findings of several studies [10, 11, 13, 14, 16, 18].

These differences may be attributed to differences in study designs, as studies of CRC survivors tend to have had smaller samples, and may be at risk of type I errors [10, 11, 16], while others examined short-term [18], long-term [13] and diverse groups of cancer survivors [13, 14].

The impact of age on cancer survivors' experiences of pain is debatable. The nature of CRC means the profile of survivors is skewed to middle-older age males and females. This study has found younger cancer survivors were twice as likely as older cancer survivors to report pain on the day of the survey and in the week preceding the survey. Previous studies have reported older cancer survivors have expressed difficulty in ascribing pain and other symptoms to cancer-related or age-related factors [9, 11, 17], while poorer QoL and greater symptom burden in younger cancer survivors have been attributed to fewer coping strategies and greater perceived threat of recurrence [4, 6]. To understand this finding, it is not unreasonable to hypothesise that younger age, and fewer comorbidities may permit more aggressive treatment strategies, contributing to a higher rate of late toxicities [6]. This is tentatively supported by the findings of the current study which associate previous radiotherapy and current chemotherapy with a greater likelihood of experiencing pain. Furthermore, younger CRC survivors may also experience a greater disturbance in their work life arising from chronic effects. This study showed that those who experience pain were more likely to indicate they were unable to work or gain fulfilment from their work compared to those who did not experience pain.

Although the mean QoL scores reported within this study are comparable to population norms [3-5], pain was significantly associated with poorer SRH and QoL on all subscales. Furthermore, differences in FACT-C scores between those who did and did not report pain are clinically significant, with disparities greater than the minimally important differences suggested by Yost and colleagues [23]. In addition, almost 95% of those who reported pain also experienced a lack of energy in the week preceding the survey, this is comparable to previous studies [13]. Pain and fatigue are potential deterrents to activity and have implications for the psychological well-being of the cancer survivor. Pain and fatigue may

signify potential recurrence or disease progression [24, 25], while late-effects of cancer may also contribute to social withdrawal, functional disability, resentment and anger in the long-term [17].

Strengths/Limitations

The results must be interpreted with cognisance of study limitations. Although this sample was drawn from multiple research sites serving various socio-economic groups, the cross-sectional nature presents a limitation to the generalisability of this study. Furthermore, the questionnaire items used to assess pain in this sample limit this study, as they are not considered profound measures of pain. However, they are drawn from instruments which have established validity and reliability for CRC survivor populations. Moreover, the measures provide suitable means to assess point prevalence of pain, consistent with prior research and within the objectives of this study.

This study has addressed many of the previously discussed limitations of cancer survivorship research including clarity of disease status, definition of survivorship and purposive sampling strategies [11]. The strong response rate of 62.3% and rigour of inclusion criteria are strengths of this study. The sample is representative of CRC survivors in Ireland, as participants were recruited from routine follow-up care in hospitals and support centers which reflect the variety of settings in which CRC follow-up care is delivered in Ireland. The inclusion criteria ensure that the sample is consistent with the definition of survivorship set forth by the Institute of Medicine [2], and the symptoms reported are not contaminated by acute consequences of treatment. The homogenous sample of CRC survivors ensure the results are generalisable to similar populations of CRC survivors, and not biased by issues pursuant to other cancer survivor groups. The findings of

this study add to the limited knowledge available regarding CRC survivors' experience of pain and its impact on QoL.

These findings present a basis to direct larger-scale epidemiological research of QoL and symptom prevalence among CRC survivors. The results of this work guide the development of a qualitative research approach within an ongoing body of mixed-methods research. The qualitative component of this study provides an opportunity to fully evaluate CRC survivors' symptom experiences, providing depth, context and coherence to the picture painted by these results.

Conclusion

The findings of this study add to the growing evidence base surrounding symptom burden and management in CRC survivors. The high prevalence of symptoms which co-occur with pain and the association between pain and poorer QoL is a cause for concern, and one which healthcare professionals must remain cognisant. It is not enough to assess and manage CRC survivors' pain in isolation. Indeed, considering pain within the bigger picture of survivors' comorbidities and cancer-related complaints is imperative to address their needs holistically. Such an approach will ensure healthcare professionals may develop appropriate pain management strategies which will assist CRC survivors to sustain reasonable QoL levels in the long-term.

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Declaration of Interest:

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Figure 1 Clustered bar chart of the ten most common symptoms experienced by CRC survivors who report pain and comparison with the proportions of those without pain who report these symptoms

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