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Frequency, Characteristics, and Correlates of Pain in a Pilot Study of Colorectal Cancer Survivors 1–10 Years Post-Treatment

Amy E. Lowery, PhD[*], **Tatiana Starr, MA**[*], **Lara K. Dhingra, PhD**[§], **Lauren Rogak, MA**[†], **Julie R. Hamrick-Price, PsyD**[**], **Maria Farberov, MPA**[*], **Kenneth L. Kirsh, PhD**[¶], **Leonard B. Saltz, MD**[‡], **William S. Breitbart, MD**[*], and **Steven D. Passik, PhD**[††]

[*]Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, New York, New York

[†]Department of Epidemiology-Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, New York

[‡]Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York

[§]Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, New York, New York

[¶]The Pain Treatment Center of the Bluegrass, Lexington, Kentucky

[**]Department of Psychosomatic Medicine, Vanderbilt University, Nashville, Tennessee

[††]Clinical Addiction Education and Research, Millennium Laboratories, San Diego, CA, USA

Abstract

Objective—The long-term effects of disease and treatment in colorectal cancer (CRC) survivors are poorly understood. This study examined the prevalence and characteristics of pain in a sample of CRC survivors up to 10 years post-treatment.

Design—One hundred cancer-free CRC survivors were randomly chosen from an institutional database and completed a telephone survey using the Brief Pain Inventory, Neuropathic Pain Questionnaire-Short Form, Quality of Life Cancer Survivor Summary, Brief Zung Self-Rating Depression Scale, Zung Self-Rating Anxiety Scale, and Fear of Recurrence Questionnaire.

Results—Participants were primarily Caucasian (90%) married (69%) males (53.5%) with a mean age of 64.7 years. Chronic pain was reported in 23% of CRC survivors, with a mean moderate intensity rating (mean = 6.05, standard deviation = 2.66) on a 0–10 rating scale. Over one-third (39%) of those with pain attributed it to their cancer or treatment. Chi-square and *t*-test analyses showed that survivors with pain were more likely to be female, have lower income, be more depressed and more anxious, and show a higher endorsement of suicidal ideation than CRC survivors without chronic pain. On average, pain moderately interfered with daily activity.

Conclusions—Chronic pain is likely a burdensome problem for a small but not inconsequential minority of CRC survivors requiring a biopsychosocial treatment approach to improve recognition and treatment. Open dialogue between clinicians and survivors about physical and emotional symptoms in long-term follow-up is highly recommended.

Reprint requests to: Julie R. Hamrick-Price, PsyD, The Center For Personal Growth, 915 Middle River Drive, Suite 307 Fort Lauderdale, FL 33304, USA. Tel: (850)-621-5176; Fax: (615)-875-3450; Julie.R.Hamrick@vanderbilt.edu.

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Keywords

Colorectal Cancer; Survivor; Pain; Quality of Life; Pain Interference

Introduction

Cancer survivors can experience a variety of lasting symptoms years after treatment ends. Chronic pain is among these symptoms, although it may be unrecognized as a burdensome problem and go untreated [1–3]. Identification of demographic, medical, and psychosocial correlates of chronic pain in cancer survivors can provide important information on specific subgroups that are most in need of pain management. Several studies have examined correlates of pain in diverse groups of cancer survivors [4–6] and found that chronic pain affects up to 50% of survivors of various cancer sites, most notably breast and lung cancer [7–13]. However, we are unaware of any studies examining correlates of persistent post-cancer pain in long-term colorectal cancer (CRC) survivors, which is the focus of the current pilot study. Limited research addressing pain in CRC survivors can contribute to underdiagnosing and undertreating chronic pain, which several studies suggest may be the case [2,3].

Of the few studies that have examined pain in CRC survivors, a prevalence range of 7–27% has been reported [14,15]. However, use of single item measures, lack of clarity with regards to disease states, exclusion of longer-term survivors, and use of convenience samples limits the reliability and generalizability of such results to the larger population of CRC survivors [14,15]. Research focusing on a comprehensive assessment of pain in a random selection of CRC survivors is needed in order to better understand the experience and impact of pain in this population.

Persistent pain has been shown to impair health-related quality of life (HRQOL) [16,17], and increase depression [18–24] and anxiety [22] in other medical and cancer survivor populations. Chronic pain is often disabling, thus having a significant impact on daily functioning in cancer survivors. Of greater concern, some studies have found that these limitations may persist for up to 20 years [25]. Ultimately, a better understanding of the prevalence, characteristics, and correlates of chronic pain in cancer survivors is essential for ensuring optimal HRQOL among CRC survivors.

A biopsychosocial conceptualization [26] was adopted in the current study in an effort to fully appreciate the multidimensional nature of the pain experience. A complete understanding of the pain experience and pain-related outcomes require consideration of physical, psychological, and social factors [27,28]. The current pilot study is part of a series of studies designed to assess pain in survivors of six different cancer sites. This study aims to report the prevalence, severity, selected demographics, and medical and psychosocial correlates of pain in a random sample of CRC survivors in an effort to identify individuals at risk for persistent, long-term post-cancer pain. We hypothesized that pain would be significantly associated with higher levels of depressed mood and anxiety. Medical factors were assessed through exploratory analyses. Identifying the correlates of pain may assist physicians and rehabilitation programs in distinguishing high-risk CRC survivors and improving their HRQOL.

Method

Participants

Adult cancer survivors from the Colorectal Service at Memorial Sloan-Kettering Cancer Center (MSKCC) were deemed eligible for this study if they were receiving ambulatory, follow-up medical care at MSKCC at the time of this study, had a previous diagnosis of colorectal cancer, were between 1 and 10 years post-treatment completion, and had no evidence of disease at the time of assessment. In addition, potential participants had to be able to be reached by telephone; read, speak, and comprehend English; be at least 18 years of age; and able to provide informed consent. Patients were considered ineligible for the study if they were undergoing active cancer treatment or had a significant psychological or physical impairment that would preclude them from providing informed consent or completing the study questionnaires. Cancer survivors who received adjuvant therapies outside MSKCC were asked to self-report the type and duration of cancer treatments received. Time since treatment was determined by review of last treatment date in medical charts. A sample size of 100 was chosen due to the descriptive nature of the analyses in this pilot study.

Measures

We selected measures that have been widely used with medical populations and whenever possible, validated with a cancer survivor population with an effort to limit participant burden.

Sociodemographic Characteristics—Participants were asked information on age, gender, race/ethnicity, marital status, education level, employment status, and income.

Medical Characteristics—Medical charts were reviewed to collect data on date of primary cancer diagnosis, tumor site and stage of disease, primary and adjuvant treatments, disease recurrence, and other comorbid conditions.

HRQOL—The Quality of Life Cancer Survivor Summary [29] is a 41-item visual analog instrument of HRQOL with items rated on an 11-point scale ranging from 0, “worst,” to 10, “best.” It is composed of four multi-item subscales: physical well-being (eight items), psychological well-being (18 items), social well-being (eight items), and spiritual wellbeing (seven items). The scale has good reliability (Cronbach’s $\alpha = 0.93$) and convergent validity with the Functional Assessment of Cancer Treatment—General Scale ($r = 0.74$) [29–31] and has been used in previous studies with long-term cancer survivors [32–34].

Psychological Distress—The Zung Self-Rating Depression Scale (ZSDS) [35] is a 20-item self-report measure of depressive symptoms. Respondents rate how they felt in the past week using a 4-point Likert-type scale ranging from 1, “none or a little of the time,” to 4, “most of the time.” Item scores are summed to produce a depression score ranging from 25 to 100. The ZSDS has demonstrated high internal consistency (Cronbach’s $\alpha = 0.84$) and validity [35]. In order to reduce patient burden, a 10-item short-form of the instrument (the Brief ZSDS) was used.

The Zung Self-Rating Anxiety Scale (ZSAS) [36] is a 20-item self-report measure that rates the presence and severity of affective and somatic symptoms of anxiety on a 4-point Likert scale ranging from 1, “none or a little of the time,” to 4, “most of the time.” Total scores range from 25 to 100. The ZSAS has demonstrated high internal consistency (Cronbach’s $\alpha = 0.93$) and validity [36].

The Fear of Recurrence Questionnaire (FRQ) [37] is a 22-item measure widely used to measure fears about cancer recurrence. Patients are asked to rate each item on a 5-point Likert-type scale ranging from 0, "strongly agree," to 4, "strongly disagree," with total scores ranging from 22 to 110. The FRQ has high internal consistency (Cronbach's α = 0.92) and validity [38].

Pain Screening—Participants were asked two criterion questions based on a widely accepted criterion and our prior research methodology [39]: "Have you experienced persistent or frequent pain during the past two weeks" or "Would you have experienced persistent or frequent pain during the past two weeks, if not for the pain medication you are currently taking?" Survivors who endorsed at least one of the items were given the structured pain interview.

Structured Pain Interview—The structured pain interview consisted of the pain history, pain type, and pain etiology questionnaires.

Pain History: The Brief Pain Inventory (BPI) [40] was used in a semistructured interview format to assess pain prevalence and characteristics of pain in the past 2 weeks. The BPI contains pain severity and pain interference subscales, and has been used in other studies of cancer survivors [41]. Pain severity items are rated on an 11-point scale from 0, "no pain," to 10, "pain as bad as you can imagine." Pain interference items are also rated on an 11-point scale from 0, "does not interfere," to 10, "completely interferes." Similar to previous research [42,43], we classified pain ratings as mild (0–3), moderate (4–6), and severe (7–10). The BPI has been well-established as a reliable (Cronbach's $\alpha \geq 0.95$) and valid pain questionnaire [40]. Items assessing alternative therapies used to treat pain were also added.

Pain Type: Three items were used from the Neuropathic Pain Questionnaire-Short Form [44], "Do you experience numbness when you have pain?," "Do you have pain that is tingling?," and "Do you have increased pain due to touch?" These items have high predictive accuracy (73%) in differentiating neuropathic from non-neuropathic pain [45].

Procedure

Institutional Review Board approval was obtained at MSKCC. Eligible CRC survivors were identified using DAVInCI, a web-based application that allows authorized researchers to access protected health information. The DAVInCI database was accessed by a trained research study assistant (RSA) to identify all survivors who met inclusion criteria. A random sample was generated from this comprehensive list of survivors by assigning each survivor a random number using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). Permission was obtained from the clinic attending physician for the RSA to contact the survivor.

Eligible participants were mailed an introductory letter and opt-out phone number. RSAs contacted participants within 2 weeks to conduct a 45- to 60-minute phone interview. Participants were compensated $15.00 for study involvement.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 19.0 for Windows (IBM SPSS Statistics, New York, NY, USA). Independent samples *t*-tests were conducted to examine demographic differences between study completers and refusers. Descriptive statistics were generated to describe demographic and medical variables, as well as the prevalence and characteristics of pain severity, treatments, and interference. Chi-square tests and independent samples *t*-tests were used to calculate

group comparisons between pain groups (pain vs no pain) on demographic, medical, and psychological variables, and compare pain intensity ratings by survivors with cancer-related pain (CRP) and those with other pain.

Results

Participants

Of the 200 CRC survivors screened and potentially eligible for the study, 100 provided informed consent and completed participation in the study. One participant's data was not able to be included in the analyses due to a large amount of missing data, resulting in a final N = 99. Reasons for not participating in the study were: unable to reach (N = 58), not interested (N = 18), too busy (N = 2), too sick/anxious (N = 1), concerns about privacy (N = 1), and other (N = 20). The only demographic variable collected on individuals who declined participation was age, which was not significantly different from study participants ($t[198] = -1.13$, $P = 0.26$). Table 1 presents demographic and disease variables. The sample was predominantly Caucasian (90%), married (69%), and had a mean age of 64.71 years (standard deviation [SD] = 12.77 years). Patients ranged from 16 to 120 months post-treatment.

Prevalence and Correlates of Pain

Participants were classified into one of four groups based on their belief about the cause of their pain: no pain (77%), CRP (9%), other pain (12%), and both CRP and other pain (2%). Therefore, a total of 23% reported pain, with 11% reporting CRP. Compared with survivors without pain, those with pain were more likely to be female ($\chi^2 = 4.24$, $P < 0.05$) and have lower income ($\chi^2 = 7.93$, $P < 0.05$). No other demographic or medical variable was significantly related to the presence of pain ($P > 0.05$). CRC survivors with pain had significantly more depressive ($t[98] = 4.14$, $P < 0.01$) and anxiety symptoms ($t[98] = 4.93$, $P < 0.01$), lower HRQOL ($t[98] = -3.16$, $P < 0.01$), and higher endorsement of suicidal ideation ($t[98] = 2.68$, $P < 0.01$) than those without pain. Fear of recurrence did not differ between survivors with and without pain ($P > 0.05$).

Subjective Characteristics of Pain

Among those with pain, intensity ratings for worst and average pain in the last week and current pain were compared between survivors with CRP and those with other pain. Overall (see Table 2), CRC survivors rated their worst and average pain as moderate and current pain as mild. None of the pain intensity ratings significantly differed between survivors with CRP and those with other pain. Slightly more than half (52.2%) reported at least one neuropathy-like symptom to describe their pain, and this prevalence did not significantly differ between survivors with CRP (62.5%) and those with other pain (38.5%) ($P = 0.38$). Pain was reported in the following sites: legs/feet (52.2%), back (30.4%), pelvis/rectum/genitalia (17.4%), arms/hands (17.4%), abdomen (13%), and neck (8.7%). Aggravating factors were reported by 83% of those with pain and included: climbing stairs (34.8%), walking (30.4%), lifting (21.7%), overextending (17.4%), standing (13%), urination/bowel movement (8.7%), sleeping (8.7%), and miscellaneous, such as weather, stress, or diet (39%).

Pain Treatment and Relief

A majority of survivors (78.3%) reported that they used complementary treatments (e.g., massage, acupuncture) for their pain. Approximately half of survivors (52.2%) with pain reported taking a prescription analgesic, with 21.7% reporting that they were taking an opioid medication. Prevalence of CRC survivors use of pain treatment did not significantly

differ between those with CRP (75%) and those with other pain (78.6%; $P = 0.24$). In addition, although not significantly different, the average percentage pain relief provided by pain treatments was higher in those with CRP (70%) in comparison with those with other pain (53%; $t(1,9) = 0.88$, $P = 0.40$).

Pain Interference

In general, survivors with CRP reported a moderate level of interference in daily activities due to pain (Table 3), while those with other pain rated their level of interference mild-moderate. Although not significantly different, there was a trend across each domain for survivors with CRP to report a higher level of interference than those with other pain (except for normal work, where survivors with other pain averaged a higher interference rating). The one area with a significant difference in ratings was relations with others; survivors with CRP reported a moderate interference due to pain and those with other pain reported a minimal level of interference.

Discussion

Pain was reported by approximately one-fourth (23%) of the survivors, which is similar to the prevalence found in other studies of CRC survivors [14,15]. The difference in this study is that the prevalence of pain was still reported in survivors as far as 10 years post-treatment, suggesting that the chronic pain they are experiencing is not likely going to improve on its own with time. Survivors with pain were more likely to be female and have lower income, which has been found in pain studies of other survivor groups [4,46]. The relationship of pain and income is not surprising, given that pain affects one's ability to work. The results suggest that chronic pain is associated with decrements in quality of life and psychological well-being (in the form of higher levels of depression and anxiety than is seen in survivors without chronic pain), as well as increases in suicidal ideation. Suicidal ideation has been found to be associated with pain in other cancer groups, particularly uncontrolled pain, and increases as pain severity increases [47–50]. Therefore, clinicians should be especially mindful to screen for thoughts of suicide in survivors with pain.

Overall, pain was rated as moderate and did not differ by attribution of pain. There was a trend for neuropathic-like pain to be reported in survivors with CRP more than those with other pain, but this difference was not significant. This lack of significant difference could reflect a misattribution of pain in those survivors who believed it was due to causes other than cancer/treatments. Future studies should include objective measures of pain etiology, such as a neurophysiologic evaluation.

Most survivors used some type of treatment for their pain, but there was a higher prevalence of use of complementary treatments for pain than prescription medications. This may reflect a greater likelihood for survivors to treat their pain on their own rather than having it treated by a professional. This could also be due to survivors' limited understanding about available pain treatments, lack of desire to see another doctor, lack of open communication with their physician about symptoms they are experiencing post-treatment, or to in part minimize medical interventions (a tendency noted in response to patients' feelings about fatigue management in a prior study) [51]. There are likely survivor-related, as well as system-related and physician-related barriers to more comprehensive assessment and treatment of chronic pain. However, this is a speculation and needs to be explored further by research.

Survivors with CRP tended to report higher levels of interference caused by pain, most notably in the area of relations to others. This is an interesting finding given that pain severity was similar across groups and may reflect the implications on intimacy that pain associated with this particular cancer has on a survivor's life. Overall, similarities were

found between survivors with CRP and those with other pain on the intensity, characteristics, and treatments used for pain, suggesting that both groups reported similar pain experiences. This further supports the notion that pain may have had similar etiologies, even though survivors had different beliefs about the cause of their pain. Further exploration is warranted in a larger sample and neurophysiologic testing to allow for a valid clinical diagnosis.

Conclusion

The results of this pilot survey must be interpreted with several caveats. Perhaps foremost among these are issues related to the generalizability of results, coming as they do from a major cancer center with a mainly affluent and Caucasian population. Our findings are based on a relatively small, cross-sectional sample from one geographic region. Although our prevalence rate is consistent with prior research, large-scale epidemiological research is needed to provide more accurate and stable estimates of pain in CRC survivors. Future studies in development will involve collaborations with other centers with a higher ethnic population. Second, our prevalence rate reflects only those CRC survivors who chose to participate in our study. Our results may overestimate the problem if survivors who chose to participate in our study were those most likely to be experiencing pain. It is also possible, however, that our results may underestimate the problem if survivors experiencing pain lacked the energy and stamina necessary for participating. The prevalence rate found in this study is comparable with the prevalence of pain found in the general US population [52]. However, the prevalence of pain in the US population represents any pain lasting more than 24 hours and may not be a true statistic of chronic pain.

Survivors' beliefs about the cause of their pain must also be interpreted cautiously, as these attributions are subject to survivors' understanding of progression of disease and are not always accurate attributions. Also, because follow-up data were not collected, there is no way to tell in the database if pain symptoms were due to heretofore undiagnosed recurrent or metastatic disease. Nonetheless, we felt it important to ask survivors about their beliefs about the cause of their pain in order to study the kinds of attributions survivors make when they have pain symptoms, even if it does not accurately reflect the cause of their pain. For example, arthritic symptoms have been found to be associated with surgical management of cancers [53]. However, could easily be misinterpreted by a survivor as arthritis.

CRC survivors face many physical and emotional challenges to making a successful post-treatment adjustment. It stands to reason that pain can complicate and impact the quality of survivorship. Although this sample was from one institution, patients managed in other settings may be receiving less optimal pain control [54]. A sizable minority of survivors with pain will transform into chronic pain patients. Pain is a fearsome symptom in cancer patients and survivors, as well as thoughts of disease progression, along with the concomitant depression and anxiety with which it goes hand in hand. A survivor's sense of vulnerability is likely to be considerably worsened by the daily reminder of being ill that pain embodies, and as one of our patients said, "after you have been treated for cancer you never again get a normal headache; it's always a brain tumor."

For survivors of cancer, ongoing symptoms (and emotional responses to these symptoms) may serve as a reminder that they will never return to their precancer beings. Emotional responses to symptoms, such as pain, can tell a lot about the meaning that is attached to them. Pain during treatment may be interpreted as treatment is working and therefore tolerated. However, pain many years after treatment can trigger feelings of anxiety, depression, and suicidal ideation. Health care professionals can screen for these feelings of

vulnerability by asking survivors directly about symptoms they may be experiencing and encouraging an open discussion of these symptoms.

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Table 1

Demographic and disease variables in CRC survivors (N = 99)

Variable	N
Age (M = 64.71, SD = 12.77, range 28–92)	90
Missing (N)	(0)
Gender (Male)	54
Missing (N)	(0)
Race	
White	90
Black/African American	3
Asian/Pacific Islander	2
Other	4
Missing (N)	(0)
Marital status	
Married	69
Single/unmarried	30
Missing (N)	(0)
Education	
High School or less	41
College degree	36
Graduate degree	22
Missing (N)	(0)
Employment	
Employed	40
Retired	48
Other	11
Missing (N)	(0)
Income	
<50,000	25
50,000–89,000	31
>89,000	40
Missing (N)	(3)
Disease stage	
Localized	46
Locally advanced	39
Metastatic	12
Missing (N)	(2)
Time since treatment (months) (M = 55.12, SD = 28.66, Range 16–120)	
1–2 (years)	29
2–5 (years)	32
5–10 (years)	37
Missing (N)	(1)

Variable	N
Treatment history	
Surgery only	31
Surgery and chemotherapy	30
Surgery, chemotherapy and radiation	38
Missing (N)	(0)

CRC = colorectal cancer; M = mean; SD = standard deviation.

Table 2

Group differences in mean pain intensity ratings (N = 99)

	CRP		Other Pain			
	M (SD)	**Range**	**M (SD)**	**Range**	***t***	***P***
Worst pain	6.00 (3.27)	2–10	6.65 (2.10)	2–9	−0.48	0.64
Average pain	6.07 (1.37)	5–8	5.81 (2.36)	0–10	0.27	0.79
Current pain	3.06 (3.63)	0–8	1.62 (2.40)	0–7	1.11	0.28

CRP = cancer-related pain; M = mean; SD = standard deviation.

Table 3

Group differences in mean pain interference ratings (N = 99)

	CRP		Other Pain			
Brief Pain Inventory	**M (SD)**	**Range**	**M (SD)**	**Range**	***t***	***P***
Overall interference	36.38 (24.59)	6–68	24.09 (14.34)	0–47	1.29	0.23
General activity	6.25 (3.73)	0–10	4.54 (3.31)	0–10	1.10	0.29
Mood	4.38 (4.27)	0–10	3.31 (3.15)	0–8	0.66	0.52
Walking ability	5.38 (4.87)	0–10	4.92 (4.46)	0–10	0.22	0.83
Normal work	3.88 (4.55)	0–10	4.38 (3.69)	0–10	−0.28	0.78
Relations with others	5.88 (4.91)	0–10	0.77 (1.74)	0–6	2.83	0.02*
Sleep	5.62 (4.34)	0–10	3.08 (3.40)	0–10	1.50	0.15
Enjoyment of life	5.00 (3.93)	0–10	3.00 (3.44)	0–9	1.21	0.24

*$P < 0.05$.

CRP = cancer-related pain; M = mean; SD = standard deviation.