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Pain is prevalent and persisting in cancer survivors: Differential factors across age groups

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Abstract

Objective—The Institute of Medicine documents a significant gap in care for long term side effects of cancer treatment, including pain. This paper characterizes age differences in the prevalence and predictive characteristics of pain to guide clinicians in identification and treatment.

Materials and Methods—A sample of 170 adults with head and neck, esophageal, gastric, or colorectal cancers were recruited from two regional Veterans Administration Medical Centers. Face to face interviews were conducted 6, 12, and 18 months after diagnosis with the PROMIS scale to assess pain and PHQ-9 scale to assess depression. Descriptive statistics characterized incidence and prevalence of pain impact and intensity ratings. Multivariate linear hierarchical regression identified clinical characteristics associated with pain in older versus younger age groups.

Results—Clinically significant pain was endorsed in one third (32%) of the sample, with younger adults reporting higher levels of the impact of pain on daily activities and work, and also higher pain intensity ratings than older adults. In younger adults, pain ratings were most associated with lower social support and higher depression, as well as advanced cancer stage. In older adults,

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pain was multifactorial, associated with baseline comorbidities, adjuvant treatment, and both combat post-traumatic stress disorder (PTSD) and depression.

Conclusions—Pain is a significant persisting problem for one in three cancer survivors, requiring ongoing assessment, even months later. Important differences in pain's determinants and impact are present by age group. Identification and treatment of pain, as well as associated conditions such as depression, may improve the quality of life in cancer survivors.

Keywords

Cancer survivorship; Pain; Depression

1. Introduction

Persisting pain after cancer treatment is drawing increasing attention given the growing numbers of cancer survivors,[1] and the documented challenges identifying and treating long term consequences of treatment.[2] Pain can be complex to understand and treat as it is multifactorial, with physiological, psychological, and social determinants.[3] In particular, across illnesses those with more medical comorbidities,[4] higher levels of depression and anxiety,[5,6] and lower social support[7] report higher levels of pain.

Pain is a predominant concern among individuals with cancer. The American Cancer Society reports that approximately 30% of patients newly diagnosed with cancer, 30–50% of patient undergoing treatment, and 70–90% of patient with advanced disease experience pain.[8] After treatment, many cancer survivors continue to experience pain,[9,10] although it is less well understood.

Pain is recognized as one of the most distressing long term side effects of cancer treatment and has been linked to poorer health outcomes and decreased quality of life among survivors.[11,12] The Institute of Medicine's (IOM) seminal report "*From Cancer Patient to Cancer Survivor: Lost in Transition*"[2] emphasizes the significant gap in identifying and treating long term side effects of cancer. Under-treatment of pain is a particularly concerning issue for cancer survivors who may experience hospital admissions related to uncontrolled pain.[13,14]

1.1. Age Differences in Pain

The literature on age differences in cancer pain is scarce and conflicting with several studies finding no differences and a few studies finding that older adults report less pain than younger adults.[4,11,15,16] It is critical to understand pain in older cancer survivors, as greater than 60% of new cancers occur in people aged 65 and older.[1] However, reports of pain vary widely, between 20 and 85% of older adults following cancer.[4,15,17,18] Our knowledge of the expected prevalence and predictors of pain in cancer survivors is limited by differences in methodology in cancer survivor research (e.g., design, sampling, measurement).[19] A common clinical measure of pain intensity is the Numeric Ratings Scale (NRS) that utilizes a 0–10 scale.[20] This measurement approach has the advantage of being efficient, but questions remain about its accuracy.[21] Pain can also be measured in terms of the impact on valued activities. This measurement approach is useful because it defines pain in terms of function — although it may complicate comparisons of younger and older adults, as these age groups may have different baseline functional levels and expectations. For example, younger adults may be more likely to be employed. Older adults may have multiple morbidities leading to chronic pain, creating background "noise" when assessing the marginal decrease in functioning associated with additional pain from a new condition. Therefore, it is especially important to consider how pain may differentially present and impact functioning older versus younger adults. In this paper we describe age differences in pain reports and delineate the variables differentially associated with pain in older versus younger survivors of oral–digestive cancers who are enrolled in care in the Veterans Health Administration (VHA).

2. Materials and Methods

2.1. Study Design and Setting

Participants were identified at the time of diagnosis from the tumor registries from VA Medical Centers in Boston and Houston, and recruited beginning at 6 months after diagnosis for an observational cohort study. Complete protocol methods including non-responder information are described elsewhere.[22]

2.2. Participants and Data Sources

Eligibility criteria included a diagnosis of one of three cancer types: head and neck (HN), esophageal and gastric (GI), or colorectal (CRC); receiving surgery, chemotherapy, and/or radiation treatment. Using a broad definition of cancer survivor consistent with the National Cancer Institute (NCI), who states that "an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life", we recruited participants of all cancer stages as long as the individual was not in end of life care, defined as being in hospice care. Participants who had a dementia disorder or psychotic spectrum disorder were also excluded. Participants completed face to face interviews 6, 12 (N = 145), and 18 (N = 122) months following their cancer diagnosis.

2.3. Variables, Data Sources, and Measurement

2.3.1. Demographics—Participants reported their age, gender, ethnicity (Hispanic/ Latino or not), race, and level of education. For the purposes of data analyses, age was dichotomized using a common standard of age 65, as older (age 65 or more, N = 79) and younger (age 64 or less, N = 91).

2.3.2. Comorbidity Score—A comorbidity score was created using electronic medical record extraction. We obtained ICD-9 data for each participant. One point was assigned for each of the 22 chronic medical conditions utilized in the Charlson Comorbidity method to create a total comorbidity score for each participant. These conditions included congestive heart failure, cerebrovascular disease, chronic lung disease and moderate to severe kidney disease. We did not mortality-adjust these conditions using the Deyo method, but rather used a total comorbidity score.

2.3.3. Social Support—Participants' ratings of social support were taken from responses to four items on the family (e.g., my family is close) and social support (e.g., I am aware of love and support from other people) subscales of the Benefit Finding Scale. Participants reported if the item "describes me" on a 3-point Likert scale ranging from 0 (no) to 2 (a lot). Family and social items were combined to create a total perceived social support scale with an internal-consistency reliability of $\alpha = .59$.

2.3.4. Cancer Information—To obtain information about the cancer site, stage, and treatments, patients' reports were confirmed in the medical record. Participants reported if they received surgery, chemotherapy, and/or radiation. For the purpose of data analyses AJCC stage ratings were dichotomized as early (stage I–II) versus advanced (stage III–IV), while treatments were dichotomized as surgery only versus surgery plus either adjuvant radiation or chemotherapy.

2.3.5. Depression—The Patient Health Questionnaire (PHQ-9)[23] was used to measure current depressive symptoms in the past two weeks. This 9-item self-report scale is based on the DSM-IV diagnostic criteria for major depressive disorder. Participants indicated how much they had been bothered by each item using a 4-point Likert scale ranging from 0 ("not at all") to 3 ("nearly every day"). A total score was created by adding the item scores for each item. In the present sample, the internal-consistency reliability was $\alpha = 0.90$.

2.3.6. Combat Post-traumatic Stress Disorder (PTSD)—To obtain information on the ongoing symptoms of combat-related PTSD, we administered the Primary Care PTSD Screen (PC-PTSD).[23] This 4-item measure uses a yes/no response format to assess the occurrence of nightmares or intrusive thoughts about the military, avoidance of thoughts or situations that are reminders of the military, feeling on guard or easily startled, and feeling numb or detached from others in the past month. A total score was created by adding the item scores for each item. In multiple regression, individuals with no combat experience were assigned a score of 0 on this variable. In the study sample, the internal consistency reliability was $\alpha = 0.88$.

2.3.7. Pain—Patient-reported Outcomes Measurement Information System (PROMIS)[24] 29 item version, was used to measure pain. This scale was developed by a collaborative group of scientists to provide a common comparison of quality of life measure across disease types. A self-report pain impact total score is obtained, comprised of four items (Table 2) rating the extent to which during the past 7 days pain interferes with daily activities, work, social activities, and enjoyment of life, rated 1 (not at all) to 5 (very much), for a possible range of 4–20. Consistent with established normative comparison data, we categorized pain severity as within normal limits (none to mild), moderate (1 standard deviation worse than community norms), or severe (2 standard deviations worse than community norms). In this paper we focus on pain impact as our main outcome variable. However, we also obtained a "pain intensity" rating on which the participant rates the intensity of pain "on average" ranging from 0 (no pain) to 10 (worse pain imaginable).

2.4. Statistical Methods

We first examined pain prevalence through descriptive statistics. We then compared older and younger groups on both pain impact and intensity using Students *t*-test. We next completed two hierarchical linear multiple regression analyses – one for each age group – to provide a concise picture of differential prediction of pain impact within age groups. To prepare these analyses we selected potential covariates identified in the literature, then examined age differences in univariate analyses using the contingency coefficient *C* or Students *t* test. We next entered variables in three steps. In the first step we entered baseline variables of physical comorbidity and social support. We did not include race or education, as these did not predict pain in univariate tests. To determine if cancer predicted pain over and above comorbidity or social predictors, we then added cancer stage and treatment variables. We did not include cancer type, as pain ratings were equivalent across cancer types in this study. Finally, we entered current psychological distress including combat PTSD symptoms and major depression symptoms which were rated concurrent to the pain variables. These variables were entered in the last step to characterize them as potentially developing or worsening after the baseline and cancer variables. In addition, as psychological distress is modifiable, we were interested to see if these potentially modifiable variables were associated with pain over and above baseline and cancer status. In the multiple regressions, missing values were imputed through mean substitution. Finally, we examined whether pain prevalence changed over time through repeated measures analysis of variance (ANOVA). We conducted analyses in SPSS 21.0.

This study was approved by the Institutional Review Boards of the VA Boston Healthcare System and the Houston VA Medical Center; participants gave informed consent to the work.

3. Results

3.1. Participants

There were 167 men and 3 women, mean age 64.66 (*SD* = 9.40, range 27–88) (Table 1). The majority of participants were White or Caucasian (81%), 92% stated that their preferred language was English, and 51% had some college education or were college graduates. Most (62%) reported that they had a spouse or partner. Less than half of the sample (*N* = 74; 43.5%) reported combat exposure. Participants had head and neck cancer (40%), esophageal/gastric cancer (10%) or colorectal cancer (50%) of American Joint Committee on Cancer Stage I (24%), II (28%), III (22%) or IV (26%); 31% received surgery only whereas 69% received surgery with adjuvant chemotherapy or radiation.

Distributions of race, education, combat status, and cancer type and stage did not differ between younger and older adults (Table 1). In addition, the mean number of comorbidities did not differ. Younger adults reported more combat PTSD symptoms and more depressive symptoms than did older adults (Table 1). In addition, younger adults were more likely to receive adjuvant treatment (*p* = 0.03).

3.2. Prevalence of Pain

In responding to individual items, about half the individuals described no impact of pain on activities, whereas the remainder described a range of pain impact (Table 2). When considered as a summary score, the mean pain impact score was $M = 8.55$ ($SD = 5.48$). Most participants (67.7%) reported pain impact within normal limits; 21.6% reported a moderate degree of pain impact on activities and enjoyment (PROMIS T score 60–69), whereas 10.8% reported severe pain impact (PROMIS T score ≥ 70); in all 32.4% reported moderate to severe pain (PROMIS T score 60 or higher) (Table 3). The pain intensity ratings ranged from 0 to 10 with a mean pain intensity score of $M = 3.31$ ($SD = 2.86$); 35.3% reported pain intensity of “5” or worse.

3.3. Age Differences in Pain

3.3.1. Pain—At 6 months post diagnosis, younger adults described higher levels of pain interfering with activities, work, and enjoyment of life than did older adults (M (SD) = 9.79 (6.01) versus 7.14 (4.44); $t = 3.20$, $p = 0.002$) (Table 3). Similarly, younger adults described higher levels of pain intensity on a 0–10 scale than did older adults (M (SD) = 3.85 (2.93) versus 2.69 (2.67); ($t = 2.66$, $p = 0.009$)). Considered as a percentage, 42.4% of younger adults report moderate to severe pain impact, whereas 20.5% of older adults do (Table 3).

3.3.2. Differential Predictors of Pain in Younger and Older Adults—In the younger adult sub-sample, lower levels of social support predicted pain impact in steps 1 and 2, even considering cancer variables (Table 4). Although the model was significant, the total amount of variance predicted was small ($R^2 = 0.07$). However, when psychological distress was added to the model, only depression was predictive of pain impact ratings, with a higher level of variance explained ($R^2 = 0.42$). In the older adult sub-sample, a different predictive model was found (Table 4). For older adults, comorbidity predicted pain impact in steps 1 and 2, even considering cancer variables while social support was not. When psychological distress was added to the model, comorbidity was predictive only at a trend level (0.09), whereas having received adjuvant treatment, the level of combat PTSD symptoms, and of depression were associated with pain impact ($R^2 = 0.54$).

3.4. Stability of Pain Over Time

At 12 and 18 months post diagnosis, pain ratings were all but unchanged (Table 3). Across both groups, the mean pain impact score was $M = 8.49$ ($SD = 5.06$) at 12 months and $M = 8.71$ ($SD = 5.34$) at 12 months. There were no differences comparing mean pain impact ratings across 117 individuals with pain ratings at all three time points ($F = 1.83$; $p = 0.34$). As shown in Table 3, similar patterns of stability were observed within the younger and older groups. At 18 months post-diagnosis, 1 in 3 individuals (30.3%) is still reporting moderate to severe pain impact.

4. Discussion

In this study we found pain to be a prevalent concern six months after cancer diagnosis for one of every three study participants. Concerns about the impact of pain on daily activities, work, and enjoyment as well as moderate to high intensity of pain (i.e., more than a “5” on a

10 point scale) continued unabated at 12 and 18 months following a diagnosis. These findings are similar to other studies of cancer survivors from non-veteran populations[4,11,15,16] although it is hard to compare across studies, as most do not assess pain at a specific point post diagnosis and few evaluations were longitudinal in nature. These findings may suggest that pain is being under-treated following diagnosis, and into treatment and survivorship, consistent with cancer survivors reports of gaps in care related to the long-term sequelae of cancer and cancer treatment.[2]

Similar to other studies,[25] younger survivors reported more pain impact and intensity than older survivors. Results of linear regression provide some cues to the variables that are differentially associated with pain reports in younger and older adults, which may begin to explain these differences. In our analyses, younger adults' pain was associated with lower social support, but most especially depression, which was significantly higher in the younger population. The Institute of Medicine reports that pain is a subjective biopsychosocial experience for many people.[3] In younger adults, reports of higher levels of pain impact could be related to higher levels of depression and greater reliance on social support. In addition, while speculative, it seems possible that younger adults may have greater sensitivity to pain as a new experience now limiting functional activities (e.g., work). In addition, our results suggest that more advanced cancer is associated with higher ratings of pain intensity.

In older adults, pain appears to be an even more complex phenomenon, associated with overall comorbidity, as well as sensitivities to adjuvant treatment, along with psychological distress. It is possible that cancer and its treatment-related sequelae become an additional chronic illness causing pain for older adults who are already limiting activities due to advancing age and illnesses. It is unclear if older patients in our study experienced less pain intensity and less impact on function, or if they under-reported pain and depression. A substantial literature documents that older adults under-endorse affective symptoms of depression.[26] Our understanding of differential endorsement of comorbid pain and depression in younger versus older adults it incomplete. In the meantime, these differences suggest that special care must be taken in assessment to insure that pain is not overlooked in abbreviated screenings.

There are numerous limitations to our methodology. Our sample has issues of both heterogeneity and homogeneity. We included participants across a range of cancer types and stages in order to gain some comparison of the potential role of cancer type and stage in pain. Although we did not find specific associations between cancer type or stage and pain in our analyses, our sample was not adequately powered to test all sample characteristics. Although our use of the term “cancer survivor” is consistent with NCI definition, more study is needed to fully describe the patient’s perspective in observing and assimilating pain into their cancer experience. At the same time, our sample was homogenous in respect to Veteran status. While veteran status is common (1 in 2 men over age 65 are veterans[32]), the extent to which the veterans sampled are different from other veterans or non-veterans on the characteristics measure here is not known. Our study of oral digestive cancers in a mostly male veteran population therefore adds to the existing cancer survivor literature which tends to focus on women after breast cancer, but limits the generalizability of this study. In addition, we were not able to adequately test race and ethnicity differences. This is important as ethnic minorities have been found to be at higher risk for unaddressed pain.[3] In addition, it is possible that those in more pain were more motivated to participate in the study; conversely it could be those with more pain felt less able to participate. We hope that our use of the PROMIS instrument and measurement at discrete time points longitudinally will permit more precise comparisons with other studies.

4.1. Clinical Implications

Clinicians should consider pain in their evaluation of cancer survivors with persistent physical and emotional symptoms following treatment. Our findings indicate the clinical importance of considering the impact of pain on one’s daily activities (i.e., pain impact) along with pain intensity, which may provide a useful avenue for assessing pain as it cannot be diagnostically “seen” in clinical practice.[27] Multiple aspects of patient’s lives may be significantly disrupted with the onset of pain[28,29] therefore it may be helpful to consider pain’s impact beyond an isolated physical issue.[30,31] Perhaps most importantly, our results point to the need to assess the long-term impact of pain following cancer treatment, so that it may be addressed and alleviated. In addition, the results demonstrating depression and combat PTSD as predictive of pain in this study suggest that patients with persistent cancer-related pain may have underlying mental health conditions (e.g., depression), that are contributing to the presentation of pain. Appropriate diagnosis and treatment may ameliorate both conditions. Clinicians might pay special attention to elderly cancer survivors to look for and treat pain, which could be under-reported.

In conclusion, our findings of high rates of persistent pain following a cancer diagnosis underscore the lasting effects of cancer treatment and the importance of regular pain assessment in cancer survivors — considering potential differences in younger and older patients. Innovative treatments for pain as well as for additional research that would identify the most effective interventions for these pain problems are needed.

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Table 1

Total and age-stratified sample characteristics.

Variable		**Total (*N* = 170)**	**Younger (*N* = 91)**	**Older (*N* = 79)**	**Statistic**
		%	**%**	**%**	***C*(*p*)**
Ethnicity and race					.16 (0.22)
Hispanic or Latino		8.1	12.1	5.1	
African American or Black		14.7	16.5	12.7	
Caucasian or White		74.1	68.1	81.0	
Other		2.4	3.3	1.3	
High school education		50.6	49.5	51.9	.02 (0.75)
Combat experience		43.5	40.7	46.8	.06 (0.42)
Cancer type					.07 (0.65)
Head and neck		40.0	42.9	36.7	
Colorectal		49.4	46.2	53.2	
Gastro-esophageal		10.6	11.1	10.1	
Advanced cancer stage		47.6	53.8	40.5	.13 (0.08)
Surgery plus adjuvant		68.8	75.8	60.8	.16 (0.03)
	Range	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*t* (*p*)
Total comorbidities	0–9	3.49 (1.88)	3.39 (1.68)	3.61 (2.09)	−.76 (0.46)
Social support	0–15	8.35 (1.94)	8.08 (2.07)	8.65 (1.73)	−1.91 (0.06)
Combat PTSD symptoms[a]	0–4	1.59 (1.68)	1.95 (1.23)	1.23 (1.58)	1.98 (0.05)
Depression	0–27	6.76 (7.01)	8.83 (4.41)	7.79 (5.11)	4.30 (.00)

Abbreviations: *M*, mean; *SD*, standard deviations; PTSD, post-traumatic stress disorder.

[a] Totals provided for younger (N = 41) and older (N = 40) who were in combat.

Table 2

Pain impact within the past 7 days at six months post diagnosis.

Pain interferes with	**Not at all %**	**A little bit %**	**Somewhat %**	**Quite A bit %**	**Very much %**	***M* (*SD*)**
Daily activities	49.7	15.6	11.4	13.8	9.6	2.18 (1.42)
Work around the house	50.9	15.6	8.4	15.6	9.6	2.17 (1.44)
Participation in social activities	57.5	12.6	8.4	13.2	8.4	2.02 (1.40)
Enjoyment of life	53.6	10.8	12.0	10.2	13.3	2.19 (1.50)

Abbreviations: *M*, mean; *SD*, standard deviation.

Table 3

Prevalence of pain over time in younger versus older groups.

Time since diagnosis	Total sample		Younger		Older		Group
	Impaired[a] %	***M* (*SD*)**	**Impaired %**	***M* (*SD*)**	**Impaired %**	***M* (*SD*)**	***F* (*p*)**
6 months	32.4	8.55 (5.48)	42.4	9.79 (6.01)	20.5	7.14 (4.44)	3.20 (0.002)
12 months	33.8	8.49 (5.06)	43.6	9.65 (5.50)	22.4	7.13 (4.13)	3.08 (0.002)
18 months	30.3	8.71 (5.34)	35.4	9.81 (5.34)	23.2	7.41 (5.08)	2.55 (0.012)
Time *F* (*p*)		1.83 (.34)		0.20 (0.80)		1.84 (0.17)	

Abbreviations: *M*, mean; *SD*, standard deviations.

[a] Refers to percentage with a *T* score ≥ 60.

Table 4

Predictors of pain at six months post diagnosis in younger versus older groups.

Step	Variable	Younger			Older		
		β	*p*	R^2	β	*p*	R^2
1	Comorbidity	.09	.22	.06 **	**.31**	**.01**	.11 **
	Social support	**−.24**	**.00**		−.12	.29	
2	Comorbidity	.11	.17	.07 *	**.28**	**.01**	.16 **
	Social support	**−.24**	**.00**		−.12	.28	
	Advanced stage	−.08	.37		.04	.79	
	Adjuvant treatment	.01	.95		−.24	.07	
3	Comorbidity	.07	.23	.42 **	.15	.09	.54 **
	Social support	−.09	.14		−.03	.76	
	Advanced stage	−.10	.18		.05	.60	
	Adjuvant treatment	−.04	.63		**−.22**	**.03**	
	Combat PTSD	.06	.33		**.19**	**.05**	
	Depression	**.59**	**.00**		**.52**	**.00**	

Variables with beta weight and p values in bold denote statistically significant predictor variables in the regression model.

* $p < 0.05$.

** $p < 0.01$.