Pain among Older Adults with Cancer - Results from the Cancer and Aging Resilience Evaluation (CARE) Registry

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Abstract

Purpose: The impact of pain on functional status and mental health among older adults with cancer is a relevant, yet understudied. We sought to identify the prevalence of pain at diagnosis in older adults with cancer and evaluate the association of pain with functional status limitations, cognition, and mental health.

Methods: This study included older adults (age ≥60) with cancer enrolled in the CARE Registry. Pain measured in numeric rating scale from 0-10. We utilized the literature based cut off for moderate-severe as ≥4. Logistic regression used to assess differences in functional status, falls, cognitive complaints, and depression/anxiety associated with moderate/severe pain, adjusted for sex, race, education, ethnicity, marital status, cancer type/stage, and treatment phase.

Results: Our cohort included 714 older adults with an average mean age of 70 years and 59% male. Common diagnoses included colorectal (27.9%) and pancreatic (18%). 43.3% reported moderate/severe pain. After multivariate adjusting for covariates, participants with self-reported moderate/severe pain were more likely to report limitations in instrumental activities of daily living (adjusted Odds Ratio [aOR] 4.3 95% confidence interval [CI] 3.1-6.1, $p<.001$), limitation in activities of daily living (aOR 3.2 95% CI 2.0-5.1, $p<.001$), cognitive complaints (aOR 2.9 95% CI 1.4-6.0, $p<.004$), anxiety (aOR 2.2 95% CI 1.4-3.4, $p<0.01$), and depression (aOR 3.7 95% CI 2.2-6.5, $p<.001$).

Conclusions: Pain is common amongst older adults with cancer and is associated with functional status limitations, cognitive complaints, and depression/anxiety. Strategies to reduce pain and minimize its potential impact on function and mental health warrant future research.

Introduction

Despite improvements in cancer prevention and therapeutics, the incidence of cancer in developed countries is increasing largely due to the shift in population demographics and population aging. Indeed, The United States (U.S.) population is aging with a projection that 20% of the population by 2030 will be above 65 years of age [1]. More than 50% of cancer cases occur in individuals older than 65 years of age and cancer is considered one of the leading causes of mortality in older individuals [2]. Compared to younger patients, the management of cancer in older patients poses several challenges including physiological decreases in organ function, the burden of comorbidities, variable functional independence, and underrepresentation in clinical trials [3–5]. One additional challenge of cancer care in older patients is pain management and its impact on quality of life. Unfortunately, up to 80% of patients with early- to advanced-stage cancer report chronic pain [6].

Undoubtedly, objective measurement of pain is quite challenging due to its complex subjective multimodal nature [7]. There is a compendium of research addressing assessment of pain in the older individuals as well as in patients with cancer, which is a fundamental step toward more effective chronic pain management. There are numerous available validated subjective pain measurement tools including

the visual analog scale, the numeric rating scale (NRS), and the verbal descriptor scale [8]. The NRS, which measures the perceived level of pain on a scale from zero (no pain) to 10 (most severe pain ever experienced), is one of the most widely used tools in U.S. healthcare institutions and has been shown to be a valid assessment of cancer-related pain [9].

There is mounting evidence that a high prevalence of pain has a detrimental effect on quality of life in older patients including higher incidences of depression, sleep disturbances, and social isolation [10 11]. Moreover, Shega and colleagues reported that moderate or higher pain was independently associated with frailty in a cross-sectional study of persons aged 65 and older in Canada [12]. In addition, older adult survivors of blood or marrow transplantation had a 2.6 fold greater odds of reporting pain in comparison to their siblings and those reporting pain were more likely to have impaired physical performance and develop frailty [13 14]. Pain management in older patients with cancer requires a multidisciplinary approach including optimal utilization of pharmaceuticals and non-pharmaceutical resources [15].

Over the past three decades, researchers from different disciplines examined different pain assessment tools and the best approaches to the management of pain in patients with cancer, however, little is known about the impact of pain on the growing number of older adults with cancer. In this study, we sought to identify the prevalence of pain at diagnosis in older adults with cancer and evaluate the association of moderate/severe pain with functional status limitations, cognitive complaints, and mental health.

Methods

Study design and Participants

This is an observational (cross-sectional) study of older adults diagnosed with cancer and referred to be seen by an oncologist at the University of Alabama at Birmingham (UAB) clinics, which include The Kirklin Clinic, UAB Acton Road clinic, and Colorectal Cancer multidisciplinary clinics, enrolled in the Cancer & Aging Resilience Evaluation (CARE) Registry. The CARE Registry is an ongoing prospective study that was launched in September 2017 [16]. For this study, older patients (aged 60 years and above) recruited into the CARE Registry between September 2017 and June 2021 with a diagnosis of cancer (colorectal cancer, gastroesophageal cancer, hepatobiliary cancer, pancreatic cancer, and others) who performed GA at the time of their initial consultation were included. Patients who were non-English speakers, were 59 years or younger, or declined participation were excluded from the study (Figure 1). The collection of data for the Registry and subsequent uses of the data for investigative and analytic pursuits such as this, was approved by the institutional review board of UAB (IRB-300000092), and all patients provided written consent.

Pain

As part of the GA, patients completed the National Institutes of Health's 10-item Patient-Reported Outcomes Measurement Information System (PROMIS®) global health scale (PROMIS Global 10) short-form [17]. PROMIS Global 10 utilized the question to assess perceived pain: “In the past 7 days, how

would you rate your pain on average?" Responses ranged from zero representing "no pain" and 10 represented as "worst pain ever experienced" [17]. The history of this tool was initially presented back in 1991 [18]. In this pain scale, pain categorized into; no pain (0), mild pain (1-3), moderate pain (4-7), or severe pain (8-10) on a linear numeric scale [19–21].

Geriatric Assessment

All participants submitted a self-reported GA, a modified version of the Cancer and Aging Research Group GA [16 22 23]. The CARE tool consists of various validated tools to screen for potential impairments of physical function, functional status, nutrition, cognition, social activity, polypharmacy, and performance status [16 19 24]. Data of patient-reported pain assessment were collected at the time of enrollment (at baseline) with the use of our CARE tool as well as other health information relevant to the management of patients' cancers were retrieved from medical records. For our cohort analysis we highlighted impairments in functional status as assessed by the Older Americans Resources and Services (OARS) assessment [25]. The CARE tool contains of 6-items assessing instrumental activities of daily living (IADL) which include an assessment of ambulation capacity, ability to procure groceries for self, ability to conduct daily home maintenance, ability to successfully take own prescriptions, ability to cook and prepare own meals, and ability manage own budget; as well as 3-items assessing activities of daily living (ADL) that include ability to get in and out of bed, ability to dress and undress, and ability to bathe one-self [19 20]. The CARE tool also assesses the presence of cognitive complaints, depression, and anxiety via PROMIS 4-item short forms [26–29]. Depression was assessed using PROMIS® Depression Short Form 4a v1.0, which involved likert answers (Never, Rarely, Sometimes, Often, Always) to four independent disclosures : "I felt worthless," "I felt helpless," "I felt depressed," and "I felt hopeless" within a week [26 27 29]

Other Covariates

Demographic variables included age and sex were abstracted from the medical record while race, ethnicity, educational level, and marital status were self-reported as part of the CARE tool [16 22 24]. Cancer-related variables included cancer stage, which was classified via TNM staging (stage I/II, III, and IV), and treatment phase, which was categorized as (pre-chemotherapy, during chemotherapy, and post-chemotherapy). Treatment stage and phase designation were determined by an oncologist, and extracted from the electronic medical record according to each participant [19].

Statistical Analyses

We report the prevalence of moderate to severe pain in older patients with cancer, and identify associations with functional status limitations, cognition, and mental health issues. As previously indicated, depression responses were translated to the appropriate t-score, and then severity was categorized into no depression (t-score 55), mild depression (t-score 55-59), moderate depression (t-score 60-69), and severe depression (t-score 70+) [26 30]. Responses to pain scale were dichotomized as no pain to mild pain (0-3) versus moderate to severe pain (4-10). Descriptive statistics were calculated for the overall study population and according to pain status, using frequencies and proportions for

categorical variables and, means and standard deviations for continuous variables. Differences in characteristics by pain status were examined using t-tests for numerical variables and Fisher's exact test for categorical variables. To avoid multicollinearity of GA measures, separate logistic regression models were estimated to identify associations between moderate/severe pain and IADL dependence, ADL dependence, falls, cognitive complaints, anxiety, and depression. In addition to unadjusted models, adjusted models were measured for each GA measure adjusting for age, sex, race, education level, marital status, employment, cancer type, cancer stage, and treatment phase [31 32]. These covariates were selected on an a priori basis given the available literature, in association with application of clinical knowledge [19 20 24]. Analyses were performed using statistical software SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Baseline Characteristics

In the CARE Registry, 1,286 patients aged 60 and higher were included, with an average age of 75-79 years. After excluding cases who did not consent to the study and those with missing survey data of CARE survey for the variables of interest, 714 patients were included in our analyses (see Figure 1). Overall, our study population was 58.9% male, 19.1% Black, and 1.7% Hispanic (Table 1). Most participants were married (65.0%) and retired (60.0%). The most frequent cancer types included colorectal (27.9%), pancreatic (18.0%), and hepatobiliary (11.5%) tumors. Most participants had not begun treatment at the time of data collection (70.0%) and stage IV cancer was most common (46.7%).

Table 1

Patient Demographics and Characteristics.

Demographics & clinical variables	All patients (n=714)	None/mild Pain (n=405)	Moderate/Very Severe Pain (n=309)	*p*
Age, mean (SD)	70, (6.8)	70.0 (6.9)	69 (7.1)	0.058
Age, n (%)				
60-64	205, (28.7)	107, (26.4)	98, (31.7)	
65-69	179, (25.1)	98, (24.2)	81, (26.2)	
70-74	157, (22.0)	94, (23.2)	63, (20.4)	0.259
75-79	102, (14.3)	66, (16.3)	36, (11.7)	
80+	71, (9.9)	40, (9.9)	31, (10.0)	
Sex, n (%)				
Male	421, (58.9)	238, (58.8)	183, (59)	0.902
Female	293, (41.0)	167, (41.2)	126, (40.8)	
Race, n (%)				
White	565, (79.0)	338, (83.5)	227, (73.5)	**0.004**
Black	136, (19.1)	60, (14.8)	76, (24.6)	
Other	13, (1.8)	7, (1.7)	6, (1.9)	
Ethnicity, n (%)				
Hispanic	12, (1.7)	6, (1.5)	6, (1.9)	0.636
Non-Hispanic	702, (98.0)	399, (98.5)	303, (98.1)	
Educational Level, n (%)				
Less than high school	89, (12.5)	35, (8.6)	54, (17.5)	
High school graduate	198, (27.7)	103, (25.4)	95, (30.7)	
Some College		72, (17.8)	78, (25.2)	**<.001**

Associate/Bachelors	150, (21.0)	129, (31.9)	63, (20.4)	
Advanced Degree	192, (27.0)	66, (16.3)	19, (6.2)	
	85, (12.0)			
Marital Status, n (%)				
Single	40, (5.6)	20, (4.9)	20, (6.5)	
Widowed/Divorced.	209, (30.0)	109, (26.9)	100, (32.4)	0.148
Married	465, (65.0)	276, (68.2)	189, (61.2)	
Employment, n (%)				
Retired	425, (60.0)	248, (61.3)	177, (57.3)	
Disabled	84, (12.0)	27, (6.7)	57, (18.5)	
Part-time (<32hr/wk)	23, (3.2)	17, (4.2)	6, (1.9)	**<.001**
Full-time (>32hr/wk)	95, (13.3)	71, (17.5)	24, (7.8)	
Other	87, (12.2)	42, (10.4)	45, (14.6)	
Cancer type, n (%)				
Colorectal	199, (27.9)	128, (31.6)	71, (23.0)	
Gastroesophageal	46, (6.4)	31, (7.7)	15, (4.9)	**0.029**
Hepatobiliary	82, (11.5)	43, (10.6)	39, (12.6)	
Pancreatic	128, (18.0)	64, (15.8)	64, (20.7)	
Other	259, (36.3)	139, (34.3)	120, (38.8)	
Cancer Stage, n (%)				
I/II	200, (28.0)	119, (29.4)	81, (26.2)	
III	181, (25.4)	102, (25.2)	79, (25.6)	0.628
IV	333, (46.7)	184, (45.4)	149, (48.2)	
Treatment Phase, n (%)				
Pre-treatment		273, (67.4)	226, (73.0)	

During-treatment	499, (70.0)	66, (16.3)	50, (16.2)	0.090
Post-treatment	116, (16.3)	66, (16.3)	33, (10.7)	
	99, (14.0)			

Abbreviation: SD, Standard deviation, IQR, Inter-quartile Range. **P*-value is a comparison between those with and without moderate/severe pain*Abbreviations: IADL, instrumental activities of daily living; ADL; activities of daily living; ecog ps, eastern cooperative oncology group performance status; mod/sev, moderate/severe.

Prevalence of pain and Association with demographic and clinical characteristics

In the study population, 43.3% of participants reported moderate to severe pain and 56.7% reported mild or no pain. Participants reporting moderate to severe pain were more likely to be Black (24.6% vs 14.8%, p=0.004), have lower levels of education (advanced degree completion (6.2% vs 66%, p<0.001), report disability for employment (18.5% vs 6.7%, p<0.001), and more likely to have pancreatic cancer (20.7% vs 15.8%, p=0.029) (Table 1). Conversely, there was no association between pain and age, sex, ethnicity, marital status, cancer stage, or treatment phase. In the unadjusted odds ratios (OR) of demographic and clinical characteristics with the presence of pain, we found no differences by age sex, or ethnicity. Older black patients (unadjusted Odds Ratio [OR] =1.9, 95% CI 1.3-2.8, reference White) and older patients with pancreatic (unadjusted OR=1.8, 95% CI 1.1-2.8, and colorectal cancer (unadjusted [OR] = 1.80, 95% CI 1.15-2.83 were more likely to experience moderate to severe pain. (Table 2).

Table 2
Unadjusted Odds Ratios of demographics and clinical variables to pain

Demographics & clinical variables	Unadjusted OR (95% CI)
Age group	
60-64	REF
65-69	0.90 (0.60-1.35)
70-74	0.73 (0.480-1.11)
75-74	**0.60 (0.37-0.97)**
80+	0.85 (0.49-1.46)
Sex	
Female	REF
Male	1.02 (0.75-1.38)
Race	
White	REF
Black	**1.89 (1.29-2.75)**
Other	1.28 (0.42-3.85)
Ethnicity, n (%)	
Non-Hispanic	REF
Hispanic	1.32 (0.42-4.12)
Education Level	
Less than high school	REF
High school graduate	0.60 (0.36-1.00)
Some college	0.70 (0.41-1.20)
Associate/Bachelors	0.32 (0.19-0.53)
Advance Degree	0.19 (0.10-0.37)
Marital Status	
Single	REF
Separated/Divorced	0.92 (0.47-1.81)
Married	0.69 (0.36-1.31)

Demographics & clinical variables	Unadjusted OR (95% CI)
Employment	
Full-time (>32hr/wk)	REF
Retired	2.11 (1.28- 3.49)
Disabled	**6.25 (3.26- 11.98)**
Part-time (<32hr/wk)	1.04 (0.37- 2.95)
Other	3.17 (1.70- 5.92)
Cancer Type	
Colorectal	REF
Pancreatic	**1.80 (1.15-2.83)**
Hepatobiliary	1.64 (0.97-2.75)
Gastroesophageal	0.87 (0.44-1.72)
Other	1.56 (1.07-2.27)
Cancer Stage	
I/II	REF
III	1.14 (0.76-1.71)
IV	1.19 (0.83-1.70)
Treatment Phase	
Pre-treatment	REF
During-treatment	0.92 (0.61-1.38)
Post-treatment	0.60 (0.38-0.95)

Association of pain with functional status limitations, mental health, and other geriatric assessment impairments

Pain was associated with all GA impairments included in this study (Table 3). Participants with moderate to severe pain were more likely to report IADL dependence (70.6% vs 33.3%; $p<0.001$), ADL dependence (25.2% vs 8.6%; $p<0.001$), falls (30.1% vs 15.1%; $p<0.001$), and limitations in walking one block (72.0% vs 31.1%; $p<0.001$). They were also more likely to have impaired self-reported ECOG performance status (48.5% vs 13.8%; $p<0.001$), take ≥ 9 medications per day (33.3% vs 15.6%; $p<0.001$), report ≥3

comorbidities (59.2% vs 42.7%; *p*<0.001), and have malnutrition (46.9% vs 36.3%; *p*=0.004). Those with moderate to severe pain reported more cognitive complaints (10.0% vs 3.0%; *p*<0.001), limitations in social activities (42.7% vs 16.3%; *p*<0.001), anxiety (24.6% vs 12.4%; *p*<0.001), and depression (19.7% vs 5.7%; *p*<0.001).

Table 3
Geriatric assessment impairments in those with and without moderate/severe pain.

Variable	Overall (n=714)	None / Mild pain (n=405)	Moderate / Severe pain (n=309)	*p**
Geriatric Assessment Domain				
Any IADL dependence, n (%)	353, (50)	135, (33.3)	218, (70.6)	**<.001**
Any ADL dependence, n (%)	113, (16.0)	35, (8.6)	78, (25.2)	**<.001**
Falls (≥1), n (%)	154, (21.6)	61, (15.1)	93, (30.1)	**<.001**
Reported limitations in walking on block, n (%)	348, (49)	126, (31.1)	222, (72.0)	**<.001**
Impaired ecog ps (≥2), n (%)	206, (29)	56, (13.8)	150, (48.5)	**<.001**
Medications (≥9 daily), n (%)	166, (23.3)	63, (15.6)	103, (33.3)	**<.001**
Comorbidities (≥3), n (%)	356, (50)	173, (42.7)	183, (59.2)	**<.001**
Malnutrition, n (%)	292, (41)	147, (36.3)	145, (46.9)	**0.004**
Cognitive complaints (mod/sev.), n (%)	43, (6.0)	12, (3.0)	31, (10.0)	**<.001**
Limitations in social activities, n (%)	198, (28.0)	66, (16.3)	132, (42.7)	**<.001**
Anxiety (mod/sev.), n (%)	126, (18.0)	50, (12.4)	76, (24.6)	**<.001**
Depression (mod/sev.), n (%)	84, (12.0)	23, (5.7)	61, (19.7)	**<.001**

**p*-value from the bivariate comparison of those with moderate/severe versus none/mild pain

Logistic regression analyses adjusting for demographic and cancer-related variables showed an association between moderate to severe pain and IADL dependence (adjusted Odds Ratio [aOR]=4.3, 95% CI 3.0-6.1, *p*<0.001), ADL dependence (aOR=3.2, 95% CI 2.0-5.1, *p*<0.001), falls (aOR=2.4, 95% CI 1.6-3.6,

p<0.001), cognitive complaints (aOR=2.9, 95% CI 1.4-6.0, *p*=0.004), anxiety (aOR=2.2, 95% CI 1.4-3.4, *p*=0.004), and depression (aOR=3.7, 95% CI 2.2-6.5, *p*<0.001) .(Table 4).

Table 4
Multivariable model of associations of moderate/severe pain with impairments in instrumental activities of daily living and activities of daily living, falls, and psycho-neurological disorders.

Variable	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*p**
IADL dependence	4.79 (3.48-6.60)	4.28 (3.01- 6.09)	**<.001**
ADL dependence	3.57 (2.32-5.49)	3.15 (1.96-5.06)	**<.001**
Falls	2.43 (1.67-3.50)	2.41 (1.61-3.59)	**<.001**
Cognition	3.65 (1.84-7.23)	2.91 (1.41-6.02)	**0.004**
Anxiety	2.32 (1.56-3.43)	2.18 (1.42-3.36)	**0.004**
Depression	4.09 (2.46-6.77)	3.74 (2.16-6.50)	**<.001**

Abbreviations: IADL, Instrumental Activities of Daily Living; ADL, Activities of Daily Living; OR (Odds Ratio).

**p*-values for individual regression models adjusted for age, sex, race, ethnicity, education level, marital status, employment, cancer type, cancer stage, and treatment phase

Discussion

This study found that 43% of older adults with primarily gastrointestinal malignancies report moderate to severe pain, and the presence of moderate-severe pain is associated with functional status limitations, cognitive complaints, anxiety, and depression. the prevalence of pain among older adults and the association of pain with Regression models found IADL dependence, ADL dependence, falls, cognitive complaints, anxiety, and depression were associated with pain after adjusting for demographic and cancer-related clinical factors.

The prevalence of moderate to severe pain in our study population was 43%, which is consistent with previous findings. Notably, a 2016 meta-analysis examined 122 studies published between 2005-2014, on the prevalence of pain in patients of all ages with cancer and found that overall, 38% of participants reported moderate to severe pain [33]. Similarly, a 2007 meta-analysis including 52 studies looked at pain prevalence grouped by cancer stage and type and found overall rates of moderate to severe pain reported in 31%- 45% of participants [31].

While previous literature has found that female patients with cancer report higher levels of pain compared to male cancer patients, our analyses did not find any differences in pain by sex [32 34]. These inconsistencies may be explained by discrepancies in proportions of cancer type between study populations. For instance, previous studies have found that patients with breast cancer are more likely to

report pain than patients with other cancer types [33 34]. Importantly, studies which found that females report more pain also had large proportions of patients with breast cancer in their study. In contrast, patients with breast cancer were not included in our study population, which could explain the inconsistency of this finding [32 34].

Our study found that respondents aged 75-79 were less likely to report moderate to severe pain compared to patients between 60-64 years. No other differences were found between age categories. These results are not surprising as previous research on age and cancer pain has produced inconsistent findings [31]. Also congruent with previous literature, our study found that patients on disability reported significantly more pain than those working full-time [35]. It is important to note that the measurement of pain in our study does not specify pain related to cancer. Consequently, when considering the relationship between pain and functional impartments in patients with cancer, it is unclear whether cancer-related pain increases the likelihood of being functionally impaired, or if people with functional impairments simply tend to report greater pain in general.

Black participants were significantly more likely to report moderate to severe pain compared to White participants. Previous research suggests several possible explanations for this discrepancy including that Black patients are less likely to be prescribed pain relieving medication and that pain medication adherence is poorer among Black patients [36 37]. Black patients also may have an increased difficulty in obtaining pain medications given pharmacies in many predominantly Black neighborhoods often inadequately stock opioids as well as potential financial barriers in obtaining pain medications[38 39]. These findings highlight the need to ensure that Black patients with cancer are thoroughly assessed for pain and provided assistance in accessing pain medications if a pain prescription is warranted.

Bivariate and multivariate analyses revealed significant association between IADL and ADL dependence and moderate to severe pain. While there is a robust literature examining pain and IADL dependence in non-cancer populations, limited research has evaluated the relationship between the presence of pain and IADL/ADLs dependence in older adults with cancer [40–42]. Patients in our cohort with moderate to severe pain experienced more cognitive complaints and anxiety.

Our study is not without limitations. Perhaps most importantly, we employed a cross-sectional study design and therefore we cannot establish causality between pain and outcome variables. Participants were recruited from a single center. This solitary source of collection exists in primarily underserved areas in Alabama, which is located in the “Deep South” region of the Southeastern United States (a historically underserved and disadvantaged region). Therefore, the results of this study may not be generalizable to other populations. Our study did not account for pain medications, or other analgesics, prescriptions or administration among participants, which could have theoretically impacted the levels of pain perceived by study subjects. Furthermore, while we did control for treatment phase with regard to chemotherapy in our regression model, we did not include consideration of patients who received surgical vs non-surgical treatments.

Moderate to severe pain was frequently reported in our study population. Pain was more frequently reported in patients who were Black, had lower levels of education, had pancreatic cancer, and were on disability. Additionally, moderate to severe pain was associated with several important GA impairments that are known predictors of adverse outcomes. Notably, our findings suggest that pain is associated with IADL and ADL dependence in older adults with malignancies. Given functional independence is a recognized priority of older adults, these results highlight the potential importance of screening for and managing pain in older patients with cancer [43]. Future longitudinal research is necessary to better understand the relationship between pain and GA impairments with a specific focus on the source(s) of pain and the impact of pain management.

Declarations

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Consent to participate: All enrolled participants have been consented by IRB-approved study personnel, according to UAB IRB rules and regulations.

Consent for publication: All authors reviewed and agreed to submission with an intent for publication.

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Figures

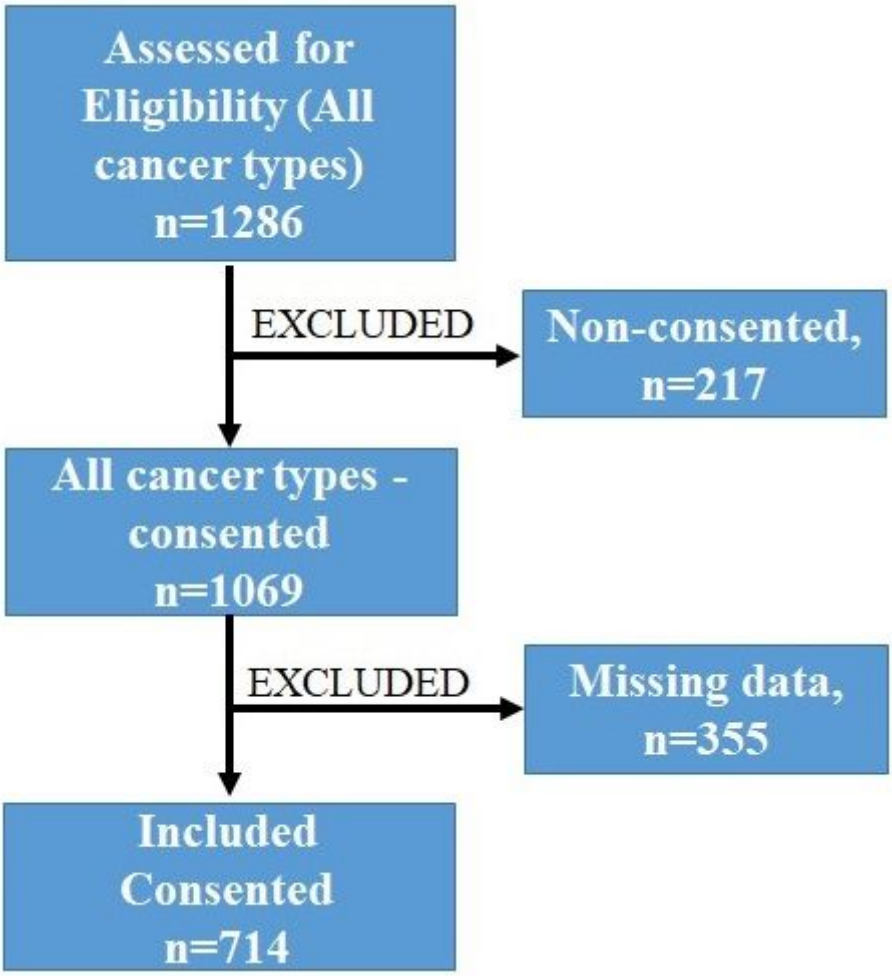

Figure 1

Selection of participant flow chart (Consort figure)

Flow Chart showing the process of study cohort selection. This figure illustrated how we excluded the patients who were not eligible in our study's criteria.