Symptom Clusters in Patients With Colorectal Cancer and Diabetes Over Time

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OBJECTIVES: To examine symptoms and symptom clusters in patients with colorectal cancer (CRC) with or without diabetes at three key periods (0–6 months, 12–18 months, and 24–30 months) post–initial chemotherapy.

SAMPLE & SETTING: Patients with CRC from a cancer center in the midwestern United States between January 2007 and December 2017.

METHODS & VARIABLES: Eight of the most common symptoms (fatigue, gastrointestinal issues, depression, anxiety, peripheral neuropathy, physical function, cognition, and sleep disturbance) reported by patients with CRC and patients with diabetes were extracted from electronic health records. Exploratory factor analysis was used to identify symptom clusters, which were assessed for patterns and clinical relevance.

RESULTS: Gastrointestinal issues and fatigue were the most prevalent symptoms in patients with CRC at each period. Across the three periods, patients with CRC and diabetes had more symptom clusters (n = 7) compared to patients with CRC without diabetes (n = 4). No stable symptom clusters were identified for either group.

IMPLICATIONS FOR NURSING: Oncology clinicians must recognize that patients with CRC and diabetes may present with exacerbated symptoms or symptom clusters. Ongoing assessment and monitoring of patients with CRC and diabetes for symptoms and symptom clusters is important because they may be at an increased risk for higher symptom burden.

KEYWORDS colorectal cancer; diabetes; symptoms; symptom clusters; survivors; comorbidity

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Estimates suggest that there are 1.5 million patients with colorectal cancer (CRC) in the United States (American Cancer Society, 2023). Advances in prevention, screening, and treatment for CRC have improved overall survivor rates (Benitez Majano et al., 2019; Van Cutsem et al., 2014). With increased cancer survival rates, the risk of living with other comorbidities is also increased (Pule et al., 2019; Rowley et al., 2017). About 33% of patients with CRC have at least one comorbid condition (Michalopoulou et al., 2021). Type 2 diabetes is a common comorbidity in patients with CRC and is prevalent in as much as 20% of the CRC population (Storey et al., 2021) compared to 11% in the noncancer population (Centers for Disease Control and Prevention, 2022). Given the increasing cancer survival rates, diabetes as a comorbidity among patients with cancer is an issue of growing importance for patients and healthcare providers.

Researchers describe similar symptoms, such as fatigue, gastrointestinal (GI) issues, depression, anxiety, peripheral neuropathy, decrements in physical function and cognition, and sleep disturbance, in patients with CRC and diabetes (Brady et al., 2022; Hershey et al., 2012; Hershey & Pierce, 2015; Vissers et al., 2016). CRC and diabetes initiate inflammatory processes (Giovannucci et al., 2010; Hammer et al., 2019), which trigger physiologic interactions that may contribute to or intensify symptoms. In addition, symptoms may co-occur, forming symptom clusters which are defined as two or more co-occurring symptoms (Kim et al., 2005; Miaskowski et al., 2004, 2007). Symptom clusters have not been well studied across multiple chronic conditions like diabetes and CRC.

In the authors' previous work with patients with breast cancer, patients with diabetes as a comorbidity reported greater symptoms (e.g., poorer physical and attention function, more sleep disturbance, greater fatigue) than patients without this comorbidity (Storey et al., 2019). However, little is

known regarding how diabetes affects the symptoms of patients with CRC. Among patients with CRC, only one study examined neuropathic symptoms in patients with CRC and diabetes (n = 218) compared to patients with CRC without diabetes (n = 957) (Vissers et al., 2015). The researchers noted that patients with CRC and diabetes experienced more neuropathic symptoms than patients with CRC without diabetes (Vissers et al., 2015). However, the study focused on only that one symptom. Even less is known about the symptom clusters of patients with CRC and diabetes. Although symptom cluster research has been conducted in patients with CRC (Agasi-Idenburg et al., 2017; Hao et al., 2021; Li et al., 2019; Potosky et al., 2022) and in patients with diabetes (Brady et al., 2022; García et al., 2019; Hammer et al., 2003), there is a paucity of research examining symptom clusters in patients with CRC and diabetes throughout the cancer trajectory. In the presence of comorbid diabetes, it is plausible that the summative consequences of symptoms and symptom clusters experienced by patients with CRC may be exacerbated. As the prevalence of CRC and diabetes is predicted to increase, it is imperative that clinicians understand the effect of diabetes on the symptom clusters in patients with CRC across time (Rowley et al., 2017).

To the authors' knowledge, no longitudinal studies have examined symptom clusters in patients with CRC and diabetes from initiation of chemotherapy through cessation of treatment. Therefore, the purpose of this study was to use data from electronic health records (EHRs) to examine individual symptoms and symptom clusters in patients with CRC and diabetes compared to patients with CRC without diabetes at three key periods across the cancer trajectory (after initial chemotherapy and through cessation of treatment). Specific aims included the following: (a) Determine the prevalence of individual symptoms in patients with CRC with and without diabetes; (b) identify the individual symptoms that constitute symptom clusters in patients with CRC with or without diabetes; and (c) compare symptom clusters between patients with CRC with or without diabetes at the following three key periods: time 1 (T1) (0–6 months), time 2 (T2) (12–18 months), and time 3 (T3) (24–30 months). Because patients with cancer are living longer with their disease, a comprehensive understanding and characterization of symptom clusters specific to patients with CRC and diabetes are critical to guide clinical practice. Findings from this study will provide pertinent information to clinicians who treat patients with CRC and diabetes.

Conceptual Framework

The conceptual framework for this study was adapted from the conceptual model of hyperglycemia in patients with cancer (Hammer et al., 2019). This original model describes the physiologic links between hyperglycemia (a characteristic of diabetes) and cancer and identifies the downstream effects of hyperglycemia on four primary symptoms (pain, fatigue, depression, and sleep disturbance) frequently experienced by patients with cancer. However, the model does not specifically examine symptom clusters. For this study, the current authors expanded the model in the following ways: (a) included three additional symptoms (GI issues, anxiety, and peripheral neuropathy) that are common among patients with CRC and patients with diabetes; (b) identified the prevalence of symptoms and the grouping of symptoms into clusters; and (c) examined the symptoms and symptom clusters across three key periods during the cancer trajectory.

Methods

Study Design, Setting, and Sample

This retrospective cohort study used EHRs from a large statewide health repository from the Regenstrief Institute that included clinical health data from five health systems in central Indiana (McDonald et al., 1999). Eligibility criteria included the following: (a) having a nonmetastatic diagnosis of CRC (stage II–III) per statewide cancer registry data and International Classification of Diseases (ICD) codes; (b) receiving chemotherapy alone or in combination with other adjuvant therapy (e.g., surgery, radiation therapy); (c) having CRC with no diagnosis of diabetes or had CRC and a diagnosis of type 2 diabetes prior to the CRC diagnosis per ICD codes and medication lists for antidiabetes medications; and (d) being aged 21 years or older. Exclusion criteria included the following factors: (a) having another diagnosis of cancer, except basal or squamous skin cancer; (b) having metastatic CRC; and (c) receiving subsequent chemotherapy after the initial chemotherapy for their cancer diagnosis. Data from January 2007 through December 2017 were identified through a statewide cancer registry and ICD codes. There were 5,629 patients with CRC identified during the study time period. Indiana University's institutional review board approved this study. All procedures performed

TABLE 1. Colorectal Cancer Cohort Characteristics

	With Diabetes (N = 712)		Without Diabetes (N = 1,581)		All (N = 2,293)		
Variable	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**p**
Age (years)	63.16	10.85	57.53	12.78	59.28	12.48	< 0.001
Body mass index (kg/m^2)	30.43	7.41	27.68	6.87	28.66	7.19	< 0.001
CCI	2.18	3.03	1.24	2.43	1.53	2.67	< 0.001
Characteristic	**n**	**%**	**n**	**%**	**n**	**%**	**p**
Gender							0.297
Male	385	54	840	53	1,225	53	
Female	326	46	741	47	1,067	47	
Other	1	< 1	–	–	1	< 1	
Race							0.116
Black	76	11	128	8	204	9	
White	626	88	1,440	91	2,066	90	
Unknown	1	< 1	1	< 1	2	1	
Other	9	1	12	1	21	1	
Stage							0.021
II	208	29	539	34	747	33	
III	504	71	1,042	66	1,546	67	

CCI—Charlson Comorbidity Index
Note. Because of rounding, percentages may not total 100.
Note. Higher CCI scores indicate more comorbidities noted in the electronic health record.

in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Procedures

A natural language processing pathway was developed to identify and extract symptom data from clinical notes in the EHR (Luo et al., 2021). The most common symptoms reported by patients with cancer and patients with diabetes (fatigue, GI issues, depression, anxiety, peripheral neuropathy, physical function, cognition, and sleep disturbance) were selected a priori to facilitate data extraction of symptoms from the clinical notes. Relevant seed terms (i.e., synonyms and phrases) that corresponded with the symptoms of interest were used to capture the varied descriptions of symptoms. For example, synonyms used to identify depression included depression, symptoms of depression, failure to thrive, sad, despair, misery, unhappy, melancholy, hopeless, and others. The natural language processing pathway first used the Unified Medical Language System MetaMap (Aronson & Lang, 2010) to extract the symptom expressions. The word sense disambiguation and negation detection were configured to ignore negative cases. Then, based on the given seed terms, a semantic analysis was used to include more expressions of the symptoms of interest that were not in the list of seed terms but were mentioned in the clinical notes (Luo et al., 2021). For example, the semantic analysis added new symptom expressions, such as feeling down, to the synonyms for depression, and added terms like situational stress, nervousness, shaking, trembling, and feeling jittery to the synonyms for anxiety.

Because of the large number of individual descriptive terms for GI symptoms in the clinical notes of the EHR, symptoms were combined into the GI symptom category based on previous literature (García et al., 2019; Han et al., 2020; Hao et al., 2021; Potosky et al., 2022).

Data Collection

Demographic (e.g., age, body mass index, gender, race) and medical (e.g., Charlson Comorbidity Index, cancer stage) characteristics were extracted

TABLE 2. Prevalence of Individual Symptoms by Diabetes Status in Patients With Colorectal Cancer

	With Diabetes (N = 712)						Without Diabetes (N = 1,581)					
	T1		T2		T3		T1		T2		T3	
Symptom	n	%	n	%	n	%	n	%	n	%	n	%
Anxiety	194	27	77	16	44	13	353	22	167	15	124	14
Depression	168	24	72	15	44	13	288	18	139	12	110	13
Fatigue	334	47	123	26	87	25	676	43	251	22	212	24
GI issues	472	66	194	41	131	38	1,034	65	451	39	357	41
Physical function	33	5	17	4	10	3	49	3	22	2	20	2
PN	183	26	76	16	41	12	321	20	122	11	102	12

GI—gastrointestinal; PN—peripheral neuropathy; T1—time 1 (0–6 months post–initial chemotherapy); T2—time 2 (12–18 months post–initial chemotherapy); T3—time 3 (24–30 months post–initial chemotherapy)

from the EHRs. A modified Charlson Comorbidity Index (excluding diabetes and CRC) was used to account for comorbidities.

Symptom data were collected at three key periods in the cancer treatment trajectory post–initial chemotherapy: 0–6 months (T1), 12–18 months (T2), and 24–30 months (T3). These periods were chosen because symptom clusters are typically related to treatment and/or disease and may vary over time. Studying only the period around the initiation of chemotherapy may not be an accurate reflection of symptoms and symptom clusters, given the acute side effects associated with the days following initial treatment (Foltran et al., 2014; Giesinger et al., 2014; Pettersson et al., 2014; Röhrl et al., 2019). A more accurate picture of the symptom profile may be found at later periods in the cancer trajectory because these symptoms and symptom clusters may fluctuate across time (Röhrl et al., 2019).

Therefore, the rationale for the three key periods was as follows: (a) 0–6 months is typically when chemotherapy is initiated and acute symptoms are first noticed; (b) 12–18 months is when treatment regimens are continuing or beginning to cease, and patients may demonstrate the cumulative effect of treatment on symptom clusters; and (c) 24–30 months represents the cessation of therapy, when patients with CRC may experience lingering symptoms post-treatment.

Data Analysis

Group comparisons of demographic and medical characteristics were evaluated using the chi-square test for categorical variables and TIBCO Analysis of Variance for continuous variables. Statistical significance was declared at $\alpha = 0.05$. Exploratory factor analysis was used to identify clusters among the eight symptoms (fatigue, GI issues, depression, anxiety, peripheral neuropathy, physical function, cognition, and sleep disturbance) during each of the three measurement periods for patients with CRC with or without diabetes. Exploratory factor analysis with the IBM Promax rotation was performed. Promax rotation, an oblique rotation, is used in factor analysis when it is anticipated that two or more variables are correlated (Field, 2018). A Cronbach's alpha greater than 0.6 and item-total correlations greater than 0.3 were considered acceptable (Oh et al., 2016). The results of the exploratory factor analysis for two and three factors were examined for each period. The three-factor solution was selected because it led to the best clinical interpretation. Symptom clusters were categorized by the symptoms with the highest factor loading. All statistical analyses were conducted with R software, version 4.1.2.

Results

Characteristics of Cohort

A total of 5,629 patients with CRC were identified for the study, of which 2,293 met the inclusion criteria for analysis. Table 1 provides the demographic and medical characteristics of patients with CRC in the study cohort (N = 2,293). Overall, most of the sample was male and White, and had stage III CRC. Overall, 712 (31%) patients with CRC also had a diagnosis of diabetes. Statistically significant differences were noted between patients with CRC and diabetes and patients with CRC without diabetes. In particular, patients with CRC and diabetes were older, with stage III CRC, had higher body mass index, and had modified Charlson Comorbidity Index scores. Cognitive and sleep disturbance symptoms were excluded from the analysis because of

low occurrences at each key period (less than 0.1%), leaving six symptoms (fatigue, GI issues, depression, anxiety, peripheral neuropathy, and physical function) for symptom and symptom cluster analysis.

Symptom Prevalence

Table 2 shows the prevalence of the individual symptoms across the three periods by diabetes status. Across the three periods, the most prevalent symptoms in patients with CRC, with or without diabetes, were GI issues and fatigue.

Symptom Clusters

T1: Table 3 shows the symptom clusters based on their highest loading on a factor within each period post–initial chemotherapy. At T1, the authors found three symptom clusters made up of two individual symptoms in each cluster in patients with CRC and diabetes, and only one symptom cluster made up of three individual symptoms in patients with CRC without diabetes.

Among patients with CRC and diabetes, the symptom clusters identified included fatigue/GI issues (cluster 1), anxiety/depression (cluster 2), and peripheral neuropathy/physical function (cluster 3). For patients with CRC without diabetes, the symptom cluster included GI issues/fatigue/anxiety (cluster 1). Overall, for T1, patients with CRC and diabetes had more symptom clusters (three versus one) that consisted of more individual symptoms (six versus three) than patients with CRC without diabetes.

T2: At T2, two symptom clusters were identified for patients with CRC with or without diabetes. The two symptom clusters identified in patients with CRC and diabetes were GI issues/fatigue/depression (cluster 1) and anxiety/peripheral neuropathy/depression (cluster 2). The two symptom clusters in patients with CRC without diabetes were depression/anxiety/GI issues (cluster 1) and peripheral neuropathy/fatigue (cluster 2). Although the number of symptom clusters was the same for each group, like T1, the symptom clusters in patients with CRC and diabetes contained more individual symptoms (six versus five) than the clusters in patients with CRC without diabetes at T2 (see Table 4).

T3: At T3, two symptom clusters were identified in patients with CRC and diabetes. Cluster 1 consisted of anxiety/depression/fatigue, and cluster 2 consisted of peripheral neuropathy/GI issues. In patients with CRC without diabetes, only one symptom cluster was identified: peripheral neuropathy/fatigue/depression/anxiety (cluster 1). Similar to T1, the number of symptom clusters was higher (two versus one), and, as in T1 and T2, the number of individual symptoms was higher (five versus four) in patients with CRC and diabetes at T3 (see Table 5).

The number of individual symptoms that made up the symptom clusters across the three key periods ranged from a minimum of two to a maximum of four for each group. Table 6 shows the symptom clusters across the three time periods. Patients with CRC and diabetes had more symptom clusters (n = 7) than patients with CRC without diabetes (n = 4). Although the symptom clusters in patients with CRC and diabetes and in patients with CRC without diabetes consisted of various configurations of

TABLE 3. Symptom Cluster by Diabetes Status at Time 1 (0–6 Months) Post–Initial Chemotherapy

	With Diabetes (N = 712)			Without Diabetes (N = 1,581)
Symptom	**Fatigue Cluster[a]**	**Anxiety Cluster[a]**	**PN Cluster[a]**	**GI Cluster[a]**
Anxiety	–	0.96	–	0.369
Depression	–	0.459	–	–
Fatigue	0.808	–	–	0.639
GI issues	0.685	–	–	0.999
Physical function	–	–	0.485	–
PN	–	–	0.742	–
Calculation	**Fatigue Cluster[a]**	**Anxiety Cluster[a]**	**PN Cluster[a]**	**GI Cluster[a]**
Cronbach's alpha	0.792	0.661	0.602	0.768

[a] Symptom clusters characterized by highest loading factor
GI—gastrointestinal; PN—peripheral neuropathy
Note. The highest factor loading indicates the most predominant symptom of the symptom cluster.

individual symptoms, the authors did not find any symptom clusters to be stable (i.e., repeated) across the three periods in either group.

Discussion

To the authors' knowledge, this is the first study to use clinical data from EHRs to comprehensively examine symptoms and symptom clusters of patients with CRC and diabetes across three key periods throughout the cancer trajectory. Using a large dataset, a cohort of patients with CRC was identified, 31% of whom had diabetes, which exceeds previous studies in which the prevalence of diabetes among patients with CRC was 20% (Storey et al., 2021). The current study expanded the conceptual model of hyperglycemia in patients with cancer (Hammer et al., 2019) to include the examination of symptoms and symptom clusters in patients with CRC and diabetes at three key periods in the cancer treatment trajectory. Findings from this study demonstrate the relationship between diabetes and the number of symptoms and symptom clusters in patients with CRC. These findings support and expand the relationships in the model and elucidate the need for future prospective studies to examine the role of diabetes and/or hyperglycemia on symptoms and symptom clusters.

Symptom Prevalence

In this study, GI symptoms were the most prevalent, followed by fatigue, for patients with CRC with or without diabetes in each period. In a systematic review and meta-analysis of 35 studies by Han et al. (2020), fatigue was found to be the most prevalent symptom among patients with CRC during active treatment and for years beyond treatment. It is plausible that GI symptoms associated with chemotherapy (nausea, vomiting, diarrhea) contribute to fatigue in patients with CRC (Husson et al., 2015). In addition, poor nutritional status (Wei & Li, 2018), malabsorption, and bowel motility (Han et al., 2023) issues may persist beyond treatment and may continue to contribute to fatigue. Future studies should examine the role of diabetes on fatigue and explore the differences in GI symptoms between patients with CRC and diabetes and patients with CRC without diabetes. Understanding whether patients with CRC and diabetes experience unique symptoms can inform the development of tailored interventions to mitigate symptoms.

Symptom Clusters

The results from the current exploratory factor analysis demonstrated that patients with CRC and diabetes had a greater number of symptom clusters at the T1 and T3 periods. These findings from T1 indicate that patients with CRC and diabetes may come into treatment with poorer overall health (Dowling et al., 2013; O'Shea et al., 2015) and have more latent symptoms than patients with CRC without diabetes. In particular, across all time periods, patients with CRC and diabetes had seven symptom clusters, and patients with CRC without diabetes had four symptom clusters. However, none of the symptom clusters in this study were repeated across the three periods, limiting the ability for direct comparison. More research is needed to identify key periods in the cancer trajectory during which patients with CRC and diabetes may experience more symptom clusters, which can inform oncology clinicians of critical time periods that may require more intense assessment and treatment of symptom clusters.

TABLE 4. Symptom Cluster by Diabetes Status at Time 2 (12–18 Months) Post–Initial Chemotherapy

	With Diabetes (N = 712)		Without Diabetes (N = 1,581)	
Symptom	**GI Cluster[a]**	**Anxiety Cluster[a]**	**Depression Cluster[a]**	**PN Cluster[a]**
Anxiety	–	0.932	–	0.589
Depression	0.555	0.367	1.146	–
Fatigue	0.97	–	–	0.832
GI issues	0.97	–	0.308	–
PN	–	0.377	–	0.898
Calculation	**GI Cluster[a]**	**Anxiety Cluster[a]**	**Depression Cluster[a]**	**PN Cluster[a]**
Cronbach's alpha	0.928	0.74	0.787	0.81

[a] Symptom clusters characterized by highest loading factor
GI—gastrointestinal; PN—peripheral neuropathy
Note. The highest factor loading indicates the most predominant symptom of the symptom cluster.

TABLE 5. Symptom Cluster by Diabetes Status at Time 3 (24–30 Months) Post–Initial Chemotherapy

	With Diabetes (N = 712)		Without Diabetes (N = 1,581)
Symptom	**GI Cluster[a]**	**Anxiety Cluster[a]**	**PN Cluster[a]**
Anxiety	0.987	–	0.551
Depression	0.971	–	0.563
Fatigue	0.882	–	0.673
GI issues	–	0.364	–
PN	–	1.074	0.688
Calculation	**GI Cluster[a]**	**Anxiety Cluster[a]**	**PN Cluster[a]**
Cronbach's alpha	0.95	0.614	0.728

[a] Symptom clusters characterized by highest loading factor
GI—gastrointestinal; PN—peripheral neuropathy
Note. The highest factor loading indicates the most predominant symptom of the symptom cluster.

Studies of symptom clusters in patients with CRC are limited, with even fewer studies examining symptom clusters in patients with CRC and diabetes. The authors found only four studies that examined symptom clusters among patients with CRC. Agasi-Idenburg et al. (2017) conducted a secondary analysis comparing symptom clusters associated with fatigue in younger and older patients with CRC. These researchers found three clusters (emotional, pain, and dyspnea) in both age groups. However, they did not report the time frame (active or post-treatment) of the sample at the time of the study, which may affect symptoms and symptom clusters (Agasi-Idenburg et al., 2017). Hao et al. (2021) examined patients with CRC (N = 149) and identified five symptom clusters (psychologic, GI issues, urinary, lack of energy, and pain) during the first year postcolostomy. However, the study focused on patients with colostomies, which may result in different symptom clusters. Potosky et al. (2022) studied co-occurring symptoms and functioning deficits in patients with CRC (N = 909) to identify subgroups with a low, moderate, or high quality of life. These researchers found that about one-third of patients with CRC experienced a physical and psychosocial symptom cluster highly correlated with functional deficits and poorer quality of life. However, the study did not define the specific symptoms within the clusters (Potosky et al., 2022). Li et al. (2022) examined whether biomarkers predicted symptom clusters in patients with radically resected CRC. The authors identified four chemotherapy-related symptom clusters that included fatigue–psychological, GI issues, neurotoxic symptoms, and constipation–abdominal distension (Li et al., 2022). However, it was a cross-sectional study conducted three days after chemotherapy administration, which captured symptoms at their peak but did not reflect symptom clusters across the cancer treatment trajectory (Li et al., 2022). All four of these studies failed to examine symptom clusters by diabetes diagnosis, which may alter symptom clusters. Future studies should examine the role of glycemic biomarkers such as blood glucose (fasting or random) or glycated hemoglobin on the symptom clusters of patients with CRC and diabetes. Glycemia is a modifiable risk factor, which may improve symptom clusters with optimal monitoring and management.

The authors found only one exploratory study that examined the severity and patterns of preselected symptoms (pain, fatigue, change in appetite, nausea, and vomiting) in a heterogeneous population of individuals with cancer and diabetes (N = 43) during chemotherapy administration (Hershey & Pierce, 2015). These researchers found two distinct clusters based on severity. In cluster 1, patients with cancer and diabetes experienced mild symptoms (i.e., no pain, mild fatigue, change in appetite, and nausea) at baseline, which remained mild throughout the study period. In cluster 2, patients with cancer and diabetes experienced mild symptom severity progressing to moderate symptom severity, with marked increases in fatigue, nausea, numbness, and tingling (Hershey & Pierce, 2015). However, only four patients in the study had CRC, limiting generalizability. The study also included patients with types 1 and 2 diabetes, which are distinctly different diseases and may have influenced the findings (Hershey & Pierce, 2015). Finally, the study was conducted over only an eight-week period and did not examine key periods within the treatment trajectory (Hershey & Pierce,

TABLE 6. Symptom Clusters Across Three Time Periods

	With Diabetes (N = 712)			Without Diabetes (N = 1,581)		
Symptom Cluster	**T1**	**T2**	**T3**	**T1**	**T2**	**T3**
Anxiety						
Anxiety	●	●	●			
Depression	●	●	●			
Fatigue			●			
Peripheral neuropathy		●				
Depression						
Anxiety					●	
Depression					●	
GI					●	
Fatigue						
Fatigue	●					
GI	●					
GI						
Anxiety				●		
Depression		●				
Fatigue		●		●		
GI		●		●		
Peripheral neuropathy						
Anxiety						●
Depression						●
Fatigue					●	●
GI			●			
Peripheral neuropathy	●		●		●	●
Physical function	●					

GI—gastrointestinal; T1—time 1 (0–6 months post–initial chemotherapy); T2—time 2 (12–18 months post–initial chemotherapy); T3—time 3 (24–30 months post–initial chemotherapy)
Note. The bullet points indicate the presence of the symptoms and the symptom clusters across the three time points.

2015). The findings from the current study suggest that patients with CRC and diabetes experience multiple and unique symptom clusters at key periods in the cancer treatment trajectory. Understanding the contribution of diabetes to symptom clusters can inform the development of screening tools to identify at-risk patients with cancer. Prospective research is needed to confirm the findings from this study.

Strengths

This study had several strengths. One strength was that the data were extracted from EHRs. Using EHR data allowed examination of symptoms and symptom clusters in a large cohort of patients with CRC, which would have been costly and difficult to obtain in a longitudinal study. In addition, the descriptions of symptoms reported directly from patients with CRC (with or without diabetes) to healthcare clinicians provide valuable insight into their experiences. Finally, this study provided a foundation for developing prospective studies that can measure symptoms and symptom clusters in patients with CRC and diabetes in real time at key periods during the cancer trajectory.

Limitations

This study had several limitations. First, the descriptive retrospective study design precluded the ability to establish causality. However, this study provided preliminary data useful to guide the development of future prospective studies. One goal of this study was to compare symptoms and symptom clusters of patients with CRC with or without diabetes at three

periods in the cancer trajectory. Therefore, other comorbidities that may have also affected symptoms and symptom clusters were not examined. More prospective research is needed to understand the influence of diabetes and multiple comorbid conditions on symptom clusters in patients with cancer. As in most symptom cluster studies, the authors preselected symptoms to include eight of the most common symptoms reported by patients with CRC and patients with diabetes and also collapsed the variety of GI symptoms into a preset GI symptom cluster based on previous literature (García et al., 2019; Hao et al., 2021; Potosky et al., 2022). Future studies may benefit from including additional symptoms for a more in-depth assessment and analysis of GI symptoms. Finally, clinicians may have incorrectly assigned or omitted some health data and ICD codes in the EHR. However, to moderate this risk, the diagnosis of diabetes was verified by reviewing medication lists. Despite these limitations, the findings from this study have implications for clinical practice and future research.

Implications for Nursing

Oncology clinicians will likely be challenged with treating patients with CRC and comorbid diabetes, given that patients with CRC live longer and the prevalence of diabetes is estimated to increase by 51% by 2045 to include more than 548 million people worldwide (Saeedi et al., 2019). Within the context of concurrent comorbidities, symptoms and symptom clusters may be underreported. Therefore, oncology clinicians must recognize that patients with CRC and diabetes may present with exacerbated symptoms or symptom clusters. Ongoing assessment and monitoring of patients with CRC and diabetes for symptoms and symptom clusters is important because they may be at an increased risk for higher symptom burden.

Conclusion

The findings of this study suggest that having a concurrent diagnosis of CRC and diabetes may exacerbate symptoms and symptom clusters, compared to patients with CRC without diabetes. Prospective research is needed to determine whether patients with CRC and diabetes experience specific and/or a greater number of symptoms and symptom clusters throughout the treatment trajectory. It is plausible that challenges in self-management of diabetes during treatment for CRC may further intensify the symptoms or symptom clusters. Future research should include studies with interventions that facilitate self-management of diabetes, which may improve symptoms and/or symptom clusters in patients with CRC and diabetes. In addition, survivorship models that include multispecialty practitioners are warranted to assess and assist in the medical management of patients with CRC and diabetes.

KNOWLEDGE TRANSLATION

- Patients with colorectal cancer (CRC) and diabetes may experience more symptom clusters at key periods during the cancer treatment trajectory than patients without diabetes, and oncology nurses should include a thorough assessment of symptoms and symptom clusters in this patient population.
- Natural language processing is an effective tool to identify symptoms and symptom clusters for a large population of patients with CRC across the cancer care trajectory without imposing additional burdens on patients.
- Prospective studies are needed to examine the impact of diabetes on symptoms and symptom clusters in patients with CRC and diabetes across the cancer care trajectory.

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