The impact of type 2 diabetes on long-term gastrointestinal sequelae after colorectal cancer surgery: national population-based study

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Abstract

Background: Long-term gastrointestinal sequelae are common after colorectal cancer surgery, but the impact of type 2 diabetes (T2D) is unknown.

Methods: In a cross-sectional design, questionnaires regarding bowel function and quality of life (QoL) were sent to all Danish colorectal cancer survivors, who had undergone surgery between 2001 and 2014 and had more than 2 years follow-up without relapse. The prevalence of long-term gastrointestinal sequelae among colorectal cancer survivors with and without T2D were compared while stratifying for type of surgical resection and adjusting for age, sex, and time since surgery.

Results: A total of 8747 out of 14 488 colorectal cancer survivors answered the questionnaire (response rate 60 per cent), consisting of 3116 right-sided colonic, 2861 sigmoid, and 2770 rectal resections. Of these, 690 (7.9 per cent) had a diagnosis of T2D before surgery. Survivors with T2D following rectal resection had a 15 per cent (95 per cent c.i. 7.8 to 22) higher absolute risk of major low anterior resection syndrome, whereas survivors with T2D following right-sided and sigmoid resection had an 8 per cent higher risk of constipation ($P < 0.001$) but otherwise nearly the same long-term risk of bowel symptoms as those without T2D. For all types of colorectal cancer resections, T2D was associated with a 6–10 per cent higher risk of severe pain ($P < 0.035$) and a 4–8 per cent higher risk of impaired QoL.

Conclusion: T2D at time of surgery was associated with a higher risk of long-term bowel dysfunction after rectal resection, but not after colon resection excluding a higher risk of constipation. T2D was associated with a slightly higher frequency of severe pain and inferior QoL after both rectal and colonic cancer resection.

Introduction

Colorectal cancer and type 2 diabetes (T2D) are common diseases, both with increasing incidence worldwide[1,2]. colorectal cancer is the third most common type of cancer[3]. T2D affects 247 million people world-wide[2], increases the risk of developing colorectal cancer[4,5], and approximately 10 per cent of newly diagnosed patients with colorectal cancer have T2D[6]. T2D has been shown to worsen the prognosis of colorectal cancer[4,5].

Due to advances in early detection, diagnostic precision, and improved treatment regimens, approximately 80 per cent of patients with colorectal cancer are now diagnosed at an early stage without detectable metastasis with more than two-thirds of non-metastatic patients alive after 5 years[7,8]. It is well established that late sequelae to cancer treatment are common[9–11] and are an important healthcare issue.

The most frequent sequela after colorectal cancer resection is bowel dysfunction characterized by constipation, diarrhoea, clustering of defecation, urgency, flatus, and faecal incontinence. These symptoms in patients that have had a rectal resection can be defined low anterior resection syndrome (LARS)[12–14]. Another frequent symptom is chronic pain reported by 13–22 per cent of colorectal cancer survivors[15,16]; however, bowel dysfunction and abdominal pain are frequently observed in individuals with T2D without colorectal cancer[17]. The symptoms are mainly caused by diabetic autonomic neuropathy, but enteric myopathy, alterations in blood glucose, and side effects to medication also contribute[18,19]. Despite the common symptomatology in individuals with T2D and in colorectal cancer survivors, no studies have investigated whether bowel dysfunction and abdominal pain after colorectal cancer resection occurs more frequently among survivors with T2D.

The primary aim of this study was to assess associations between T2D and long-term bowel dysfunction, severe pain, and impaired quality of life (QoL) among colorectal cancer survivors. The hypothesis was that all colorectal cancer resections in patients with T2D was associated with an increased risk of developing long-term gastrointestinal sequelae.

Methods

Study population

The study was based on a large population-based survey regarding long-term sequelae and QoL. All Danish colorectal cancer survivors who had undergone cancer surgery between 2001 and 2014, had more than 2 years of follow-up after surgery, and no known relapse of cancer were eligible[20,21]. Data were retrieved from the Danish Colorectal Cancer Group Database (DCCG), which has a high degree of completeness (more than 95 per cent) and thus represents the population of Danish colorectal cancer patients undergoing surgical resection[22]. The data were furthermore linked to the Danish Civil Registration System ensuring that patients who emigrated, died, or had research protection were excluded.

Patients with disseminated or recurrent disease, other previous cancer (except from non-melanoma skin cancer), permanent stoma, other major surgical procedures performed (total colectomy or pelvic exenteration), radiotherapy for other cancer than rectal cancer, or dementia were excluded.

Identifying individuals with type 2 diabetes

Individuals with T2D were identified in the Danish registries using the civil registration number, which is a unique personal identification number assigned to all Danish residents. All data are recorded with reference to this number and permits accurate linkage of recorded health information at the personal level. Data from the Danish National Patient Register (comprising information on diagnoses given during all hospital contacts in Denmark), the National Prescription Registry (comprising information on all prescriptions filled at any pharmacy in Denmark), and the Danish National Health Service Register (comprising information on podiatrist services) were used to identify individuals with diabetes as previously described by Bendix *et al.*[23]. Individuals were classified as having type 1 diabetes if they had only prescriptions of insulin and a diagnosis of type 1 from a medical department, otherwise diabetes was classified as T2D.

Subgroups according to anatomical site of cancer

Colorectal cancer survivors were subdivided into three subgroups according to the anatomical site of the cancer and the surgical procedure. The subgroup 'right-sided colonic cancer resection' (Right-CC) contained all patients with caecum or ascending colonic cancer, the subgroup 'sigmoid cancer' (Sig-C) contained all patients with sigmoid cancer, and the subgroup 'rectum cancer' (Rec-C) contained all patients with rectum cancer. Short segmental resections of the transverse colon, splenic, or isolated descending resections were excluded due to a combination of low numbers and uncertainty regarding the surgical procedure.

Patient-reported outcomes

A detailed description of the survey data has been published elsewhere[14,24–27]. In the present study, bowel function was evaluated using the same single items (constipation, diarrhoea, faecal incontinence, urgency, clustering of defecation, and flatus incontinence) and cut-offs as for assessing LARS. Constipation was defined as bowel movements less than once per day, and diarrhoea was defined as a need to open the bowel four times or more a day. Faecal incontinence was defined as leakage of liquid stool on a weekly basis. Urgency, clustering, and flatus incontinence were only considered if the symptoms occurred on a weekly basis[14]. The total LARS score, and thus major LARS, was only computed among rectal cancer survivors as the score is only validated in this group[28].

Severe pain was assessed using the PAIN score, which originally examined chronic pain in the abdomen, pelvis, and lower extremities after rectal cancer surgery[24]. Patients with major pain were classified as having severe pain and those with minor or no significant pain as having no severe pain.

The impact of bowel dysfunction on health-related QoL was examined by a single question: 'Overall, how much does your bowel function affect your QoL?' Those who responded 'some' or 'major' impact were categorized as having impaired QoL, whereas 'little' or 'no' were categorized as having no impaired QoL.

Statistical analysis

Descriptive statistics were used to compare baseline characteristics and symptoms between groups. Differences were tested using Pearson's chi-squared test and Student's *t* test. A binomial regression was used for estimation of risk differences adjusted for covariate effects (generalized linear model for binary outcomes with an identity link function). Model 1 adjusts for age at surgery, sex, and time from surgical treatment to answering the survey. Model 2a additionally adjusts for chemotherapy (no/yes) in the Right-CC and Sig-C subgroups, and Model 2b further adjusts for chemotherapy (no/yes), radiotherapy (no/yes), and tumour height (5 cm or smaller, 5–10 cm, more than 10 cm from anus) in the Rec-C subgroup. The OR was calculated by using logistic regression when needed for comparison with results from other papers. Results were presented with 95 per cent confidence interval (c.i.) when relevant. In sensitivity analyses, we expanded the definition of urgency, clustering, and flatus to symptoms at a daily basis instead of weekly, whereas we restricted the definition of constipation to less than once a week and diarrhoea to more than six times daily. Furthermore, the definitions of LARS, pain, and QoL were expanded to include the 'minor/little' category.

All analyses were conducted using Stata version 17 (StataCorp, College Station, Texas, USA).

Results

In total, 53 617 patients were identified in the DCCG database (*Fig. 1*) of whom 24 124 met the inclusion criteria and received a letter of invitation to participate in an electronic survey concerning long-term functional outcome after colorectal cancer surgery. The letters of invitation were sent between November 2015 and January 2016. Based on the answers additionally 5397 patients were excluded because they met at least one of the exclusion criteria. Surgical procedure other than right-sided colectomy, sigmoid, and rectal resections were excluded (3420 patients). Finally, individuals with a diagnosis of type 1 diabetes (52 patients) were excluded, as well as those who developed T2D after the date of surgery and until the end of follow-up (date of answering the questionnaire) (767 patients).

Baseline characteristics

A total of 14 488 colorectal cancer survivors were eligible for the study, and 8747 (60 per cent) answered the questionnaire
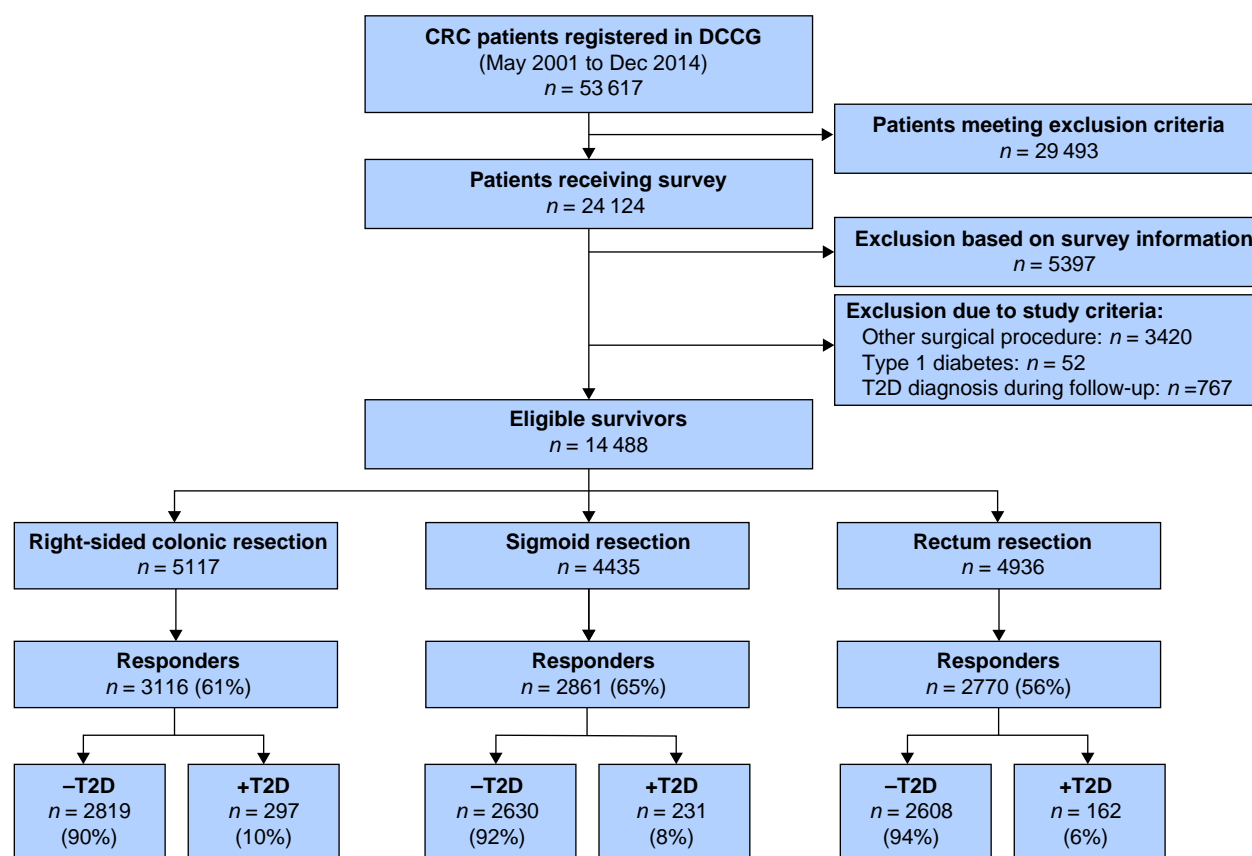
Fig. 1 Number of colorectal cancer survivors based on surgical resection type with or without type 2 diabetes after applying exclusion criteria

*Exclusion criteria were patients with disseminated or recurrent disease, other previous cancer (except from non-melanoma skin cancer), permanent stoma, other major surgical procedures performed (total colectomy and pelvic exenteration), radiotherapy for other cancer than rectal cancer, or dementia. DCCG, Danish Colorectal Cancer Group Database; CRC, colorectal cancer; T2D, type 2 diabetes.

(*Fig. 1*). Compared with responders, the non-responders were significantly older (66 *versus* 70 years, $P < 0.001$), more likely to be women (49 *versus* 53 per cent, $P < 0.001$), more co-morbid according to ASA score (63 *versus* 76 per cent, $P < 0.001$), more often had a previous diagnosis of T2D (7.9 *versus* 12 per cent, $P < 0.001$), and were more often diagnosed with rectal cancer (32 *versus* 38 per cent, $P < 0.001$) (*Table S1*).

Table 1 displays the study population divided into surgical subgroups (3116 Right-CC, 2861 Sig-C, and 2770 Rec-C). A total of 690 (7.9 per cent) had a diagnosis of T2D at the time of colorectal cancer surgery. Compared with Right-CC, the other surgical subgroups were younger ($P < 0.001$), more often men ($P < 0.001$), less often classified as having an ASA score greater than II ($P < 0.001$), and less often had a diagnosis of T2D ($P = 0.047$). The differences were most pronounced when comparing Right-CC with the Rec-C subgroup. Furthermore, within each surgical subgroup, those with T2D were significantly older ($P < 0.001$), were more often men ($P = 0.005$), had higher BMI ($P < 0.001$), and were classified in higher ASA groups than those without diabetes ($P < 0.001$).

The impact of T2D on bowel symptoms in all surgical subgroups

Within each subgroup of Right-CC and Sig-C, those with T2D had almost the same frequency of long-term bowels symptoms as those without diabetes (*Table 2*), with the exception of a higher frequency of constipation (23 per cent *versus* controls 15 per cent, $P = 0.001$) and flatus (45 per cent *versus* controls 37 per cent, $P = 0.016$) among Right-CC survivors, and a higher

frequency of constipation (26 per cent *versus* controls 17 per cent, $P = 0.001$) and urgency (30 per cent *versus* controls 22 per cent, $P = 0.008$) among Sig-C survivors.

In the rectal cancer subgroup, T2D was associated with higher frequencies of symptoms related to defaecation control (clustering, urgency, and faecal incontinence), and the risk of suffering from major LARS was higher (60 *versus* 48 per cent, $P = 0.002$). The adjusted risk difference of major LARS was 15 per cent (95 per cent c.i. 7.8 to 22 per cent) higher among Rec-C survivors with T2D compared with survivors without T2D (*Table 3*), and the adjusted OR was 1.9 (95 per cent c.i. 1.3–2.7). In the sensitivity analyses, the results remained unchanged (data not shown).

Bowel symptoms and surgical procedure

Overall, patients in the Right-CC and Sig-C subgroups had the same prevalence of most bowel symptoms (*Table 2*) with the exception that those having undergone Right-CC were more likely to suffer from faecal incontinence (6.8 per cent *versus* Sig-C 3.5 per cent $P < 0.001$) and those having undergone Sig-C were more likely suffer from urgency for defaecation (37 per cent *versus* Right-CC 23 per cent, $P < 0.001$). In contrast, Rec-C had a significantly higher frequency of almost all bowel symptoms except constipation.

Severe pain

The three surgical subgroups had about the same risk of major severe pain (prevalence 13–15 per cent, data not shown). Within each surgical subgroup, the adjusted risk difference of severe

Table 1 Baseline characteristics of study cohort

	Total	Right-CC		Sig-C		Rec-C	
		−T2D	+T2D	−T2D	+T2D	−T2D	+T2D
Number	8747 (100)	2819 (90)	297 (9.5)	2630 (92)	231 (8.1)	2608 (94)	162 (5.8)
Age (years) (s.d.)	65.0 (10.0)	68.1 (10.4)	72.2 (7.6)	65.0 (9.6)	69.3 (7.9)	63.3 (9.7)	66.9 (7.1)
BMI (s.d.)	25.8 (4.4)	25.3 (4.4)	28.4 (5.5)	25.8 (4.3)	29.0 (4.6)	25.6 (4.0)	28.9 (4.7)
Sex ratio (M:F)	4468:4279	1196:1623	155:142	1373:1257	155:76	1479:1129	110:52
Smoking status							
Never smoker	3061 (35)	975 (34)	89 (30)	933 (35)	83 (36)	924 (35)	57 (35)
Smoker	1245 (14)	413 (15)	46 (16)	359 (14)	23 (10)	387 (15)	17 (11)
Former smoker	3232 (37)	1011 (36)	134 (45)	938 (36)	95 (41)	982 (38)	72 (44)
Missing	1209 (14)	420 (15)	28 (9.4)	400 (15)	30 (13)	315 (12)	16 (10)
ASA score*							
I	3036 (35)	886 (31)	10 (3.4)	1002 (38)	10 (4.3)	1120 (43)	8 (4.9)
II	4745 (54)	1537 (55)	197 (66)	1411 (54)	152 (66)	1326 (51)	122 (75)
>II	822 (9.2)	333 (12)	90 (30)	168 (6.4)	69 (30)	130 (5.0)	32 (20)
Missing	144 (1.7)	66 (2)		49 (1.9)		32 (1.2)	
Stage of disease							
I/II	5591 (64)	1897 (67)	212 (71)	1729 (66)	148 (64)	1502 (58)	103 (64)
III/VI	2497 (29)	819 (29)	77 (26)	812 (31)	74 (32)	677 (26)	38 (23)
Unknown	659 (7.5)	103 (3.7)	8 (2.7)	89 (3.3)	9 (3.9)	429 (16)	21 (13)
Treatment							
Chemotherapy	3139 (36)	1004 (36)	91 (31)	969 (37)	79 (34)	940 (36)	56 (35)
Radiotherapy	397 (14)					379 (15)	18 (11)

Right-CC, right-sided colon cancer resection (caecum and ascending colon); Sig-C, sigmoid cancer resection. Rec-C, rectum cancer resection; + (with) or − (without) T2D (type 2 diabetes). *ASA physical scale.

Table 2 Frequency of long-term bowel symptoms based on surgical resection type with or without type 2 diabetes

	Constipation*		Clustering†		Diarrhoea‡		Urgency†		Incontinence†		Flatus†	
Right-CC												
Reply 'yes'/all replies	468/3010	(16)	684/3066	(22)	259/3010	(8.6)	1150/3073	(37)	182/3079	(6.9)	1172/3078	(38)
- TD2	405/2730	(15)§	610/2778	(22)	234/2730	(8.6)	1039/2783	(37)	162/2790	(5.8)	1043/2789	(37)§
+TD2	63/280	(23)§	74/288	(26)	25/280	(8.9)	111/290	(38)	20/289	(6.9)	129/289	(45)§
Missing	106		50		106		43		37		38	
Sig-C												
Reply 'yes'/all replies	495/2809	(18)	606/2829	(21)	323/2809	(12)	654/2831	(23)	99/2836	(3.5)	1271/2834	(45)
- TD2	437/2582	(17)§	549/2600	(21)	298/2582	(12)	586/2606	(22)§	87/2608	(3.3)	1162/2607	(45)
+TD2	58/227	(26)§	57/229	(25)	25/227	(11)	68/225	(30)§	12/228	(5.3)	109/227	(48)
Missing	52		32		52		30		25		27	
Rec-C												
Reply 'yes'/all replies	332/2722	(12)	1440/2743	(53)	1056/2722	(39)	1212/2749	(44)	303/2742	(11)	1665/2749	(61)
- TD2	316/2561	(12)	1340/2582	(52)§	992/2561	(39)	1125/2587	(43)§	274/2580	(11)§	1561/2589	(60)
+TD2	16/161	(10)	100/161	(62)§	64/161	(40)	87/162	(54)§	29/162	(18)§	104/160	(65)
Missing	48		27		48		21		28		21	

Values are n (%). Right-CC, right-sided colon cancer resection (caecum and ascending colon); Sig-C, sigmoid cancer resection. Rec-C, rectum cancer resection; + (with) or − (without) T2D (type 2 diabetes). *Defaecation six or fewer times a week. †On a weekly basis. ‡Diarrhoea is defaecation more than three times a day. §$P < 0.050$.

Table 3 Risk differences of severe pain, impaired quality of life and major low anterior resection syndrome after different types of colorectal cancer resections in patients with and without type 2 diabetes (adjusted and unadjusted analysis)

	-T2D	+T2D		+T2D		+T2D	
		RD unadjusted	P	RD adjusted model 1	P	RD adjusted model 2a/b	P
Right-CC							
Severe pain	1 (ref)	4.6 (−0.01; 9.8)	0.085	5.6 (0.38; 10)‡	0.035	5.7 (0.55; 11)*	0.030
Impaired QoL	1 (ref)	3.1 (−1.6; 7.9)	0.180	4.1 (−0.01; 8.9)	0.090	4.0 (−0.69; 8.8)*	0.094
Sig-C							
Severe pain	1 (ref)	7.9 (2.0; 14)‡	0.009	9.1 (3.2; 15)‡	0.002	9.2 (3.4; 15)*	0.002
Impaired QoL	1 (ref)	4.8 (−0.01; 10)	0.085	6.1 (0.72; 11)‡	0.026	6.1 (0.72; 11)*	0.026
Rec-C							
Major LARS	1 (ref)	13 (5.1; 21)‡	0.001	13 (5.8; 21)‡	0.001	15 (7.8; 22)†	<0.001
Severe pain	1 (ref)	7.6 (0.6; 15)‡	0.034	9.1 (2.1; 16)‡	0.011	10 (2.9; 18)†	0.006
Impaired QoL	1 (ref)	6.4 (−1.4; 14)‡	0.110	7.6 (0.1;15)‡	0.046	4.4 (−03.5; 12)†	0.27

Values are risk difference percentage (95 per cent c.i.). Right-CC, right-sided colon cancer resection (caecum and ascending colon); Sig-C, sigmoid cancer resection; Rec-C, rectum cancer resection; + (with) or − (without) T2D (type 2 diabetes); LARS, low anterior resection syndrome; QoL, quality of life. Model 1, adjusted for age at surgery, sex, and time from surgical treatment to answering the survey; *Model 2a, model 1 + chemotherapy (no/yes); †Model 2b, model 1 + chemotherapy (no/yes) + radiotherapy (no/yes) + tumour height (5 cm or less, 5–10 cm, and more than 10 cm from anus). ‡Indicates significant results.

pain was higher in those with T2D than in those without (Table 3). This was most pronounced in the Sig-C and Rec-C subgroups, where those with T2D had a 9.2 per cent (3.4–15 per cent) higher absolute risk of severe pain after sigmoid resection and a 10 per cent (2.9–18 per cent) higher absolute risk after rectal resection compared with those without T2D.

Quality of life

In the Right-CC and Sig-C subgroups, 16–17 per cent experienced impaired QoL, whereas the frequency was 34 per cent in the Rec-C subgroup (data not shown). Those with T2D had only a slightly higher risk of impaired QoL (4–8 per cent) than those without T2D (Table 3).

Discussion

This national cross-sectional study of colorectal cancer survivors with diabetes, demonstrated right-sided and sigmoid resection was associated with almost the same risk of long-term bowel symptoms as those without diabetes, except for an 8 per cent higher risk of constipation. In contrast, patients with rectal resection and T2D had a higher a risk of symptoms related to defaecation control (clustering, urgency, and faecal incontinence) and a 15 per cent (95 per cent c.i. 7.8 to 22) increased risk of major LARS. In all resection types, T2D was associated with a slightly higher risk of severe pain and impaired QoL.

Several studies have examined long-term bowel complications after rectal resection using the LARS score. In 2018, a meta-analysis based on 11 studies was published and the estimated prevalence of major LARS was 41 per cent (95 per cent c.i. 34 to 48)[12]. This is in line with our findings among Rec-C survivors without diabetes. In a randomized setting (242 non-stoma patients), Chen *et al.*[29] investigated the long-term bowel function (median follow-up 14.7 years) after total mesorectal excision with or without preoperative short-course radiotherapy. They reported a similar higher OR of 1.8 (99 per cent c.i. 0.6 to 5.6) associated with diabetes as observed in the present study. The non-significant result in the study by Chen *et al.* might be explained by an underpowered study cohort. The present study confirmed previous findings, showing that bowel symptoms and major LARS were associated with poor health-related QoL[27,30,31], and the prevalence was higher among survivors after rectal resection compared with colonic resection[30,32].

However, bowel symptoms are also commonly reported in the general population. A Danish study on a random sample of 3440 adult citizens from the general population demonstrated that 12–18 per cent of the adult female and 10–11 per cent of the adult male population suffered from symptoms corresponding to major LARS, and the symptoms were associated with unspecified physical disease[33]. A similar prevalence of 12 per cent was found in a general Dutch population, whereas the authors reported a prevalence of symptoms of major LARS at 24 per cent among individuals with diabetes[34]. Similar higher frequencies of small and large intestinal symptoms in individuals with T2D were reported in two reviews[35,36]. Both papers found a higher prevalence of diarrhoea and constipation among individuals with T2D compared with those without. Additionally, a higher frequency of faecal incontinence, severe pain, and bloating was found in one of the studies[36].

The hypothesis was that there would be a higher frequency of long-term bowel dysfunction associated with T2D among colorectal cancer survivors due to well described diabetic gastroenteropathy[17]. A major pathological driver of diabetic enteropathy is believed to be changes in the enteric motor and sensory functions, leading to manifest symptoms such as those related to motility and secretory function[37]; however, the bowel symptoms associated with diabetes among colorectal cancer survivors differed to some extent from the general diabetes population. Diarrhoea was not associated with diabetes, whereas higher frequencies of constipation were only observed in the Right-CC and Sig-C subgroups, and otherwise T2D had only minor impact on long-term bowel symptoms in these two subgroups. In contrast, rectal cancer survivors with T2D had higher frequencies of clustering, urgency, and faecal incontinence when compared with those without T2D. These symptoms can occur due to disruption of the reflexes controlling defaecation and continence. The observed higher influence of T2D on long-term bowel dysfunction in the Rec-C subgroup when compared with the Right-CC/Sig-C subgroups can all be related to impaired nerve function associated with diabetes. Colonic function mainly comprises motility and secretion, whereas rectal function is much more complex. The colon is predominantly influenced by enteric neuronal and hormonal functioning, whereas rectal function is more dependent on direct nerve innervation controlling the defaecation and continence function. During rectal resection, nerves lie near the dissection plane and risk direct surgical injury, as well as the delayed impact of scarring, fibrosis, and the side effects of neoadjuvant treatment[38,39]. In patients with existing neuropathy, it is likely that these effects could be more pronounced.

The observed higher prevalence of severe pain among colorectal cancer survivors with T2D compared with those without diabetes could also be attributable to nerve function. Overall, the prevalence of severe pain was similar in the surgical subgroups and in the same range as formerly published studies of pain after cancer surgery[15,16,40] and colorectal surgery in general[41]. It is plausible that people with diabetes had pre-existing sensory symptoms as any autonomic and sensory neuropathy associated with long-standing diabetes affects many structures of the neuroaxis involved in pain processing[17]; however, the frequency of severe pain after surgery in diabetics is higher than expected, and it is likely that the surgical trauma in addition to chemoradiotherapy increase any pre-existing neuropathy or may be responsible for its *de novo* development. Only one previous study investigated the impact of diabetes, and in contrast with our findings, it did not find any association between diabetes and pain after colorectal cancer surgery[15]. The difference may be explained by heterogeneous study populations and more importantly, by a different time of pain assessment (6 months after surgery *versus* more than 2 years after surgery as in the present study).

Bowel dysfunction following treatment of pelvic cancers is treatable. Several studies from the UK show that patients benefit from algorithm-based management and a multidisciplinary treatment approach[42–44]. If cancer survivors undergo clinical evaluation and the underlying pathophysiology to their bowel dysfunction is found, they can receive targeted treatment with marked improvement in up to 38 per cent[45]. Rectal cancer survivors with LARS may be treated with conservative treatment in a nurse-led clinic with 75 per cent of patients experiencing an improvement in LARS score[46]. Larsen *et al.* have shown that when asked in a survey, 10 per cent of Danish colonic cancer survivors have bowel dysfunction and are interested in clinical evaluation and treatment[47]. If cancer survivors with long-term bowel

sequelae are identified, evaluated, and treated, there is a potential for helping a large patient group, including those with diabetes.

The core strengths of the present study include the population-based data with large patient numbers, the prospectively collected disease- and treatment-related data, as well as register-based identification of the diabetes population. The study is limited by a response rate of 60 per cent. Compared with respondents, the non-respondents were older, classified in higher ASA groups, and had more often a previous diagnosis of T2D and rectal cancer. This selection bias may influence the results of this study in both directions. It is possible that colorectal cancer survivors suffering from long-term sequelae are more likely to answer the survey due to personal interest in potential treatments, which could lead to an overestimation of the symptoms. Another possibility is that a lower attendance of survivors with T2D might lead to underreporting in this group; however, we do not find any reason to believe that the selection bias is different within the three surgical subgroups and therefore, we consider the observed difference between colon and rectal resected survivors to be reliable.

Funding

Acknowledgements

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

Due to the Danish law it is not possible to make national health registers available, but on request we would like to collaborate and discuss reasonable access to data.

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