International Journal of Colorectal Disease (2019) 34:1517–1528
https://doi.org/10.1007/s00384-019-03342-x

REVIEW

Quality of life in patients treated for anal carcinoma—a systematic literature review

Anton Sterner[1,2] · Kristoffer Derwinger[1,2] · Caroline Staff[3] · Hanna Nilsson[1,2] · Eva Angenete[1,2]

Accepted: 30 May 2019 / Published online: 19 July 2019

Abstract

Purpose Anal cancer is a mainly treated with chemoradiotherapy. A small number of patients undergo salvage surgery. There are few published studies investigating quality of life and functional outcome after treatment for anal cancer. The aim of this review was to explore the literature and identify areas for further research.

Methods A search was conducted in Medline using MESH terms related to anal cancer and quality of life. Two investigators selected and reviewed articles based on titles and abstracts. Three investigators read and reviewed the included articles and collected relevant data. The included articles were evaluated using the minimum standard checklist, and key findings were summarised in a chart.

Results Some 15 articles, and a total of 802 patients, were deemed eligible. The results differed slightly among the studies. The incidence of symptoms such as fatigue, nausea, insomnia and appetite loss was higher than among healthy volunteers. Bowel function, urinary function and sexual function were negatively affected. Some studies found that, compared with the normal population, anal cancer survivors scored clinically significant worse in the functional scales in QLQ-C30.

Conclusion In conclusion, it is apparent that several functional problems affect the quality of life of patients with anal cancer. There are few studies which have investigated quality of life after treatment for anal cancer. Interventions to address issues related to anal cancer treatment may improve long-term quality of life in this patient group.

Trial registration CRD42017059787

Keywords Anal cancer · Oncology · Morbidity · Radiotherapy

Introduction

Anal cancer (squamous cell carcinoma) is a rare disease with an annual incidence between 1 and 2 per 100,000 inhabitants accounting for 1–1.5% of all gastrointestinal malignancies. In Sweden, 150–200 new cases are registered each year with increasing incidence [1]. Like cervical cancer, anal cancer is strongly associated with the human papillomavirus (HPV), which is the leading cause of approximately 80–85% of the tumours [2, 3].

Radio and chemotherapy (RCT) has been the cornerstone treatment of anal cancer since the 1970s, when studies by Nigro et al. showed that the survival rate for patients treated with RCT was as good or higher than for patients who underwent surgery alone [4–6]. Today, a majority of patients with anal carcinoma are treated with fluorouracil (5-FU) and

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00384-019-03342-x) contains supplementary material, which is available to authorized users.

✉ Anton Sterner
anton.sterner@vgregion.se

[1] Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[2] Region Västra Götaland, Sahlgrenska University Hospital, Department Of Surgery, Gothenburg, Sweden

[3] Department of Surgery, Capio S:t Görans Sjukhus, Stockholm, Sweden

mitomycin C (MMC) in combination with radiotherapy, in doses normally up to 45–60 Gy, depending on TNM-stage. A small group of patients undergo salvage surgery with a permanent colostomy due to lack of treatment response or tumour recurrence. A large Nordic study recently showed that inclusion in a treatment protocol has a positive effect on outcome [7].

Studies investigating QoL after treatment for anal cancer are rare. A review article by Sodergren et al. summarised the few published studies up to 2014 and found that the most common complications after treatment for anal cancer were skin conditions, faecal incontinence and sexual problems, but psychological side effects such as depression and fatigue also occurred [8]. However, since then, some longitudinal studies with baseline data have been published [9–12].

Quality of life in other types of malignancy in the gastrointestinal canal than anal cancer has been widely investigated using standardised questionnaires such as focusing on anorectal, bladder and sexual function after treatment. These questionnaires were designed for patients treated for rectal cancer and other malignancies in the gastrointestinal canal. Recently, however, Sodergren et al. published an EORTC questionnaire for anal cancer, EORTC QLQ-ANL27, which has not yet been used in any other study [13] as far as we know. The aim of this review article is to investigate the existing research on quality of life and evaluate the need for further research in the subject.

Materials and methods

Protocol and registration

The trial is registered in the PROSPERO International prospective register of systematic reviews, registration number: CRD42017059787.

Eligibility criteria

Eligible studies were published prior to December 2016. Endpoints were quality of life after treatment of anal cancer. Case reports, editorials, review articles and comments were excluded.

Information sources/search strategy

The PICO that was set up was patients with anal cancer, treatment with chemoradiotherapy and or surgery, no control was used, the outcome was functional outcome and quality of life. A search using the PICO was conducted in Medline, for English language articles only. A combination of MESH terms and other terms related to anal cancer, treatment, and quality of life were used (see Table 1). Articles of interest, found through references in the published articles, were also assessed for eligibility.

Study selection

Two investigators independently reviewed and selected articles by reading the titles and abstracts. Articles concerning other diseases than carcinoma of the anal canal, and studies lacking quality of life as an endpoint after treatment of anal carcinoma, were excluded. We included randomised controlled trials, case-report trials and prospective trials. Disagreement between the two independent investigators was solved by discussion.

Data collection process

Three reviewers read the full articles that were selected for a closer investigation. Relevant data were retrieved and collected in a data form as Tables 1, 2 and 3.

Data items

Data about main author, year of publication, type of trial, number of patients, method of evaluating quality of life, and main findings were abstracted by two authors and collected in a data form.

Risk of bias in individual studies

Two investigators assessed risk of bias by studying the included articles using the minimum standard checklist developed by Efficace et al. [14].

Summary measures

The quality of the included studies was evaluated using the minimum standard checklist for studies assessing QoL, developed by Efficace et al. [14].

Synthesis of results

The key findings and study characteristics from all included studies were summarised in a chart.

The results regarding general quality of life, symptom scales and long-term results from the studies that used the EORTC QLQ-C30 for evaluating quality of life were summarised in a table and compared with a cohort of healthy volunteers.

Risk of bias across studies

Risk of bias was assessed by one author and summarised in the results.

Table 1 Characteristics of included studies

Main author	Year	Study design	Primary endpoint	No. patients	Median age, years	Evaluation method	Follow-up months, med.	Study strength/ limitations	Key findings
Joseph	2016	Prospective longitudinal cohort study	Evaluation of QoL after helical tomotherapy	54	57 (37–83)	QLQ 29, 30	26 (0–66)	Longitudinal study, short follow-up	General QoL deteriorated directly after treatment but improved within 12 months. Urinary incontinence, diarrhoea and dyspareunia were persistently worsened during follow-up
Sunesen	2015	Multi-centre, cross-sectional, register study	Long-term adverse events/extent of distress	84	58 (35–85)	Own questionnaire	33 (5–92)	Response rate 89%. Non-validated questionnaire	> 50% of patients experienced faecal incontinence causing great distress in majority. 60% of women experienced dyspareunia causing great distress in 50%
Knowles	2015	Single-centre, cross-sectional	Adverse events, long-term QoL	42	54 (11)	EORTC QLQ-30 and CR38	64 (41–94)	Inclusion period 17 years, response rate 46%	54% had more than 4 bowel movements/day, 22% leakage of stool, high symptomatology for sexual problems
Han	2014	Single-centre, longitudinal cohort study	Acute toxicity and QoL	58	56 (39–88)	EORTC QLQ- and CR29	12	Prospective evaluation, 67% response 12 months	General QoL deteriorated after treatment but returned to baseline within 3 months. Rate of impotence increased after treatment
Fakhrian	2013	Single-centre, cross-sectional	Critical adverse events and QoL	42	64 (50–86)	FACT-C	68 (9–222)	Long inclusion period of 23 years	Largest difference in QoL was seen for grade 3 stool incontinence, grade 3 stool frequency and grade 3 dyspareunia, vs no problem
Bentzen	2013	National cohort, cross-sectional	Long-term HRQoL	128	61 (40–89)	EORTC QLQ-C30, CR29	66 (25–112)	Large cohort compared to other studies	Compared with volunteers, the scores were poorer in all scales and single items. Faecal incontinence in 57% vs 8% of volunteers. 67% impotence, 24% severe dyspareunia
Welzel	2011	Single-centre, cross-sectional	Long-term QoL	52	62	QLQ-C30, QLQ-CR38, LENT/SOMA	36 (5–137)	Low answer % for sex questions. Long inclusion	QoL in anal cancer patients was reduced and 5 major concerns were identified, including urological/gastrointestinal complains as well as impairment of sexual function
Tournier	2016	Single-centre longitudinal cohort study	QoL is secondary endpoint	119	59	QLQ-C30, AS-CT, MSK-AF	27 (0–66)	Subgroup of locally advanced tumours. Short follow-up	After treatment GHS, emotional function, insomnia, appetite loss and constipation were clinically and significantly approved compared with baseline data
Provencher	2010	Single-centre, cross-sectional	QoL och tumour control	30	53 (36–84)	QLQ-C30, QLQ-CR29	51 (15–132)	Long inclusion period vs small study size	47% reported some faecal incontinence. 65% of women lacked sexual interest
Das	2010	Single-centre cross-sectional	Long-term QoL	32	51	FACT-C, MOS (medical outcome study), sexual problem scale	60 (36–156)	Single-centre, small size, low response rate, 40%	55% were very dissatisfied with their sexual life, 65%, 71% and 72% experienced lack of sexual interest,

Table 1 (continued)

Main author	Year	Study design	Primary endpoint	No. patients	Median age, years	Evaluation method	Follow-up months, med.	Study strength/ limitations	Key findings
									inability to relax and enjoy sex or becoming sexually aroused
Oehler-Janne	2007	Single-centre, cross-sectional	Clinical outcome	34	62	QLQ-C30, 38		QoL was not a primary endpoint	No difference in quality of life between two different radiation therapies
Jephcott	2004	Single-centre, cross-sectional case control study	Long-term QoL	50	69 (45–89)	QLQ-C30, 38	62 (28–146)	Case control study, volunteers were recruited by posters might cause bias	QoL differed between anal cancer survivors and volunteers, and for sexual enjoyment and sexual problems the different reached very much changed
Vordermark	2001	Single-centre, cross-sectional	Clinical outcome	14		GIQLI	53 (12–95)	Small cohort, 14 patients	Manometry found a decreased resting and maximal sphincter pressure in patients treated because of anal carcinoma
Allal	1999	Single-centre cross-sectional	Long-term QoL	41	60 (42–75)	QLQ-C30, 38	116 (37–218)	No patients above 80 years	Overall quality of life was significantly associated with severity of late complication and anal function score. Low sexual functioning
Vordermark	1999	Single-centre, cross-sectional	Long-term	22		GIQLI	37 (7–151)	Small study	No difference was found in QoL assessed by GIOLI between patients with anal cancer, anorectal disease or healthy workers. Patients with faecal incontinence scored significantly worse

Table 2 Evaluation of studies according to minimum standard checklist by Efficace

HRQoL issue	No.	Reports %
Conceptual		
A priori hypothesis stated	14/15	
Rationale for instrument reported	13/15	
Measurement		
Psychometric properties reported	13/15	
Cultural validity verified	1/15	
Adequacy of domains covered	11/15	
Methodology		
Instrument administration reported	10/15	
Baseline compliance reported	14/15	
Timing of assessments documented	14/15	
Missing data documented	9/15	
Interpretation		
Clinical significance addressed	13/15	
Presentation of results in general	15/15	

Result

Study selection and literature search

After screening 736 potential studies using title and abstract, 15 articles were found eligible and in total, 802 patients were included in the review (see Fig. 1).

Study characteristics

Characteristics of the 15 included observational studies are listed in Table 1. Twelve studies were cross sectional out of which ten were single-centres with inclusion periods varying from 8 to 24 years. Two Scandinavian multi-centre cross-sectional studies retrieved patients using national registers recruiting relatively large cohorts. Three studies were longitudinal assessing quality of life before and after treatment of anal cancer; in one of these, the authors compared two different techniques of radiation [15]. The earliest inclusion period started in the 1970s, but the majority of patients received treatment during the 1990s up to the 2010s.

The quality of the QoL items reported was generally high with a mean of 8.3 for the 15 studies, well above the recommended level of 8 (Table 2) [14].

The time interval from treatment to assessment of QoL differed between the studies. In order to ensure long-term QoL evaluation, five studies required a minimum follow-up period of 2 years. Two of the longitudinal studies measured QoL in time intervals up to several years after treatment, while the third longitudinal study assessed QoL at two occasions only, before and directly after treatment.

The number of patients enrolled varied from 14 to 128. The two largest studies, including 128 and 84 patients, respectively, were based upon national registries [10, 16]. Median age varied from 51 to 69 years and the response rate of QoL assessment was between 40 and 89%.

Drop-out analysis

A drop-out analysis was performed in 8 of the 14 studies. Knowles and Bentzen reported that patients who declined participation were older with more comorbidities, but no differences in tumour characteristics were seen [11, 16]. Tournier-Rangeard found that patients, who answered the follow-up QoL questionnaire, had higher QoL in the baseline questionnaire [17]. Drop-out analyses in the remaining studies showed no difference in characteristics between responders and non-responders concerning tumour characteristics, age or comorbidities.

QoL instruments

In the absence of a disease-specific quality of life questionnaire designed for anal cancer survivors, most authors have used previously validated QLQ-CR38/QLQ-CR29 or FACT-C designed for colorectal cancer [18]. These questionnaires collect information regarding anxiety, body image, sexual function, urinary function and anorectal function.

QLQ-C30, a generic cancer instrument, has previously been validated numerous times for different cancer cohorts [19, 20] in different countries and cultures [21–24], as well as for patients with curable and palliative disease. QLQ-C30 contains 30 items, 5 multi-item functional scale (physical, role, emotional, cognitive and social functioning), 6 single-item symptom scale (including fatigue, nausea/vomiting, pain, dyspnoea, insomnia, appetite loss, constipation diarrhoea and financial difficulties) and a multi-item named global health score measuring the overall physical condition and general QoL. A low global health score indicates poor physical condition and/or low overall quality of life [25]. In nine of the included studies, QoL was assessed using QLQ-C30 with the addition of QLQ-CR29 or QLQ-CR38 [26].

When analysing and comparing results from QLQ-C30, the authors have used the recommendations of Osoba et al. [27] grading a change of less than 5 to be small, 5–10 to be moderately relevant and any change above 10 points to be clinically significant.

Two authors chose to evaluate QoL using the validated FACT-C, a part of the Functional Assessment of Chronic Illness Therapy (FACIT) [28, 29] measurement system. This questionnaire contains self-reporting instruments for evaluating QoL in patients with cancer and other chronic

Table 3 QLQ-C30 for patients included in the six cross-sectional studies below

QLQ-C30	Bentzen		Welzel [1]		Jephcott [2]		Allal	Provencer	Knowles	Michelson [3]	
Cohort group	Anal cancer	Volunteer	Anal cancer	German control [4]	Anal cancer	Volunteer	Anal cancer	AC	Anal cancer	Women 60–69	Men 60–69
Mean (SD)	68 (25)	83 (19)	61	63	66 (28)	78 (20)	71 (21)	70 (25)	67	78 (22)	77 (21)
Physical function											
Mean (SD)	77 (22)	90 (15)	70	84	74 (29)	89 (14)	80 (22)	87 (14)	87	87 (16)	88 (17)
Role function											
Mean (SD)	69 (31)	91 (19)	60	82	76 (33)	87 (25)	85 (21)	77 (26)	67	87 (24)	87 (24)
Emotional function											
Mean (SD)	77 (25)	87 (16)	57	77	74 (28)	81 (16)	77 (25)	77 (26)	67	84 (20)	86 (18)
Cognitive function											
Mean (SD)	77 (26)	89 (15)	76	88	75 (24)	82 (20)	76 (23)	85 (25)	83	90 (17)	87 (16)
Social functioning											
Mean (SD)	71 (29)	91 (18)	60	89	73 (35)	90 (20)	82 (28)	74 (34)	67	92 (19)	91 (18)
Fatigue											
Mean (SD)	38 (28)	20 (18)	23	41	36 (39)	20 (21)	27 (22)	28 (29)	33	20 (22)	20 (21)
Nausea/vomiting											
Mean (SD)	6 (13)	3 (10)	8	6	6 (17)	1 (4)	6 (15)	1 (4)	0	3 (12)	2 (8)
Pain											
Mean (SD)	25 (30)	14 (23)	34	22	23 (31)	14 (22)	15 (21)	20 (25)	17	21 (26)	18 (22)
Dyspnoea											
Mean (SD)	27 (33)	10 (20)	30	13	23 (33)	8 (16)	13 (22)	18 (26)		16 (24)	17 (25)
Insomnia											
Mean (SD)	35 (35)	20 (26)	40	24	29 (32)	22 (28)	24 (29)	26 (31)		23 (28)	19 (26)
Appetite loss											
Mean (SD)	14 (24)	3 (12)	14	7	13 (22)	3 (15)	10 (19)	10 (23)		4 (15)	2 (10)
Constipation											
Mean (SD)	22 (28)	14 (22)	17	6	24 (32)	8 (16)	15 (21)	7 (19)		9 (21)	4 (14)
Diarrhoea											
Mean (SD)	27 (32)	12 (21)	37	2	27 (32)	5 (12)	28 (36)	28 (40)		5 (16)	5 (14)
Financial difficulties											
Mean (SD)	14 (27)	4 (14)	37	10	23 (37)	8 (20)	15 (28)	20 (31)		7 (21)	5 (16)

illnesses [30]. FACT-C combines FACT-G, assessing general QoL with the 9-item colorectal cancer subscale (CCS). Two of these items address issues concerning stoma. FACT-C contains four items: physical, social, emotional and functional wellbeing [31, 32]. In all, FACT-C contains 36 items presented on a 5-point Likert scale.

Two studies used a questionnaire developed by Eypasch for gastrointestinal disease, not limited to cancer [33]. Sunesen and co-workers constructed their own anal cancer–specific questionnaire [10]. This questionnaire is based on existing validated questionnaires and an expert panel including three colorectal surgeons and one radiation oncologist.

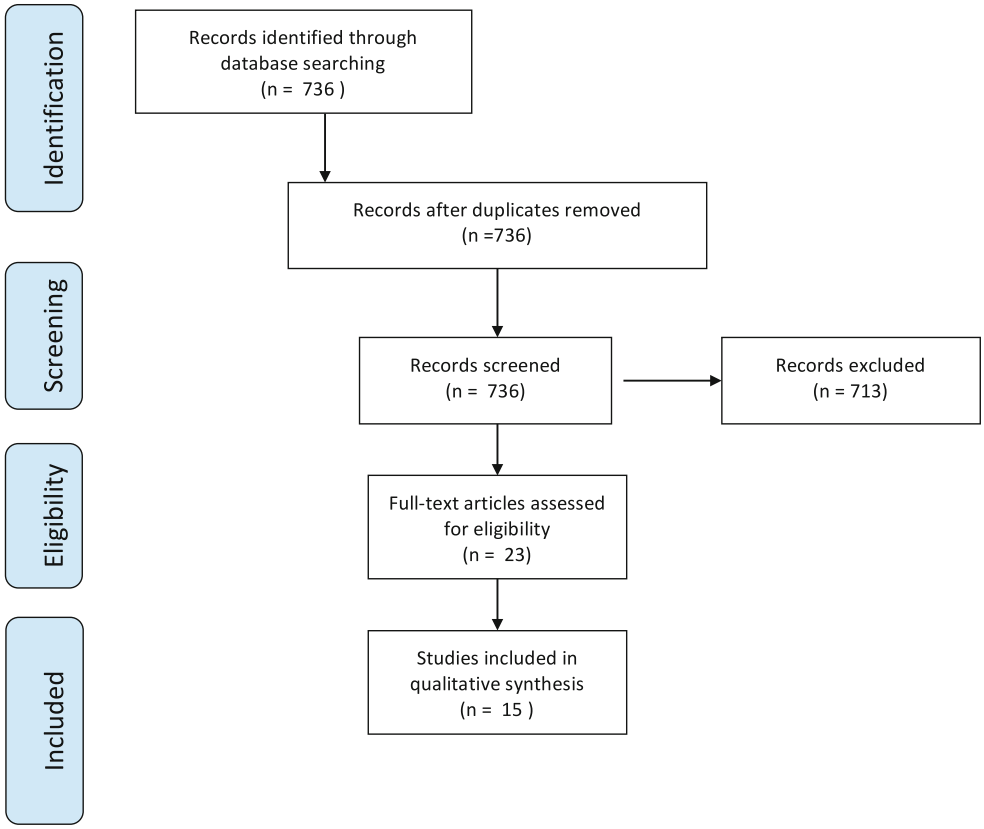

Fig. 1 Flow chart over included articles

Synthesis of studies

General quality of life

Results from the QLQ-C30 questionnaire from six cross-sectional studies [11, 16, 34–37] are listed in Table 3, together with reference data from a Swedish [38] and a German [39] healthy cohort. The numerical value of global health status, after treatment of anal carcinoma, varies from 60 to 72.

Data of QLQ-C30 score from the three longitudinal studies [9, 12, 17] are displayed in Table 4. After an initial decrease immediately after treatment, global health status increased to baseline levels [12] or well beyond a few months after treatment [9, 17].

In several studies [34, 36, 40, 41], sphincter function was found to independently affect overall QoL. Fakhiran as well as Vordermark found that stool incontinence as well as urgency (only Fakhiran) lowered QoL [ref. 42]. Dyspareunia also negatively affected QoL (ref. Fakhiran) as did higher age [43].

Functioning scales in QLQ-C30

Bentzen et al. [16] and Welzel et al. [34] found that anal cancer survivors scored clinically significantly worse for all five functional scales in QLQ-C30 compared with the normal population. The largest difference (> 20p) was seen for role and social functioning. Provencher [37] also found a clinically significant difference for social function and Jephcott [35] demonstrated a difference for all functions, but clinically non-significant for emotional and cognitive functioning.

As with global health score, however, functional scales were back to baseline values within a year, except from role function and social function, which had improved clinically significantly compared with baseline data.

Symptom scales, long-term results

General cancer–specific symptoms addressed in QLQ-C30 are listed for the applicable studies in Tables 3 and 4. Compared with volunteers, Bentzen et al. [16] found that anal cancer survivors scored worse for all symptoms and single items in QLQ-C30 and CR29. Similar findings were made by Welzel et al. who compared their cohort with the German background population. In their study T3/4, low tumour localisation, a long follow-up time, surgery, male gender and being physically inactive had a significantly negative impact on role function and fatigue [34].

One year after treatment, as assessed by Joseph et al. [9], fatigue, pain, appetite loss and constipation were clinically significantly improved compared with baseline data, as was financial difficulties.

Table 4 QLQ-C30 for patients included in the three longitudinal studies

QLQ-C30	Joseph et al.			Tournier et al.		Han et al.		
Time of evaluation	Baseline	After treatment	1 year	Baseline	After treatment	Baseline	After treatment	1 year
Global health status								
Mean (SD)	61 (22)	42 (19)	72 (18)	65 (23)	71 (21)	68 (20)	*50 (19)*	70 (20)
Physical function								
Mean (SD)	82 (17)	62 (23)	85 (17)	88 (17)	86 (17)	87 (15)	*66 (22)*	88 (15)
Role function								
Mean (SD)	69 (35)	41 (23)	80 (23)	82 (28)	81 (28)	75 (29)	*44 (29)*	86 (25)
Emotional function								
Mean (SD)	69 (21)	64 (22)	77 (22)	65 (26)	74 (25)	70 (23)	*72 (22)*	78 (21)
Cognitive function								
Mean (SD)	77 (23)	70 (25)	83 (24)	81 (23)	80 (24)	79 (20)	*72 (23)*	79 (18)
Social functioning								
Mean (SD)	69 (28)	50 (27)	81 (22)	86 (25)	82 (26)	70 (27)	*47 (30)*	83 (20)
Fatigue								
Mean (SD)	37 (24)	62 (25)	27 (20)	29 (28)	33 (25)	32 (23)	*51 (20)*	24 (18)
Nausea/vomiting								
Mean (SD)	8 (16)	21 (19)	7 (16)	6 (18)	7 (17)	8 (15)	*14 (17)*	6 (16)
Pain								
Mean (SD)	34 (31)	59 (30)	18 (22)	30 (21)	20 (26)	33 (32)	*55 (29)*	19 (24)
Dyspnoea								
Mean (SD)	16 (23)	22 (27)	14 (21)	13 (22)	19 (27)	11 (17)	*20 (24)*	9 (15)
Insomnia								
Mean (SD)	40 (31)	43 (32)	33 (30)	41 (35)	27 (32)	36 (32)	*39 (27)*	29 (27)
Appetite loss								
Mean (SD)	23 (27)	49 (30)	10 (23)	22 (29)	13 (21)	21 (28)	*36 (27)*	11 (20)
Constipation								
Mean (SD)	26 (30)	18 (27)	4 (4)	26 (35)	14 (28)	12 (22)	*33 (32)*	8 (17)
Diarrhoea								
Mean (SD)	14 (21)	49 (35)	23 (27)	14 (23)	17 (25)	12 (22)	*31 (25)*	12 (21)
Financial difficulties								
Mean (SD)	38 (34)	38 (35)	17 (24)	12 (28)	11 (24)	28 (33)	33 (34)	19 (29)

Bowel function

In the anal cancer–specific questionnaire created by Sunesen [10], symptoms were identified according to the extent of distress they caused, graded as none, little, moderate or great. Faecal incontinence, faecal urgency and frequency of bowel movements were common and caused great distress. Knowles et al. [11] found that 29% of patients altered their daily activity because of bowel dysfunction. As seen in Table 4, diarrhoea increased after treatment and remained increased for the study period in the longitudinal studies. Anal cancer survivors had more diarrhoea than healthy volunteers (Table 3).

Urinary symptoms

Increased urinary frequency was common among anal cancer survivors [9, 37, 42], as was urinary incontinence that increased 10% after treatment [9]. In Sunesen's study [10], urinary incontinence caused great distress for the majority of the 45% of patients who experienced it.

Symptoms affecting sex life

It was common with a low response rate for questions regarding sex. Women neglected to answer these questions to a larger extent than men, as did anal cancer survivors compared

Table 5 Sexual functioning assessed by QLQ-CR38

Author	Allal		Welzel		Knowles		Jephcott			
Number of patients	No. patients	Score	No. patients	Score	No. patients	Mean score	No. patients	Score	No. healthy volunteers	Score
Functional scales										
Sexual functioning	40/41	13 (20)	52/52	22 (26)	41/42	0	44	24	45	29
Sexual enjoyment	8/41	(66)	18/52	43 (34)			19	46	20	70
Sexual dysfunction among men	6/6	66 (31)	14/15	68 (38)	11/11	83	11	85	9	19
Sexual dysfunction in women	8/35	18 (14)	10/37	55 (38)	7/31	83	16	51	15	21

with volunteers. In Sunesen's study, half of the patients did not answer questions evaluating sexual function and the majority of those stated complete absence of sexual desire and activity as a reason. In Jephcott et al., only 54% of anal cancer survivors answered compared with 80% of healthy volunteers [35] and similar response frequencies have also been reported by Knowles, Welzel and Allal [11, 34, 36].

Compared with healthy volunteers, anal cancer survivors scored worse for sexual problems and men scored worse than women (see Table 5). In Joseph et al., sexual function was significantly decreased for both women and men during treatment, but returned to baseline values after treatment [9].

Bentzen found a clinically significant difference in sexual interest between anal cancer survivors and volunteers for both genders, supported by Provencher and Sunesen [10, 16, 37]. The latter also found that women not interested in sexual activity rated their sexual desire to be "severely decreased" or "non-existing".

Erectile dysfunction in men and dyspareunia in women was found to be common after anal cancer treatment. Bentzen, Sunesen and Fakhrian all report an incidence of erectile dysfunction between 60 and 71% [10, 16, 40]. Among healthy volunteers, this was 20% [16]. Up to 60% of the female patients experienced some degree of dyspareunia [10, 40] and Joseph et al. found dyspareunia to be the only symptom that did not return to baseline 1 year after treatment [9]. Bentzen et al. found that the biggest difference in QoL was found among female patients experiencing grade 3 dyspareunia compared with those free of dyspareunia, which indicates that dyspareunia is a symptom of great importance [16]. This is corroborated by Sunesen et al. [10].

Discussion

Patients treated for anal cancer have a long-term reduced quality of life compared with healthy individuals, which is accompanied by and in some part due to bowel, urinary and sexual dysfunction. Compared with pre-treatment QoL, the deterioration in QoL seen immediately after treatment improved substantially within the first year.

The decrease in global QoL seen in anal cancer survivors compared with Swedish reference material [38] and healthy volunteers [16, 35] seems to be multifactorial. Consistently throughout the studies, bowel dysfunctions such as faecal incontinence, faecal frequency and faecal urgency seem to have a large impact on quality of life [10, 11, 36, 40]. In the case of bowel dysfunction, a stoma might alleviate some of these symptoms. In one of the included studies, it was shown that patients who underwent an abdominoperineal resection, APR, experienced an increase in general health score and decrease of rectal pain after surgery. Colostomy-free survival is often used as a measure of clinical success. However, for some patients, a stoma might be a relief. In fact, in patients with rectal cancer, it is not certain that a stoma will reduce quality of life [44]. We suggest that perhaps more patients treated for anal cancer would benefit from meeting with a surgeon to evaluate the possible benefit of having a stoma.

Urinary incontinence was identified in several studies as a factor influencing quality of life. The frequency of urinary incontinence was lower than among patients operated for rectal cancer [45–50] but in contrast to patients treated for rectal cancer, it remained for a longer period of time [48].

In order to more precisely describe the aetiology of the symptoms, it is important to also evaluate QoL and body functions before treatment. A pre-treatment questionnaire could then be used to identify patients at risk and provide useful information to assist patients early in the post-treatment period to improve quality of life.

Patients treated for anal cancer have an altered sexual life. It is evident from this review that this issue needs to be addressed. The low response rate, however, makes interpretation difficult. In the future, more research should be focused on this area to improve the quality of data. Male sexual function seems to be similar to patients treated for rectal or prostate cancer [48, 51] and it is important that patients are referred

to urologists after treatment to try different treatment options. In women, dyspareunia was reported as causing distress and affecting quality of life. This can sometimes be alleviated with support from gynaecologists, but as with sexual problems in men, the issue must be addressed with the patients after treatment cessation.

Risk of bias

The quality of the included papers was assessed using the minimal checklist and the overall quality is high. However, some particular risk of bias is worth mentioning. Anal cancer is a rare disease and the retrospective studies included have inclusion periods well beyond 10 years. The heterogeneity suggests that patients have received different therapies within and across studies. There is also a difference between the trials regarding length of follow-up time, and time from treatment to first evaluation. The low response rates cause a serious risk of selection bias. Few patients in general and women in particular answered questions regarding sexual life rendering this important research field difficult to assess.

The external validity of the studies is compromised by the use of single-centred studies. Only two national cohorts were used. Reports from single-centres may be misleading on a national or international level since these centres may share a special interest in these issues and treat patients accordingly.

Only one study included a questionnaire specifically intended for patients with anal cancer. It is possible that the questionnaires used are insufficient to fully explore the functional results of anal cancer treatment and its impact on quality of life. A validated questionnaire based on in-depth interviews with patients with anal cancer has recently been published [13] and it will be interesting to evaluate whether this will facilitate proper follow-up and identification of functional problems. It is interesting to note that the base line values in several domains of QLQ C-30 are much lower than in a rectal cancer cohort prior to treatment [48]. It is difficult to interpret this, but it may be that the patients with anal cancer present with much more symptoms than patients with rectal cancer.

In summary, it is apparent that patients with anal cancer have several functional problems affecting general QoL. Interventions to address these issues may in the end improve the long-term quality of life in this patient group.

Author contributions Anton Sterner and Eva Angenete designed the study; Anton Sterner, Hanna Nilsson and Eva Angenete collected data; Anton Sterner, Hanna Nilsson and Eva Angenete analyzed the data; Anton Stener, Kristoffer Derwinger, Caroline Staff, Hanna Nilsson and Eva Angenete interpreted the results; Anton Sterner, Hanna Nilsson and Eva Angenete drafted the article; Anton Stener, Kristoffer Derwinger, Caroline Staff, Hanna Nilsson and Eva Angenete all critically revised the article and gave final approval for submission.

Funding Lion's Cancer Research Fund of Western Sweden, the Swedish Society of Medicine, The Swedish Research Council 2017-01103, The Swedish Cancer Society 2016/509, Sahlgrenska University Hospital. Agreement concerning research and education of doctors ALFGBG-493341 and ALFGBG-426501, The Healthcare Committee, Region Västra Götaland, VGRFOU 569701 and VGRFOU 644421.

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