Review

Measuring psychosocial functioning in the radiation oncology clinic: a systematic review †

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Abstract

Background: This paper aimed to systematically review the (1) prevalence, (2) risk factors, (3) interventions, and (4) measurement instruments associated with psychosocial function decline in radiation therapy (RT) patients.

Methods: A MEDLINE systematic literature review was performed to identify studies monitoring psychosocial function among RT patients as a primary endpoint.

Results: Fifty-seven and 22 risk factors for RT-related psychosocial function decline were identified and refuted, respectively, in 93 eligible studies representing 12,808 patients. Median prevalences of psychosocial function decline prior to, during, and following RT were 20%, 36%, and 25%. Prior to RT, anxiety was more prevalent than depression (20% vs 15%), but dropped following completion of RT, whereas median depression levels remained elevated (17% vs. 27%). Of the 79 identified risk factors, 17 were reported as predictive of psychosocial decline by two or more more studies, and five had robust support: (1) physical symptoms, (2) time point during RT, (3) chemotherapy reception, (4) female gender, and (5) younger age. Three interventions were consensually reported to improve psychosocial function: psychotherapy, nursing consultation/patient education, and self-management training. Eighty-six different assessment tools were used to monitor RT-related psychosocial function decline with the Hospital Anxiety and Depression Scale (25.8%) and the psychiatric interview (22.6%) being the most utilized. The distress thermometer has been used in 5 studies (5.4%) to date.

Conclusion: Psychosocial function declines in approximately one-third of RT patients. Anxiety can dissipate after initiation of RT, whereas depression can persist throughout and after RT. Severe

physical symptoms and time-related factors most robustly predict psychosocial function decline, which

can be improved by psychotherapy and interventions aimed to improve patient education.

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Introduction

Recent guidelines from the Institute of Medicine recommend that providers of cancer care 'ensure the provision of appropriate psychosocial health services' for all oncology patients [1]. Implementation of this recommendation is challenged by the need to prove the value of addressing psychosocial aspects of cancer care, provide well-designed trials establishing evidence of the effects of psychosocial support, and address the cost of supportive care to the healthcare system [2].

Little literature addressing psycho-oncologic care in radiation oncology is available. Efforts to ensure the psychosocial health of radiation oncology patients have resulted in numerous parallel attempts to screen for depression or anxiety with a variety of instruments at numerous institutions. These uncoordinated efforts have amassed inconsistent data, leaving many unanswered questions regarding psychosocial function maintenance in radiation oncology. Thus, providers desiring to implement supportive psychosocial care in radiation oncology centers currently have little evidence to expound on the National Comprehensive Cancer Network (NCCN) Distress Management Guidelines.

The purpose of this study was to perform a systematic literature review of studies monitoring psychosocial function during radiation therapy (RT) and to report (1) prevalence estimates of psychosocial function decline, (2) risk factors (both reported and refuted) of psychosocial function decline, (3) interventions improving psychosocial function, and (4) evaluation of measurement instruments.

Methods and materials

A MEDLINE literature review was performed (last accessed 1/14/2014) according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement to identify reports of psychosocial function among RT patients. Articles were individually scrutinized and then categorized

by whether psychosocial function measurement was the primary endpoint of the study or not. Primary study measures included (1) reported prevalence of psychosocial function decline either before, during, or after RT; (2) risk factors associated with psychosocial function decline; (3) interventions improving psychosocial function; and (4) the instrument(s) used to measure psychosocial function. Lastly, studies were grouped by cancer type, if reported, including a general category for papers studying patients with a variety of tumor types.

Study results were combined by tabulating (1) median and interquartile ranges of reported prevalences and (2) both risk factors for psychosocial decline and interventions reported to improve psychosocial function. Preliminary consensus was defined as two or more studies reporting similar risk factors or intervention outcomes. No other cumulative statistical analyses were performed given the variety of risk factors and interventions reported. Lack of available hazard and odds ratios limited cumulative data analysis and forest plotting. Studies reporting the prevalence of and temporal associations with psychosocial function decline were scrutinized for bias within the discussion section. Individual assessment of bias for each study was not comprehensively performed. No financial support was received for the completion of this systemic review. No online review registration was performed prior to systematic review. Data were extracted and tabulated by a single reviewer. No efforts to contact individual authors for confirmation of data, duplicate extraction, or piloted forms were performed.

'Radiation', 'radiotherapy', 'distress', 'psychological', 'psychosocial', 'coping', 'quality of life', 'depression', 'anxiety', and 'emotion' were the initial search terms. Medical Subject Headings term search was also performed. References and citations were searched for additional pertinent articles. Acceptable surrogate terms for 'psychosocial function' included 'psychological', 'psychosocial', 'anxiety', 'stress', 'distress', 'depression', and 'emotion'. Studies reporting RT effects on these terms were considered to be monitoring psychosocial function as a primary endpoint and mainly consisted of studies reporting anxiety, depression, and distress. The broader terms 'quality of life' and 'fatigue', however, were not considered to be sufficiently-specific surrogates. Studies reporting RT effects on these latter terms were reviewed further to identify any inclusion of monitoring of psychosocial function. If found, such studies were included in our initial analyses but were labeled as studies monitoring psychosocial function as a nonprimary endpoint and were eventually excluded from the final analysis. Studies monitoring non-RT-related psychosocial function as a primary endpoint in general or tumor site-specific oncology patient populations (and not specifically in RT patients) were also not included. Many of these studies included patients who received RT as part of their treatment, but were evaluating the psychosocial impact of multi-modality treatment and not RT specifically. If evaluation of the psychosocial impact

of radiation was not among the primary endpoints, they were also excluded from the final analysis.

Results

A total of 93 studies that satisfied selection criteria were identified (Appendices A–F and Figure 1) between 1969 (oldest eligible article) and January 2014. Patient psychosocial function declined prior to, during, and following RT at median prevalences of 20%, 36%, and 25%, respectively (Table 1). Prior to RT, anxiety was more prevalent than depression (20% vs. 15%) and both doubled during RT (49% vs. 33%). Anxiety dropped below initial levels after RT completion, whereas median depression levels remained elevated (17% vs. 27%). Isolated distress was reported in substantially fewer studies (N=3) but increased during RT.

Among 79 potential risk factors identified, 57 predicted psychosocial function decline, and 22 were refuted as being predictive (Table 2). Seventeen risk factors were reported with preliminary consensus: (1) severe physical side effects, (2) pre-RT anxiety, (3) history of depression, (4) palliative treatment intent, (5) pain, (6) pre-RT or early RT period, (7) post-RT period, (8) older age, (9) female gender, (10) increasing decline as RT progressed, (11) tumor stage, (12) awareness of diagnosis (all in general radiation oncology patients), (13) postmastectomy status, (14) chemotherapy reception, and (15) younger age in breast cancer patients, and (16) non-specific impaired function (cognitive/social/ emotional/physical), and (17) prior laryngectomy in head and neck cancer patients (Table 2). Of these, physical symptoms, time dependence, chemotherapy reception, female gender, and younger age were reported with the most robust consensus and are discussed further.

Eight and two interventions were reported to improve and have no effect on psychosocial function decline, respectively (Table 2). Three were reported to improve psychosocial function decline in two or more studies: patient education sessions (nurse or therapist administered), psychotherapy (individual and group), and self-management training.

Eighty-six different assessment tools were used to monitor RT-related psychosocial function (Table 3). Eight were used in five or more studies, with the Hospital Anxiety and Depression Scale (HADS) and the psychiatric interview being the most-often-utilized tools (26.8% and 22.6% of studies, respectively). The distress thermometer (DT) was used in 5 studies (5.4%).

Discussion

This systemic review (1) identifies the prevalence of any type of psychosocial function decline as approximately one-third of RT patients, (2) coalesces 17 consensually reported and five dominant risk factors for psychosocial function decline, (3) reports three consensually supported

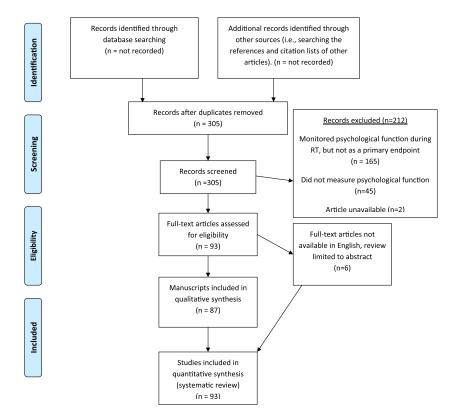


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram

interventions for improving psychosocial function during RT, and (4) delineates the HADS and psychiatric interview as the most commonly used instruments and the DT as the most recently advocated instrument of psychosocial function measurement during RT.

Prevalence

Psychosocial function is an inherently subjective entity of significant complexity. Historically, it has been objectified by classification systems identifying specific clusters of symptoms whose duration and degree define psychiatric diagnoses. Psychosocial function decline in the form of depression or anxiety can persist for months or years and is not necessarily related to the effects of a cancer diagnosis. In the late 1990s, the NCCN defined a novel term-'distress'-to better quantify acute cancer-related psychosocial impact. Distress was defined as 'a multifactorial, unpleasant, emotional experience of a psychological (cognitive, behavioral, emotional) social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness, and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis' [3]. Because distress is not necessarily related to anxiety or depression, it affords categorization of acute

needs that many patients have, which would otherwise not meet diagnosis criteria for historical psychiatric diagnoses. Division of psychosocial function into subcategories (of distress, anxiety, distress, etc.) aims to facilitate prompt and optimal treatment of both acute and chronic psychosocial function decline [3]. A recent multi-institutional clinical trial affirmed the importance and feasibility of addressing psychosocial function in radiation oncology on a national level within current cooperative groups [4].

We utilized the broad term of 'psychosocial function decline' to signify any of these psychosocial subcategories and systematically tallied the reported prevalence of each in RT patients. We found that about one-third of patients experienced psychosocial function decline during RT and discovered a temporal relationship between rates of anxiety, depression, and distress over the course of treatment (Figure 2).

The proportion of patients with anxiety prior to RT ranged broadly (14–38%) with a median of 20%, whereas a median prevalence of 49% (range 19–54%) was reported during RT that decreased to 17% (range 13–19%) following RT, indicating that anxiety increases and then decreases throughout RT. This higher prevalence rate of anxiety during RT compared with before RT requires careful interpretation because the majority of studies included in this review were not comparing pre-RT, intra-RT, and post-RT values longitudinally but rather assessed patients at a single (or perhaps at two) time point(s) during RT and often in the follow-up period (Appendices A–F).

Cancer patient population	Author	Year	Pre-RT (%)	During RT ^a (%)	Post-RT	Qualifying details (depression, anxiety, distress, or other)
General radiation oncology	Irwin et al. [48]	1987		33		Depression, RT onset to 2 months' follow-up
(multiple tumor types studied)	Chaturvedi et al. [69]	1996		4664		Rate of anxiety
	I			42–50		Rate of depression
	Maher et <i>al.</i> [9]	1996	19		13	Anxiety alone, 6% drop
			40		32	Anxiety and depression (8% drop); severe depression
						and anxiety dropped from 16% to 15%, and patients with
						no anxiety or depression increased from 25% to 40%,
						pre-RT and post-RT, respectively.
	Walker et al. [23]	1996		80	I	Cancer-related intrusive thoughts ^b
	Jenkins et al. [74]	1998		33		Clinically significant depressive symptoms
	Leopold et al. [27]	1998	ĺ	48		Diagnosis of depressive or anxiety disorder
	Chiu et al. [97]	2001	I	5.9		Percent referred to consult-liaison psychiatry; of these,
						53% and 47% had depression-related and
						anxiety-related disorders, respectively.
	Fritszche et al. [50]	2004		51		Diagnosed mental disorders; 28% of these
						were adjustment disorder.
	Steigelis et al. [98]	2004	10-20	21–54	8-48	Anxiety pre-RT, depression during and post-RT,
						meta-analysis results
	Hahn e <i>t al.</i> [99]	2004		15		Frequency of depression
	Frick et al. [100]	2007		9.5		Clinically relevant anxiety or depression
	Maurer et al. [11]	2012	33, 41			41% true or marginal anxiety and 33% true or
						marginal depression prior to RT
	Guo et <i>al.</i> [12]	2013	48, 52			Baseline anxiety (52%) and depression (48%)
	Adams et al. [26]	2014			14-19	Possible (12%) or probable (7.8%) anxiety,
						possible (9.0%) or probable (5.4%) depression,
						post RT
	Median (IQR)	I	36.5 (19—46)	33 (15–50)	22.5 (9–44)	Psychosocial function decline (approximate $^{\circ}$)
Breast	Hughson et al. [85]	1987		33		Postmastectomy RT anxiety or depression
	Maraste <i>et al.</i> [56]	1992	4	I	ļ	Morbid anxiety
			- I.5			Severe depression
	Rahn et <i>a</i> l. [47]	1998		40		Anxiety about RT
				51		Anxiety about RT side effects
	Mose et <i>al.</i> [10]	1999	40			Anxiety about undergoing RT
				19		Anxious during most of RT duration
	Mose et al. [6]	2001	48			Initially afraid of RT
					36	No reduction in anxiety at end of RT
				53		Overall feeling of distress
	Faller et al. [101]	2003	22			Anxiety score >10 on HADS
	I		ъ			Depression score >10 on HADS
	I		37	I		Distress on Hornheider Questionnaire
	Luutonen et al. [54]	2011	ļ	40		Depressive symptoms or distress
	Torres et al. [16]	2013	6	16	15	Depression

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	Median (IQR)	Ι	I8.0 (6–39)	39.8 (19–51)	25.5 (15–36)	Psychosocial function decline (approximate)
Prostate	Jongkamp et <i>al.</i> [13]	2012		01		Depression during LDR brachytherapy
	Lofti-Jam et al. [88]	2013	19.7			Distress on the DT prior to EBRT
Head and neck	Bjordal <i>et al.</i> [30]	1995		30		Prevalence of psychological distress
	Hammerlid et al. [95]	1997	I	19-40	Ι	Psychiatric distress
	Hammerlid et al. [93]	1998		33		Either clinical depression or anxiety
	De Graeff <i>et al.</i> [41]	1999	27		27	Depressive symptomatology
	Rose et al. [5]	2001	13.4		12.2	Anxiety, at 1-month follow-up: 20.6%
			10.3		41.3	Depression, up 30%, at 1-month follow-up : 29.9%
	Sehlen et al.	2003	19/15/0 (34)		33/9/5.3 (42)	Mild/marked/severe depression: 6 weeks:
						21.5/16.9/0%, 6 months: 22.2/17.3/0% (total)
	Kelly et al. [8]	2007	13.9		23	Moderate-severe depression, mid-RT: 19%
			20		18	Moderate-severe anxiety, mid-RT: 15%
	Lue et <i>al.</i> [24]	2008		51.2	I	Anxiety, post-RT endocrinopathy patients
				44.2		Depression, post-RT endocrinopathy patients
	Chen et al. [90]	2009	58			Pre-RT depression on HADS
			45			Pre-RT depression on BDI
			7		I	Pre-RT anxiety
	Neilson <i>et al.</i> [7]	2010	15		31	Mild to severe depression
			30		17	Mild to severe anxiety
	Paula <i>et al.</i> [91]	2012	19.5	26.8	31.7	Either depression or dysphoria
	Chen et al. [94]	2013			13-17	Depression at 1, 3, 5 years post-RT: 17%, 15%, and 13%
	Neilson et al. [25]	2013	15		29	Depression, fell to 8% at 18 months
	Median (IQR)		19 (14–32)	33 (19–49)	25 (17–32)	Psychosocial function decline (approximate ^C)
Cumulative median prevalence (IQR)			15 (9–42)	33 (16–46)	27 (15–36)	Studies reporting isolated depression $(N = 11)$
			20 (14–38)	49 (19–54)	17 (13–19)	Studies reporting isolated anxiety $(N = 1.1)$
			28 (19–37)	35 (22–50)	No studies	Studies reporting isolated distress ($N = 3$)
			20 (14–40)	36 (19–49)	25 (15–35)	Any psychosocial functional decline
See Table 3 for abbreviations.						

There were no reported prevalence estimates from central nervous system, or gynecologic cancer-only studies. *Reported as prevalence rate without specifying temporal relationship to RT start or completion.

^bNontraditional endpoint of intrusive thoughts was not included in average calculations. ^cMedian values were calculated using reported prevalence; for those reported as ranges of data, both the upper and lower range were included and considered as two separate data points for median calculation. See Appendices A–F for individual study details.

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Table 2. Risk factors and interventions for psychosocial function decline during radiation therapy by tumor location

Table 2. Risk factors and interventions for psychosocial functions	nction decline during radiation therapy by	tumor location
Confirmed risk factors for psychosocial function decline	Refuted risk factors	Interventions
General radiation oncology (studies of patients of various tumor types; see I. Side effect symptom severity [18–20,23,26]	 Appendix A for details) 1. Time dependence: increasing as RT progresses [11,17,78,79]; post-RT period [48] 	1. Psychotherapy , individual [12,51] or group [76]
 Time dependence: pre-RT or early RT period [17,68,69]; high pre-RT anxiety [49,68,70,71]: increasing as RT progresses [49,72] (also refuted); post-RT period [72,73] (also refuted) 	2. Gender [50]	2. Nursing-led [37] or other method of patient education [38,80]
3. Patient history of depression [27,74]	3. Country or socioeconomic status [69]	3. Self-management training [15,31] (one study qualified this as being efficacious only in patients with early-RT anxiety [31])
 4. Palliative treatment intent [9,75] 5. Pain [17,27] 6. Age: over 60 [49], over 65 [17] (also contradicted) 7. Gender: female [9,17,12,26,48,49], male [51] (also refuted) 8. Tumor stage [49] (also refuted) 9. Awareness of diagnosis [51,58,76] (also refuted) 10. Erroneous misconceptions about RT [72] 11. 3-year survivor status [77] 12. Less hope (assessed by patient questionnaire) [18] 13. Breast cancer patient [49] 14. Alcohol or nicotine addiction [49] 15. Metabolic disorder [49] 16. Marital status (lower risk if married) [49] 	4. Distress screening itself [53]	 4. Relaxation training [81] 5. Musical Intervention [32]
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Breast cancer (see Appendix B for details) I. Time dependence: pre-RT period for anxiety [10,46,47] and overall distress, if age < 45 [55], increasing as RT progressed for depression [46] and for for string listermatics [202]	I. RT reception (in postmastectomy patients) [53,85]	1. Nursing-led [59] or therapist-led [34] patient education
for functional interruption [82] 2. Chemotherapy reception in postmastectomy RT patients [16,52–83]	2. Time dependence: increasing as RT progressed for anxiety [10,46,47]	2. Cognitive and behavioral therapy and hypnosis [57]
 Postmastectomy status [56,84] Younger age [54] (<age 45="" 50–59="" [55],="" [56],<br="" ages="">and age <58 [8]) (also contradicted)</age> 	 Treatment awareness [85] Breast-conserving lumpectomy and RT [86] 	3. Exercise [33] 4. Improved communication [10]
 Pre-RT anxiety, not responsive to distraction techniques and affected by environmental factors (i.e., waiting rooms) [6] 		5. Communication support groups (refuted) [87]
 b) environmental factors (i.e., waiting rooms) [o] c. Tumor stage [84] (also refuted) 7. Menopausal symptoms and postsurgical problems [79] 8. Pessimism [84] 9. Latina ethnicity [84] 10. Educational status [16] 11. Perceived stress level [16] 12. NF-kappa-B binding [16] 		6. Stress reduction [35]
Prostate cancer (see Appendix C for details) I. Pre-RT anxiety [39] 2. RT as initial treatment (as opposed to prostatectomy) [66] 3. Younger age , English as a second language, and unmet physical needs [88]	I. RP vs. RT (no difference seen) [89] 2. Hormonal therapy [66] 3. Brachytherapy [13]	I. Patient education audio recordings (refuted) [39]
Head and neck cancers (see Appendix D for details) I. Time dependence: increasing depression and/or anxiety as RT progresses [5,8,14,21,75,90–92]; weeks 3–4 of RT [21,28,29]; during the post-RT period [5,7,14,21,28,29,90] with improvement at 4 [21], 8 [29], and 12 weeks [28]; pre-RT period [93]	1. During the post-RT period (decline improved post-RT in these two studies) [41,42]	I. Psychotherapy or counseling [36]
 Worsening physical side effects [21,25,28]; eating-related side effect symptoms [14,24]; speech problems, sexuality problems, and teeth problems [24] 	2. Tumor stage [14]	

(Continues)

Table 2. Continued

Confirmed risk factors for psychosocial function decline	Refuted risk factors	Interventions
3. Impaired function: cognitive/social [24,30] and	3. Fractionation schedule [30]	
emotional/physical function [24]		
4. Pre-RT depression [7,90]	4. Brachytherapy [95]	
5. Pain [21,30]	5.Higher education status [14]	
6. Concurrent chemotherapy [7,21]	6. Marital status [14]	
7. Laryngectomy, tracheostomy tube, or stoma [93,94]	7. Tumor grade [14]	
8. Pretreatment anxiety [7]	8. Substance abuse [14]	
9. Age < 55 [90] (also contradicted)		
 Gender: male [7] and female [21] (also refuted) 		
11. Working at time of treatment enrollment [90]		
12. Large tumor size [93]		
13. Single marital status [90]		
14. Living alone [90]		
15. Gastrostomy tube dependence [94]		
16. Continued smoking [94]		
Central nervous system cancers (see Appendix E for details)		
I. Low-grade gliomas when compared with	I. No difference seen between RT and	None reported
hematologic malignancies [96]	surgery arms [96]	
Gynecological cancers (see Appendix F for details)		
I. Time dependence: pretreatment anxiety [83]; distress increased	I. Post-RT period [45]	None reported
(1) cumulatively with brachytherapy sessions [43,83],		·
(2) at the third week of EBRT treatment [22], and		
(3) at post-RT period until 3 months [44] (also refuted)		
2. Severe physical side effects [22]		

Risk factors in bold were reported with preliminary consensus (>1 study reporting similar risk factors) (n=17).

Studies reporting anxiety levels throughout treatment found that anxiety was more prevalent before RT than during RT, decreasing after RT starts and suggesting that anxiety may be related to unfamiliarity to daily treatments that alleviates soon after starting treatment [5–8]. Maher *et al.* [9] for example, evaluated anxiety and depression longitudinally in 269 patients and reported that patients with anxiety alone decreased by 6%, between the start and completion of RT. Mose *et al.* [10] evaluated 48 breast cancer patients and reported that a majority (77%) of those reporting anxiety during RT associated it only with treatment initiation, whereas only 19% were anxious most of the time. Maurer *et al.* [11] and Guo *et al.* [12] also confirmed higher rates of anxiety compared with depression at RT onset.

Reported prevalence of depression was also markedly variably with a medium of 33% (Table 1), which was mostly consistent across tumor types with the exception of prostate cancer patients, who had a substantially lower rate (10%) if undergoing brachytherapy implantation [13]. Depressive symptoms were consistently reported to increase from baseline [8,14] after RT initiation and stay elevated into the follow-up period [15,16].

Distress was much less commonly studied because of its relative recent introduction within management guidelines but nonetheless was similarly estimated to affect about one-third of patients during RT (Table 1). Similar to anxiety, distress was not consistently reported as increasing during RT. Carter *et al.*, for example, monitored over one thousand patients with the DT and found distress to be higher before RT [17].

Risk factors

The early prediction of psychosocial function decline associated with RT may facilitate early intervention, minimize delay, prevent treatment interruption, improve quality of life, and indirectly influence cancer-specific outcomes. Seventeen risk factors predicting psychosocial function decline during RT were reported with a preliminary consensus of at least two separate studies: (1) severe physical side effects, (2) pre-RT anxiety, (3) history of depression, (4) palliative treatment intent, (5) pain, (6) the pre-RT or early RT period, (7) the post-RT period, (8) age, (9) female gender, (10) time dependence with increasing decline as RT progressed, (11) tumor stage, (12) awareness of diagnosis (all in general radiation oncology patients), (13) postmastectomy status, (14) chemotherapy reception, (15) younger age in breast cancer patients, (16) impaired function (cognitive/social/ emotional/physical), and (17) prior laryngectomy in head and neck cancer patients. Of these, we discuss five dominant risk factors, which were reported with a more robust consensus: (1) severe physical symptoms or pain, (2) time dependence, (3) female gender, (4) chemotherapy reception, and (5) younger age.

Instrument	Barriers and practical limitations to implementation	Number of studies using instrument (%) (n = 93)
HADS [104]	14 items (seven anxiety and seven depression): ranked from 0 to 3; available in >80 languages; untimed; £62.50 for 100 surveys	24 (26)
Interview (SCID)	Gold standard for assessment of psychiatric comorbidities; time intensive; not a rapid screening tool; high cost	21 (23)
EORTC QLQ-C30 [107]	30 items: ranked from 1 to 4; available in 81 languages and site-specific versions; 10- to 15-min administration time; free of charge (noncommercial use)	17 (18)
POMS [105]	65 items, ranked from 1 to 5; 5- to 10-min administration time; 37-item short-form available; \$50.00 for 25 surveys	12 (13)
BDI [102]	21 items: ranked from 0 to 3; available in Spanish; 5-min administration time; \$52.00 for 25 surveys	10 (11)
FACT [108]	27-item general form, ranked 0 to 4; available in dozens of languages; site-specific supplements available; free of charge after registration	7 (7.5)
STAI [106]	40 items (20 state and 20 trait): ranked from 1 to 4; available in 28 languages; 10-min administration time; \$100.00 for 50 surveys	8 (8.6)
DT [103]	One item: ranked from 0 to 10; problem list available to identify distress areas; ultra-rapid; NCCN recommended; free of charge	5 (5.4)

Table 3. Instruments used in studies monitoring psychosocial function decline as a primary endpoint

Psychosocial function-monitoring instruments used in at least five different studies are listed

Acronyms: BCT, breast-conserving therapy; BDI, Beck Depression Index; CNS, central nervous system; CTCAE, Common Terminology Criteria for Adverse Events; DT, distress thermometer; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire-C30; FACT, Functional Assessment of Cancer Treatment; HADS, Hospital Anxiety and Depression Scale; POMS, Profile of Mood States; QoL, quality of life; RP, radical prostatectomy; RT, radiation therapy; SCID, Structured Clinical Interview for DSM-IV; STAI, State–Trait Anxiety Index.

Other questionnaires used to measure psychosocial function decline (times used, if >1) (total number of instruments: 86): AES, Adaptation to Survivorship Experience; BAI, Beck Anxiety Index; BHS, Beck Hopelessness Scale; CBI-L, Cancer Behavior Inventory-Long Form; CARES-sf, Cancer Rehabilitation Evaluation System; CaTS, Cancer Treatment Scale; CES-D, Center for Epidemiologic Studies Depression Scale (4); Clinician Administered PTSD Scale; CAHS, Cognitive Appraisal of Health Scale; CARTS, Concerns about Radiotherapy Scale; CRI, Coping Resources Inventory; CECS, Courtauld Emotional Control Scale; Diener and Emmons mood report; EDLQ, Everyday Life Questionnaire; EPIC-26, Expanded Prostate Cancer Index Composite; QLI, Ferrans Quality-of-Life Index-Cancer Version; FQCI, Freiburg Questionnaire of Coping with Illness; FLIC, Functional Living Index-Cancer; GHQ-20 and GHQ-12, General Health Questionnaire (4); GES, General Perceived Self-efficacy; Gottschalk-Gleser Anxiety Scale (2); HAM-D, Hamilton Rating Scale For Depression; Health Status Questionnaire; QSC, Herschbach's Questionnaire: Stress in Cancer Patients; Hopkins Symptom Checklist-25 (2); Hornheider Questionnaire; IES scale, Impact of Event Scale (2); IDS-SR, Inventory of Depressive Symptomatology-Self-report (2); KPS, Karnofsky Performance Scale (5); KORTS, Knowledge of Radiotherapy Scale; KHOS, Krantz Health Opinion Survey; Leeds Self-assessment of Depression and Anxiety Scales (3); LOT, Life Orientation Test (3); LASA, Linear Analogue Scale Assessment; Maguire Observer Rating Scales of Depression and Anxiety (2); MDASI, MD Anderson Symptom Inventory; SF-36 or RAND-36, Medical Outcomes Study 36-Item Short Form by RAND (2); MSAS-SF, Memorial Symptom Assessment Scale-Short Form; MOS-SSS, Medical Outcomes Social Support Survey; Mental Component Summary Scale; MHI, Mental Health Inventory; MMACS, Mini-mental Adjustment to Cancer Scale; MMPI, Minnesota Multiphasic Personality Inventory; MUIS-C, Mishel Uncertainty in Illness Scale-Community Form (2); MFI, Multidimensional Fatigue Inventory; NEO-FFI, NEO-Five Factor Inventory; Overall Anxiety Scale; PHQ-9, Patient Health Questionnaire-9; Pearlin and Schooler's Mastery Scale; PSS, Perceived Stress Scale; PPSQ, Pienschke Patient Satisfaction Questionnaire; PIPER, Piper Fatigue Scale-revised; PANAS, Positive and Negative Affect Scale; PTCI, Posttraumatic Cognitions Inventory; PRIME-MD, Primary Care Evaluation of Mental Disorders; PAIS-SR, Psychosocial Adjustment to Illness Scale-Self-Report version (3); FBB, Questionnaire for Treatment Motivation and Need; RIES, Revised Impact of Event Scale; RSES, Rosenberg Self-esteem Scale; SADS, Schedule for Affective Disorders (3); SEIQoI-DW, Schedule for the Evaluation of Individual Quality of Life-Direct Weighting; SOMS, Screening for Somatization; SIPP, Screening Inventory of Psychosocial Problems (2); SCL-90-R, Symptom Checklist-90-R; SCBS, Self-care Burden Scale; SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale; SOCS, Sense of Coherence Scale; SIP, Sickness Impact Profile (5); SEP, Side Effect Profile; SESX, Side Effect Severity Checklist; SSQSR, Social Support Questionnaire-Short Form-Revised; PSYCH-6, Somatic and Psychological Health Report; SIRO, Stress Index Radiation Oncology; SWBI, Subjective Well-being Inventory; SCNS-SF34R, Supportive Care Needs Survey Short-Form Revised; SAS, Symptom Assessing Scale; SC90-R, Symptom Checklist 90-Revised; SDS, Symptom Distress Scale (3); SP, Symptom Profile; ULSr, UCLA Loneliness Scale; University of Washington QoL instrument (2); UCL, Utrecht Coping List; VAS, Visual Analog Scale; and additional author-designed questionnaires (7).

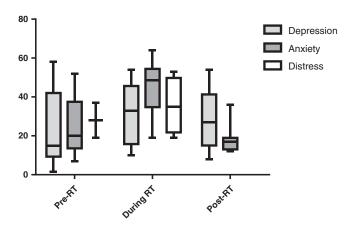


Figure 2. Radiation therapy mental health decline

Side effect symptom severity/pain

Severe physical symptoms and pain were reported as risk factors for psychosocial function decline in 12 and 4 studies, respectively, without being contradicted or refuted. Severe physical symptoms correlated to poor adjustment [18,19], negative mood [20], distress [17,21], negative emotions [22,23], disruption of function [22], anxiety [24,25], depression [14,26,27], and poor quality of life [26,28] in general oncology, head and neck, and gynecologic patients. Physical symptoms also coincided with increasing psychosocial function decline associated with head and neck treatment weeks 3 and 4, including eating, speech, sexual, and dental problems [14,21,24,28,29]. Similarly, pain was associated with psychosocial function decline consensually in four studies [17,21,27,30] without being refuted. In summary, physical side effects are a well-supported risk factor associated with psychosocial function decline.

Time dependence

A specific time point was reported as a risk factor 44 times in 38 studies and refuted 10 times in 10 studies. Specifically, 16 studies found that psychosocial function decline (mainly anxiety) was highest *prior* to treatment (seven general, five breast, one prostate, two head and neck, and one gynecologic, with no studies refuting), 17 studies identified that psychosocial function decline accelerated *during* the course of treatment (two general, two breast, 10 head and neck, three gynecologic, with seven studies refuting [four general and three breast]), and 10 studies identified accelerated decline *following* RT (two general, seven head and neck, and one gynecologic, with four studies refuting [one general, two head and neck, and one gynecologic]) (Table 2).

Among the 16 studies reporting pre-RT period association with psychosocial function decline, eight (four general, one breast, one prostate, one head and neck, and one gynecologic) specifically highlighted pre-RT anxiety. The lack of tumor site predominance suggests that pre-RT anxiety predicts psychosocial function decline independent of side effects or treatment duration, which can vary by tumor site. Interestingly, among those interventions reported to improve psychosocial function decline, 10 studies reported that addressing uncertainty or patient ignorance by a number of different interventions (Table 2 and Appendices A-F) in the pre-RT period alleviated associated anxiety [12,15,31–38]. Additionally, high pre-RT anxiety was reported as an independent predictor of negative mood [39], overall distress [6], and posttreatment anxiety [7,40].

Time dependence seemed most robustly predictive in the head and neck cancer population with 10 and 7 studies identifying acceleration of decline during RT and persisting through the follow-up period, respectively (Table 2). Interestingly, three studies specifically reported high distress near week 4 of treatment and simultaneously associated the decline with pain or severe treatment side effects [21,28,29]. Even the two studies refuting increasing psychosocial function decline in the post-RT period still reported high levels of depression both before and at the end of RT [41,42] and were similar to studies reporting elevated post-RT distress, in that they reported eventual improvement in decline over weeks to months after treatment [28,29].

Time dependence was also reported in patients receiving RT for gynecologic malignancies with heightened levels at week 3 and association with physical side effects, albeit in fewer studies [22,43–45] compared with patients irradiated for head and neck cancers. Three breast cancer studies [10,46,47] confirmed high pre-RT anxiety that improved throughout RT [10,46,47], and two studies reported increases in depression or functional interruption (but not anxiety) over time.

In summary, time dependence was the most robustly supported risk factor predicting psychosocial function decline, with anxiety dominating the pre-RT period and the highest correlation being observed in patients with head and neck cancer.

Female gender

Female gender was reported as risk factors in seven studies [9,12,17,21,26,48,49], mostly in general radiation oncology populations, whereas gender was refuted as a risk factor by one study [50], and the contradicting male gender was identified as a risk factor in two studies [9,52]. Most recently, in 178 general radiation oncology patients, Guo et al. [12] reported a 61% to 39% and 53% to 38% female to male prevalence of RT-related anxiety and depression, respectively. Adams et al. [26] also reported female gender to be predictive of psychosocial function decline (p=0.012) during pelvic RT, which showed that women experienced more bowel, urinary, and sexual dysfunctions, correlating to overall higher symptom score and depression (p < 0.001). Overall, female gender was a moderately supported risk factor for psychosocial function decline, with some refutation and contradiction requiring further investigation.

Chemotherapy

Chemotherapy reception was reported as a risk factor for depression or distress in five separate studies [7,16,21,52,53] either in patients with breast cancer receiving postmastectomy chemotherapy followed by RT or in patients with cancers of the head and neck undergoing concurrent chemotherapy and RT. In two older studies, Hughes et al. evaluated the psychosocial effect of chemotherapy and radiation versus radiation alone in patients with breast cancer treated with mastectomy on prospective trials. The first study [53] confirmed that depressive symptoms were more common in patients treated with chemotherapy (cyclophosphamide, methotrexate, and 5-fluorouracil) for up to 12 months, and the second study [52] confirmed the trend for persistent depression at 13 months following RT. More recently, Torres et al. [18] associated chemotherapy with inflammatory marker nuclear factor kappa B and with depression in breast cancer patients. In patients with cancer of the head and neck, Lewis et al. [21] reported that chemotherapy was associated with increased pain and distress 2 weeks into RT, and Nielson et al. [7] associated

chemotherapy reception with post-RT depression with high statistical significance. In summary, chemotherapy was a moderately supported risk factor for psychosocial function decline limited to patients with breast and head and neck cancers, requiring further investigation.

Younger age

Younger age was reported as risk factors in six separate studies (one general, four breast, and one head and neck) [8,54–56,88,90], but the contradicting factor of older age was identified as a risk factor in two studies [17,49] in a general radiation oncology population. One of these contradicting studies [49] measured isolated stress levels alone before, during, and 6 weeks after RT, concluding that patients 60 years of age or younger experienced a decline in stress over time and patients older than age 60 experienced increased stress. The other [17] was a large study of 1178 patients not solely comprised of RT patients, which reported age over 65 years as being associated with higher distress. The remaining studies confirmed younger age to be associated with increased pain [17], distress [6,17,54], poor psychosocial response, decreased quality of life, survivorship maladaptation [55], and anxiety [56]. Overall, younger age was only a moderately supported risk factor for psychosocial functional with some contradictory findings requiring further investigation.

Interventions

Our study identified numerous interventions used for distress relief (Table 2), but only three were reported by two or more studies: patient education sessions (nurse or therapist administered), psychotherapy (individual and group), and self-management training.

Psychotherapy was identified by five separate studies as successfully improving RT-associated psychosocial function decline [12,36,51,57,58]. Most recently, Guo et al., [12] reported results of a randomized controlled trial where psychotherapy improved anxiety and depression, and Schnur et al. [57] also prospectively randomized and reported improved positive affect and less negative affect with cognitive behavioral therapy. Nursing-led or therapist-led education sessions alleviated decline in two studies, one of which reported improvement in stress reaction only and not in overall quality of life [59]. The other, however, showed reduction in anxiety but not depression following face-to-face encounters providing sensory and procedural information and addressing emotional concerns [34]. Self-management training for stress reduction successfully lowered anxiety in a study by Krischer et al., but only in patients reporting high levels of pre-RT anxiety [31]. Self-management for patient education also successfully alleviated

uncertainty about treatment prior to RT start and decreased post-RT distress [15].

Instruments

The gold standard psychiatric interview is optimal to assess the multifaceted components of human psychosocial response but is reportedly too time-consuming for practically widespread implementation in busy clinics [60-62]. Although some of the studies we reviewed utilized the psychiatric interview for assessment of psychosocial function, many utilized shorter instruments. Efforts to identify quick reliable surrogates to the psychiatric interview have resulted in lengthy questionnaires aimed at identifying single aspects of the psyche and in rapid questionnaires aimed at identifying a zoomed-out and broadened view of a patient's global psychosocial function [63,64]. Examples of the former include the Beck Depression Index (BDI) and HADS, which use dozens of questions to arrive at a binary or tiered assessment (Table 3). Exemplifying the latter, the DT measures the distress of the entire individual with a single question using a 1-10 ordinal scale [65]. Although the specific psychiatric metrics assessed by traditional or rapid questionnaires are not equivalent, both demonstrate the trend to more practical assessments, which despite validation, can still compromise comprehensiveness.

Surrogate replacement of the psychiatric interview narrows the psychosocial experience of cancer treatment into a binary identification of depressed versus not depressed, anxious versus not anxious, and most recently, distressed versus not distressed. This narrowing necessitates a redefinition of the objectives for each type of evaluation into screening, assessment, and diagnosis. Screening for distress with the DT, for example, is inherently different from in-depth assessment with the BDI, which likewise precedes diagnosis by interview. Distress screening aims to herd a wider array of nonpsychological concerns including practical concerns of transportation, finances, and so on, which would not be included in psychological assessment. Assessment of patient depression may follow distress screening, but is aimed at identifying a single psychiatric diagnosis, which is confirmed by a diagnostic interview. Delineation of the different purposes of each type of psychosocial assessment is needed to prevent oversimplification of mental health assessment methodology.

Our review of the literature attempted to encompass all measurements of psychosocial deterioration in radiation oncology patients, using an umbrella term of 'psychosocial function decline'. We identified 86 different assessment instruments used to monitor RT-related psychosocial function decline, mostly consisting of lengthy questionnaires (Table 3). Noteworthy are the large variety

of available instruments and the lack of uniformity of use. No single tool emerged dominant. The vast majority of studies in radiation oncology utilized psychiatric interviews or lengthier questionnaires such as the HADS, BDI, or the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30, as opposed to more rapid instruments such as the DT. This may simply be a function of time, as the DT has only been available for clinical use recently. The NCCN-recommended DT has been used in 5 published studies, all published within the last 2 years except one [15]. These use trends demonstrate a recent increase in the use of global distress screening and the historical predominance of assessment of psychiatric diagnoses. The convergent use of a single measurement instrument is likely reflective of the recent emphasis on distress screening associated with the publication of the NCCN Distress Management Guidelines. Radiation oncologists should first identify whether they desire to assess for specific psychiatric diagnoses or more global cancer-related distress prior to the selection of an instrument for use.

Most studies included in this review had sample sizes less than 100 patients, with a median of 79.5 patients and a range of 16–1778. Larger studies may have reported more reproducible and externally valid findings (the sample size of large studies [200 or more participants] have been bolded in Appendices A-F); those with the five largest sample size are further discussed. The largest study by Carter et al. [17] in 2011 was a prospective cohort study of electronic administration of the DT in all patients at an Australian cancer center. They confirmed declining rates of distress of 18%, 11%, and 11% over three nonspecific sequential time points during RT treatment or follow-up in general radiation oncology and also medical and surgical oncology patients. Distress prevalence was less in RT than in medical oncology patients, and related risk factors of female gender, age over 65 (as mentioned earlier), and pain were predictive of distress. Hervout et al. [66] reported higher levels of depression and anxiety in 580 prostate cancer patients compared with 281 patients treated with radical prostatectomy, measured once during the follow-up period, and refuted the reception of androgen deprivation therapy as a contributing risk factor. Rahn et al. [47] studied 523 breast cancer patients undergoing RT as a part of breast conservation and estimated 40% anxiety prior to RT, which declined over time. A Dutch cluster randomized trial by Braeken et al. [67] with 568 general RT patients identified 21% anxiety, 7% depression, and 39% distress at 3 months following RT completion and concluded that distress screening alone does not alleviate psychosocial function decline. A recently reported (abstract-only)

multi-institutional trial performed by the RT Oncology Group (RTOG 0841) of 455 general RT patients assessed at a single point prior to RT reported a 16.5% prevalence rate of depressive symptoms using the DT and other rapid instruments [4].

Our study has numerous limitations. There was significant variability of methodology between reviewed studies, introducing significant selection and reporting bias of risk factors. Many studies did not consistently report psychological function decline at the same intervals or with similar instruments, and there was a relative lack of studies including longitudinal analyses of psychosocial function at numerous time points over the course of RT (Table 1). Significant lead-time bias, selection bias, and reporting bias may confound findings because of the time point of screening, lack of baseline functional screening, nonrandom selection of patients to receive interventions, and nonreporting of all subcategories of psychosocial function in all studies. Because numerous (as opposed to a single) risk factors were reported across studies, meta-analytic analysis of reported hazard or odds ratios was not feasible. Comparatively few studies (n = 5) utilized the DT as a measurement instrument, limiting the external applicability of our study because current NCCN guidelines advocate for its sole use as an initial screening instrument of psychosocial function in the oncologic setting. The ultimate interpretation of this review is limited to hypothesis generation.

Conclusion

Psychosocial function declines in about one-third of irradiated patients, typically in the form of anxiety, depression, or distress. Anxiety levels are high prior to RT and improve with time, whereas depression increases over the course of RT and persists into the follow-up period. Severe physical symptoms or pain, time dependence (especially in patients with head and neck cancer), female gender, chemotherapy reception, and younger age predict psychosocial function decline during RT. Psychotherapy, nursing intervention/patient education, and selfmanagement improve psychosocial function. There is marked variability in the choice of measurement instruments for psychosocial function, with the HADS and psychiatric interview being the most commonly utilized and the DT the most recent. Prospective studies are needed to confirm at-risk populations, ideal screening methodology, and interventional benefit, to further refine guidelines and resource allocation.

Conflict of interest

None to disclose for both authors.

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