Genetic testing for Lynch syndrome in the first year of colorectal cancer: a review of the psychological impact

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Abstract An increasing number of patients with colorectal cancer (CRC) receive genetic counselling within 1 year after diagnosis. Little is known whether specific subgroups are more vulnerable for genetic testing related distress. A literature review was conducted to identify the psychological impact of CRC in the first year, and the additional impact of genetic testing. The electronic databases of PubMed, PsychInfo, Embase and the Cochrane Library were searched to identify all reports published between January 1997 and October 2007 on the psychological impact of (1) CRC-diagnosis up to 1 year after treatment and of (2) genetic testing for Lynch syndrome in patients with CRC. Studies on the psychological impact of genetic testing in newly diagnosed patient with CRC were not available. Either CRC patients diagnosed several years ago were studied and the focus was also often on the psychological impact of genetic testing prior to DNA-test disclosure. They show that limitations in emotional and social functioning can persist up to 1 year after CRC treatment, especially in those with a stoma or diagnosed before age 60. Female patients and male patients diagnosed before age 50 appear to be more vulnerable to genetic testing-related distress. It is well known that being treated for CRC has great impact on psychological functioning. Little is known about the psychological impact during the first year after diagnosis and very little is known about the additional psychological effect of genetic testing for hereditary cancer in this period. We found presumptive evidence that specific subgroups of patients with CRC are more vulnerable for genetic-testing-related distress.

Keywords Colorectal cancer · Diagnostic genetic testing · Lynch syndrome · Psychological impact · Review

Introduction

Up to 5% of patients with colorectal cancer have Lynch syndrome (hereditary non-polyposis colorectal cancer (HNPPC)) [1–3]. Unfortunately, only a small proportion of the expected number of patients undergo genetic testing. Identification of a hereditary predisposition can be lifesaving. When more patients are traced with hereditary colorectal cancer, an increasing number of relatives can receive appropriate surveillance, which will prevent premature death from colorectal cancer [4]. To enhance the detection of Lynch syndrome, a special strategy has been developed for risk patients who cannot be recognized by family history. This new strategy called MIPA involves MSI-testing by pathologist in new patients with CRC below the age of 50 [5]. It is being introduced at an increasing number of hospitals. In this strategy, the pathologists select patients and tumour specimens for
microsatellite instability (MSI) testing. In case of a positive MSI test, the patient is at risk for Lynch syndrome and thus referred for genetic counseling to a clinical genetic center.

For the patients, the difference between the new strategy and the existing procedure is that genetic counseling and testing is discussed very shortly after the diagnosis of colorectal cancer, instead of a long period after diagnosis and treatment. In this early stage after diagnosis, patients with colorectal cancer may be more emotionally vulnerable. Concurrently, these patients are confronted with three major tasks: (1) to cope with their cancer, (2) to cope with the consequences of a possible genetic risk and (3) to consider informing and discussing genetic counseling and DNA-testing with their blood relatives. Extended work already has been accomplished on familial cancer in general, including colorectal patients tested for Lynch syndrome. In a number of reviews on familial cancer, colorectal cancer was included as one of the familial cancers [6, 7]. Many studies describe the psychological impact of pre symptomatic testing for Lynch syndrome [8–22]. From these studies it can be concluded that in general genetic counselling and pre symptomatic testing for Lynch syndrome can lead to increased distress immediately after DNA-test disclosure but does not lead to long-term adverse effects. Other related studies assessed experiences of patients and family members with genetic counselling for hereditary cancer and [23], the impact of attendance of a familial colorectal clinic on cancer-related concerns [24], subjective perception regarding colorectal cancer [25, 26], compliance with screening after testing [26], genetic testing for Lynch syndrome in colorectal cancer survivors who were more than 1 year after diagnosis [27] and quality of life after various surgical procedures [28].

Obviously, this new Lynch detection strategy gave rise to systematically survey relevant data related to the issue of the impact of symptomatic genetic testing in patients with colorectal cancer in their first year after colorectal cancer diagnosis. A literature review was conducted to identify the psychological impact of colorectal cancer, focusing on the impact of the malignancy during the first year after primary treatment and of the additional impact of genetic testing for Lynch syndrome in affected patients.

Materials and methods

The electronic databases PubMed and PsychInfo were searched to identify all the reports published between January 1997 and October 2007 on the psychological impact of colorectal cancer and genetic testing for hereditary colorectal cancer (Lynch syndrome) in patients during their first year of colorectal cancer. Two searches were performed in each database.

Search 1 retrieved literature on the psychological impact of the diagnosis and treatment of colorectal cancer. A sensitive search strategy was adopted using the following keywords: colorectal cancer, colorectal tumour(s), colorectal carcinoma, colorectal neoplasms, psychological distress, psychological adaptation, coping, emotional adjustment, anxiety, depression and quality of life. Using these keywords, 470 abstracts were retrieved: 415 from PubMed and 55 from PsychInfo. After removing doubles, one of the reviewers (KL) checked all the titles and abstracts. Full text copies were obtained when the studies had possible relevance. Inclusion criteria were (1) studies on patients in their first year with colorectal cancer (2) psychological outcome measurements, (3) peer-reviewed articles in English, French or Dutch. From studies with a prospective design with long-term follow-up, only the results up to 1 year were retrieved. Exclusion criteria were (1) Patients with colorectal cancer aged ≥70 years. These patients are not generally referred for genetic testing due to their advanced age. (2) Colorectal cancer disease management studies and subjective experiences. (3) Qualitative design. (4) Research into non-standard medical treatment. (5) Publications of which no relevant data (mean scores) could be retrieved. Based on these criteria, 17 studies remained (see Fig. 1).

Search 2 retrieved literature on the psychological impact of genetic testing in patients with colorectal cancer. The keywords in search 1 were used in combination with the terms genetic testing, genetic predisposition to disease, genetic screening, genetic counseling and genetics. Using these keywords, 101 abstracts were retrieved. After removing doubles, one of the reviewers (KL) checked all the titles and abstracts. Full text copies were obtained of all the possibly relevant studies. Inclusion criteria were (1) patients diagnosed with colorectal cancer (2) psychological outcome measurement, (3) peer-reviewed articles in English, French or Dutch. Exclusion criteria were (1) Pre-symptomatic/predictive testing, because our focus was on the impact of genetic testing in patients diagnosed with colorectal cancer. (2) Qualitative design. (3) Genetic testing for Familial Adenomatous Polyposis (FAP). (4) Publications of which no relevant data (mean scores) could be retrieved. Based on these criteria, ten studies remained (see Fig. 1).

Additional free text searches were performed in PubMed, PsychInfo as well as in the Cochrane Library database and in Embase using all the above-mentioned keywords to select reviews on the psychological impact of colorectal cancer and genetic testing for hereditary colorectal cancer. However, none of these searches led to any relevant publications.
Methodological quality

The studies were assessed according to the guidelines for levels of evidence and grades of recommendation, supplied by the Oxford-Centre for Evidence-based Medicine. A level of evidence (LE) 1 refers to RCT studies, LE2 to cohort studies, LE3 to case-control studies, LE 4 to case-series and LE5 to expert opinions (http://www.cebm.net/levels_of_evidence.asp).

Results

I Psychological impact of colorectal cancer

Table 1 gives a summary of each of the 17 papers [29–45] included in our review. The vast majority of the patients with colorectal cancer were older than 50 years. As a result of the heterogeneity of psychological variables and used measurement instruments of the retrieved studies, a limit was set in describing those studies that used the European Organization for Research and Treatment in Cancer (EORTC) QLQ-C30 scale. In ten out of the 17 studies, the European Organization for Research and Treatment in Cancer (EORTC) QLQ-C30 scale had been used to measure the quality of life of the patients [29–32, 35, 41, 43–46]. This scale has frequently been used to assess health-related quality of life in various groups of cancer patients [47].

The mean scores on functional status were retrieved from the studies, because an important aim of this review was to evaluate functioning after treatment for colorectal cancer. The scores are presented in Table 2. Our comparison may not do justice to the special qualities of each individual study, as their designs were intended to provide answers to specific research questions, not to facilitate comparability. Nevertheless the comparison adds new dimensions to our knowledge in this area. To evaluate the significance of these function scores, they were compared to reference data from a random sample (n = 2081) of the general (non-cancer) adult population [47] and from breast cancer patients [48] (Table 2). According to the MIPA (MSI test by pathologist) procedure, MSI-positive patients are usually informed about the results and offered genetic testing within 3 months after surgery. Therefore, clear distinction is made between psychological functioning in the first 3 months after treatment and in the subsequent period up to 1 year after treatment. In the publications of Schmidt [42] and Tsunoda [44] the EORTC-QLQ-C30 data were presented in graph and mean data could not be obtained and used reliably. The study of Wilson et al. [45], only presented mean data on EORTC-QLQ-C30 Global Health Status. Therefore, these three studies are not reflected in Table 2.

Regarding the psychosocial impact of CRC with other instruments than the EORTC-QLQ-C30, it appeared that often different questionnaires were used, concerning patients at different ages, with different types of colorectal
| Author          | LE | N   | Mean age at inclusion years (SD) [range] | Time of data collection | Study method/questionnaires | Main outcome measures | Main psychological findings                                                                 |
|-----------------|----|-----|-----------------------------------------|-------------------------|-----------------------------|-----------------------|-----------------------------------------------------------------------------------------------|
| Kopp et al.     | 1  | 79  | 72.4 [53–90]                           | At discharge and 6 months after treatment | EORTC QLQ-C30/CR38         | Quality of life       | Six months after surgery, global quality of life approximated normal values but deficits remained in role, physical and social functioning |
| Marijnen et al. | 1  | 990 | 64 [NP]                                 | Pre-treatment, 3, 6, 12, 18 and 24 months after treatment | RSCL; VAS                 | Health-related quality of life and overall perceived health | Few QoL differences between PRT+ and PRT− group. PRT negative effect on sexual functioning, deteriorating over time |
| Allal et al.    | 2  | 53  | 58 (11)                                | Pre- and 12–16 months post | EORTC QLQ-C30/CR38         | Quality of life       | Compared to pre-RT scores, at 1 year, improvement in emotional state, perspective of the future, global QoL. Sexual dysfunction increased, particularly in men |
| Amdt et al.     | 2  | 309 | 65.1 (9.4)                              | 1 year after diagnosis | EORTC QLQ-C30              | Quality of life       | Severe limitations in emotional and social functioning predominantly in patients younger than 60 years |
| Engel et al.    | 2  | 299 | <70 n = 212; >70 n = 87                 | At treatment and annually to 4 years follow-up | EORTC QLQ-C30/CR38         | Quality of life       | Compared to a general population sample, patients had the largest differences with regard to role and social functioning |
| Fatma et al.    | 2  | 160 | 50 [18–83]                              | During visit first line | FACT-C; Spitzer QoL         | Quality of life       | >40% of the patients reported signs of psychological distress, 35% expressed fear of dying |
| Femsler et al.  | 2  | 121 | 51.9 [26–82]                           | Through computer networks | DOII; SWBS                  | Demands of illness; spiritual well-being | DOI greater among men, the youngest subjects (26–45 years), who received treatment in the previous 2 months. Women reported greater spiritual well-being than men |
| Gall et al.     | 2  | 338 | <60 n = 43; 60–69 n = 77; >70 n = 218   | 6 weeks, 6 months after treatment until 2 years follow-up | HADS; SF12; PSVQ           | Anxiety, depression, health-related quality of life | At baseline, mental HRQoL scores consistent with average values in the population. Levels of anxiety and depression consistent with or lower than population norms |
| Guren et al.    | 2  | 42  | 67 [38–78]                              | Start and end treatment and 4–6 weeks follow-up | EORTC QLQ-C30/CR38         | Quality of life       | At the end of RT, physical and social functioning and global quality of life poorer than population norms. HR QoL scores returned to pre-treatment levels 4–6 weeks after RT |
| Klemm et al.    | 2  | 21  | 51.9 (NP)                               | Via online CRC support group | DOII                      | Demands of illness   | The 10 most intense demands predominantly psychosocial and existential concerns. Respondents in the youngest age group (<45 years) greater demands |
| Nordin and Glimelius | 2 | 139 | 67 (NP)                                 | <12 weeks after diagnosis | RDCQ; IES; MAC; HADS       | Diagnosis reactions; impact of event; adjustment to cancer, anxiety; depression | Patients with CRC more confrontational attitude than those with gastric cancer; avoidance in men lower than in women, mental adjustment better in women |
| Norum           | 2  | 94  | 62 [40–76]                              | 16 months after treatment | IES                       | Impact of event       | Less than one-third of the patients reported a moderate to high level of psychological distress |
| Author          | LE  | N      | Mean age at inclusion years (SD) [range] | Time of data collection | Study method/questionnaires | Main outcome measures | Main psychological findings                                                                 |
|-----------------|-----|--------|------------------------------------------|-------------------------|-----------------------------|-----------------------|---------------------------------------------------------------------------------------------|
| Ross et al.     | 2   | 249    | 64.5 (NP)                                | 3, 6, 12 and 24 months after initial treatment | EORTC QLQ-C30/CR38         | Quality of life        | Patients with stoma higher levels of depression and poorer social functioning than non-stoma patients. Male patients with stoma more sexual problems than males without |
| Schmidt et al.  | 2   | 253    | <70 \( n = 168 \); >70 \( n = 85 \)  | Pre-surgery, 3, 6,12 and 24 months after treatment | EORTC QLQ-C30/CR38         | Quality of life        | Role functioning better in patients <70 years. Younger patients more sexual problems |
| Schmidt et al.  | 2   | 368    | 64.9 (11.1)                              | Pre-surgery, at discharge, 3, 6, 12 and 24 months after treatment | EORTC QLQ-C30/CR38         | Quality of life        | QoL below baseline early postoperative period, after 3 months, global health, emotional and physical functioning improved. Men high levels of strain related to sexual problems |
| Tsunoda et al.  | 2   | 100    | 64 [33–83]                               | Pre-treatment and monthly follow up to 1 year | EORTC QLQ-C30              | Quality of life        | Physical and role functioning below preoperative values 1 month after surgery, returned to preoperative values <3 months. Global health, emotional and social functioning improved within 3 months |
| Wilson et al.   | 2   | 201    | 68.2 [36–91]                             | 6 weeks after treatment | EORTC QLQ-C30; FACT-C; SF12; EQ-5D | Physical and mental health-related quality of life | Patients <65 years and those with a stoma poor health-related quality of life |

**Questionnaires**
- EORTC QOL-C30/CR38, DOH, SWBS, FACT-C, Spitzer QoL, SF12, PVSQ, RSCL, VAS, IES, EQ-5D, RDCQ, MAC
- NP, not present; MD, medical doctor; RT, radiotherapy; PRT, pre-operative radiotherapy; (HR)QoL, (health-related) quality of life; LE, level of evidence
| Time of data collection | Physical | Role | Emotional | Cognitive | Social | Global health status |
|------------------------|----------|------|-----------|-----------|--------|---------------------|
| Refilata Servaes et al. [48] | 6–70 months after breast cancer treatment | 72.6 (18.8) | 71.4 (22.7) | 71.2 (21.8) | 73.7 (24.0) | 82.5 (22.8) | ND |
| Schwarz and Hinzb [47] | A-selected non-cancer population | Male 92.0 (15.6) Female 88.7 (17.5) | Male 89.8 (21.7) Female 86.6 (23.7) | Male 81.8 (18.8) Female 76.3 (22.2) | Male 92.7 (15.0) Female 90.1 (18.4) | Male 92.0 (18.3) Female 90.3 (20.1) | 72.7 (22.2) Female 69.2 (21.9) |
| Schmidt et al. [43] | Before surgery | 86.1 (20.4) | 78.5 (22.0) | 82.7 (30.5) | 76.7 (30.3) | 66.5 (23.8) | 58.5 (26.0) | 85.1 (19.6) | 80.8 (23.9) | 78.4 (26.1) | 75.1 (30.9) | 62.4 (25.2) | 57.7 (24.1) |
| | At discharge | 64.4 (27.1) | 50.6 (25.7) | 41.3 (39.5) | 37.2 (38.6) | 63.4 (23.5) | 52.6 (25.4) | 75.5 (26.1) | 72.8 (26.5) | 58.2 (32.3) | 75.7 (33.5) | 47.5 (19.6) | 43.3 (22.8) |
| | 3 months after surgery | 74.5 (22.8) | 60.4 (24.8) | 66.0 (32.2) | 58.6 (32.5) | 70.8 (25.0) | 66.0 (25.4) | 80.4 (25.4) | 78.0 (24.4) | 63.5 (29.6) | 57.1 (31.8) | 61.4 (20.3) | 54.4 (21.2) |
| | 6 months after surgery | 76.8 (20.9) | 66.4 (23.5) | 68.6 (32.3) | 64.5 (30.8) | 71.4 (23.6) | 66.9 (23.8) | 81.6 (23.2) | 80.8 (23.5) | 64.4 (30.1) | 64.9 (31.4) | 63.3 (19.5) | 58.1 (20.5) |
| | 12 months after surgery | 78.1 (21.8) | 68.3 (25.5) | 72.0 (31.4) | 70.5 (31.0) | 71.3 (23.6) | 68.2 (24.3) | 81.8 (22.7) | 82.2 (23.7) | 68.5 (30.3) | 64.9 (33.2) | 65.3 (20.1) | 61.0 (23.9) |
| Kopp et al. [37] | At discharge | 54.5 | 46.5 | 66.3 | 70.9 | 72.1 | 52.6 |
| | 6 months after surgery | 69.9 | 61.6 | 73.3 | 73.7 | 74.9 | 63.6 |
| Arndt et al. [30] | 1 year after diagnosis | 79.5 (24.0) | 74.4 (33.4) | 67.0 (28.2) | 78.5 (26.6) | 74.7 (30.9) | 62.8 (22.4) |
| Engel et al. [32] | 1 year after surgery | 81.8 | 65.2 | 68.9 | 82.6 | 73.7 | 65.3 |
| Ross et al. [41] | Follow-up after surgery | No stoma 75.2 (1.8) | FU stoma 79.3 (1.9) | Initial stoma 83.9 (1.5) | Initial stoma and FU stoma 84.7 (1.5) | 93.8 (1.3) | 72.9 (1.5) |
| | Initial stoma | 67.3 (4.3) | 68.2 (6.0) | 80.1 (4.1) | 75.4 (4.1) | 84.1 (3.7) | 65.1 (4.3) |
| | Initial stoma and FU stoma | 82.2 (4.4) | 84.4 (5.9) | 86.7 (4.1) | 88.8 (4.1) | 92.3 (3.6) | 73.5 (4.4) |
cancer and often with different times of data collection. Still, an overall impression was obtained that demands of illness, especially psychosocial and existential concerns, were greater among the youngest age group below 45 years. Moreover, patients with a stoma showed higher levels of depression and poorer social function than non-stoma patients. Especially men with a stoma reported sexual problems as did patients after treatment for rectal cancer.

Impact of colorectal cancer on functional status

Up to 3 months after treatment

Table 2 shows that compared to the reference data, colorectal cancer led to reduced social functioning (especially in the patients with a stoma) as well as to decreased role and physical functioning [29, 30, 32, 37, 41, 43]. Patients of younger than 65 years and those with a stoma reported reduced health-related quality of life 6 weeks after surgery [45]. In the group with rectal cancer the men suffered from more problems with their sexual functioning after abdominoperineal resection than the women [43]. It can be concluded that immediately after treatment for colorectal cancer, physical, social and role functioning were diminished especially in patients with a stoma, compared to levels of physical, social and role functioning of a selected sample of adults [47] and of patients with lung cancer (another common malignancy worldwide) [49, 50].

Between 3 and 12 months after treatment

Reduced role, emotional and social functioning continued up to 1 year after treatment. The women reported poor physical functioning [43] compared to the reference data [47] and the scores from a severely fatigued disease-free breast cancer group [48]. Global health status scores of the patients with colorectal cancer were also poorer than the reference data [47]. Severe limitations were found in emotional and social functioning up to 1 year after treatment. These problems were especially likely to affect patients of younger than 60 years [30]. In the men, strain due to sexual impairment appeared to persist [29, 43, 46]; the men with a stoma had more sexual problems than those without [41]. Rectal cancer patients reported poor role and social functioning compared to the reference data [47] up to 1 year after treatment [32]. In the patients who had pre-operative radiotherapy, emotional functioning was impaired compared to the norm data [47]. At 12–16 months after radiotherapy, these scores had returned to normal levels [29]. Thus, severe problems with emotional and social functioning persisted up to 1 year after treatment.
especially in the patients of younger than 60 years and in those with a stoma.

Impact of colorectal cancer on demands of illness and spiritual well-being

In two studies, patients younger than 45 years reported greater demands of illness (hardships or stressors that require coping or adjustment to illness) than the older patients [33, 36]. Fernsler et al. [33] also showed that such demands of illness were greater in men and in men and women who had received treatment in the previous 2 months; in contrast, the women reported significantly higher spiritual well-being than the men. This leads to the conclusion that colorectal cancer caused more hardships and stressors in men and in patients diagnosed before the age of 45 years.

II Psychological impact of genetic testing for Lynch syndrome

Summaries of the ten relevant studies are shown in Table 3. Nearly all the studies had gathered data on the patients before disclosure of the genetic test result. Two studies had made assessments pre-test and post-test [16, 51], whereas one study had only made assessments post-test [52]. Very few studies gave specific details about the time interval since the diagnosis of colorectal cancer and inclusion in the study [53, 54]. Table 3 also shows the diversity in outcome measures and (self-administered) questionnaires to gather data [16, 51, 55–58]. The aim of this review was to determine how patients with colorectal cancer reacted to (the offer of) genetic testing. Therefore, the psychological reactions were documented according to stage of genetic testing the patients had reached at the time of the studies. The process of genetic counselling was divided into three distinct stages: (1) Period of genetic counselling and if desired, having a blood sample taken. (2) Period of waiting for the result of the DNA analysis. (3) Period after disclosure of the genetic test result.

Psychological reactions before genetic counselling

The three relevant studies showed that patients with colorectal cancer tended to have positive attitude towards genetic testing [56, 57, 59]. Their most common motivation to undergo genetic testing was concern about the risk of colorectal cancer in close relatives. Motivation was the highest in the younger patients, in those with early stage disease and in those who had more frequent thoughts about hereditary colorectal cancer [57]. In a group of patients with colorectal cancer who attended an information session about Lynch syndrome, 28% developed a clinically significant level of cancer-worry-related distress [56]. In conclusion, motivation to undergo genetic testing was primarily the need to know if close relatives were at increased risk for colorectal cancer and was strongly present in younger patients.

Psychological reactions before and after genetic counseling

Other studies obtained data on the patients after patients had consented to have a blood sample taken for DNA analysis. Keller [55] and Murakami found clinically relevant depression scores before and after genetic counseling in 19 and 5% of the patients, respectively [51]. Another study reported clinically relevant anxiety levels in 32% of the patients before genetic counseling, whereas the scores dropped to 16% after genetic counseling [55]. In a group of patients who had given a blood sample for genetic testing, the prevalence of depressive symptoms was 24%, although all the scores remained within the clinically normal range [54]. Patients in the age group of younger than 50 years had higher levels of anxiety and depression but the scores were within the normal range; their data also showed significant associations between pre-test distress, a history of familial mortality from colorectal cancer and anticipation of becoming depressed post-test [53]. Characteristics associated with depression were female sex, less formal education, fewer sources of social contact; associations with anxiety were younger age, less formal education, Non-Caucasian race, more severe disease and fewer sources of social contact [54]. Intrusion scores reached clinically relevant levels in 14% of the patients [55]. Higher intrusion and avoidance scores were found in women and in the patients who had been diagnosed with colorectal cancer less than 1 year previously, although all the scores remained within the normal clinical range [53]. Clinically relevant cancer-worry-related distress was detected in 25% of the patients before genetic counseling, but after genetic counseling, this dropped to 13% [55]. In conclusion, most psychological distress scores remained within the normal range before the result of the genetic test was disclosed, although a minority of the patients developed clinically relevant anxiety and depression levels. Vulnerable subgroups were female patients and male patients diagnosed before the age of 50 years.

Psychological reactions after disclosure of the genetic test result

Disclosure of the genetic test result led to significant depression scores in 7% of the patients and post-traumatic
| Author         | N   | Inclusion age mean (SD)/median [range] | Time of data collection | Study method/questionnaires | Main outcome measures                                                                 | Main psychological findings                                                                                                                                                                                                 |
|---------------|-----|---------------------------------------|-------------------------|-----------------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Esplen et al. [53] | 220 | 63 (9.6)                              | At pre-test             | IES, STAI, CES-D            | Impact of event, state and trait anxiety and depression                                  | Women higher levels of intrusion and avoidance compared to males. Patients diagnosed before 50 years significantly higher levels of anxiety and depression than those diagnosed after 50 years. Diagnosed within one year significantly lower levels of intrusion and avoidance, than those over 2 years after diagnosis. Significant associations between pretest distress, family history of CRC and mortality related to CRC and anticipation of becoming depressed at post-test |
| Gritz et al. [16] | 155 | >50 n = 56; <50 n = 99                 | At pre-test, 2 weeks, 6 and 12 months after result disclosure | CES-D, STAI, RIES, QLI and Saq | Depression, state and trait anxiety, impact of event test result, quality of life, cancer worries and perceived cancer risk | Mean scores of all outcome measures within normal limits for cancer-affected participants. Affected and unaffected carriers higher mean test-specific distress scores at 2 weeks post result disclosure compared to non-carriers; scores decreased in affected carriers and all unaffected participants from 2 weeks to 12 months post result disclosure. Unaffected mutation carriers may experience increased distress during the immediate post result disclosure period. |
| Ho et al. [59] | 62  | 42 (9.9)                               | Pre and post result disclosure | DBS, C-HADS, C-MBSS, LOT     | Decisional consideration, attitude genetic testing, anxiety, depression, coping style | Participants even more concerned about well-being and reactions of their significant others than their own well-being in their decisional consideration process. Those with higher depression levels tended to emphasise more on the negative consequences of learning test results |
| Keller et al. [55] | 65  | Patients 50.3 (12.2); at risk persons 37.0 (9.1) | Pre and 4–6 weeks after genetic counselling | MOS-SF12, GBB, HADS, IES and Saq | Health state and complaints, anxiety, depression, impact of event, evaluation of counselling | Distress and HNPPC related worries declined after counselling. Distress decrease partly attributable to increase in personal self-confidence. One-third reported enhanced family communication specific to hereditary cancer. Twenty-five per cent reported cancer-related worries before testing. This dropped to 13% post-genetic counselling. |
| Keller et al. [56] | 73  | 49 (17)                                | After information session on HNPCC | Saq                         | Cancer worry, attitude genetic testing, family communication                           | Distress clinically significant in 28% of participants. Restricted family communication was reported frequently. Positive attitude towards obtaining a genetic test result predominated |
| Kinney et al. [57] | 98  | 64 (13)                                | Before genetic counselling or testing | Saq                         | Knowledge and risk perception CRC genetics, health behaviour, knowledge/interest genetic test | 61% worries about relative’s CRC risk, 64% concerned about being a carrier. 81% had never heard of genetic test for hereditary CRC. 72% stated they would take the test. Predictors to take the test: younger age, less advanced stage of disease and more frequent thoughts about CRC being hereditary |
Table 3 continued

| Author                  | N   | Inclusion age mean (SD)/median [range] | Time of data collection | Study method/questionnaires | Main outcome measures | Main psychological findings |
|-------------------------|-----|---------------------------------------|-------------------------|-----------------------------|-----------------------|-----------------------------|
| Loader et al. [52]      | 36  | 59.9 (6.7)                            | 3 and 12 months after result disclosure | SF36, IES, SSSQ, BSS       | Health state, impact of event, social support, preventive behaviour | At 12 months post result disclosure more knowledge in carriers, younger when DNA tested or younger at CRC diagnosis. All but one told relatives about their gene mutation. Self-assessed mental health better in married patients |
| Murakami et al. [51]    | 42  | 50 [21–69]                            | After first genetic counselling session for HNPCC and 1 month after result disclosure | SCID ASD/PTSD/PTSS and Saq | Acute stress disorder, post-traumatic stress disorder or symptoms and feelings of guilt | None of the participants met the criteria for major depression, ASD or PTSD 1 month after result disclosure. 7% met the criteria for minor depression and 5% had PTSS. The only predictor of psychological distress was the presence of a history of major or minor depression. 12% had feelings of guilt |
| Vernon et al. [54]      | 200 | ORPS                                  | After provision of blood sample for DNA analysis | CES-D, STAI, SSSQ, MBSS    | Depression, state and trait anxiety, social support, quality of life and coping style | Prevalence of depression symptoms was 24%. Female sex, less formal education, fewer sources of social contacts and less satisfaction with them were associated with high scores on the CES-D scale. Characteristics associated with high anxiety were younger age, less formal education, non-White race, advanced local-regional disease, fewer social contacts and less satisfaction with them |
| Vernon et al. [58]      | 269 | <50 n = 105; >50 n = 164              | After provision of blood sample for DNA analysis | CES-D, STAI, MBSS, SSSQ,QLI and Saq | Depression, anxiety, coping style, social support, quality of life and intention genetic testing | 90% intended to learn genetic test results. Intention positively associated with income, quality of life, a belief that being tested will help family members prevent cancer, being worried about carrying an altered gene and belief that one has ability to cope with test results. Negative association with belief that genetic counselling is too much trouble relative to benefits |

**Questionnaires** (R)IES, CES-D, STAI, (C)HADS, SF12, (C)MBSS, Sarason SSS, QLI, DBS, LOT, SCID

Saq, self-administered questionnaires; ORS, only presented in relation to psychological scores; CRC, colorectal cancer; HNPCC, hereditary non-polyposis colorectal cancer (Lynch syndrome)
stress symptoms in 5% [51]. Lynch syndrome mutation carriers showed higher test-specific distress than non-carriers but these scores returned to baseline between 2 and 12 weeks after receiving the test result [16]. The only predictor of psychological distress after disclosure of the test result was a history of depression [51]. It can be concluded that disclosure of the genetic test result did not lead to any relevant levels of psychological distress in most patients. Vulnerable subgroups seemed to be patients with pre-test distress, high familial mortality from colorectal cancer and a history of depression. Therefore, a subgroup of vulnerable patients whose genetic test discloses Lynch syndrome mutation carrier ship may benefit from extra psychological counselling.

Discussion

This literature review shows that little is known about the additional psychological impact of obtaining a genetic test disclosure in newly diagnosed patients with colorectal cancer. Only ten studies were identified on diagnostic genetic testing in colorectal patients. Most of these studies measured distress prior to genetic test disclosure, but did not obtain data after disclosure of the test result. Prior to disclosure of the genetic test result, female patients and men who were diagnosed with colorectal cancer before the age of 50 years appeared to be more vulnerable to genetic-test-related distress. A history of depression and high levels of pre-test distress were strongly associated with genetic-test-related distress and cancer related worries. It is generally known that a young age at diagnosis and multiple family members with cancer are hallmarks of heredity. Therefore, significant levels of anticipated psychological distress prior to disclosure of the genetic test result in patients with a history of familial mortality from cancer [53] can also be regarded as relevant to patients with colorectal cancer who are suspected of Lynch syndrome carrier ship.

The few studies available on distress after disclosure of the genetic test result revealed ambiguous results. For patients with different types of cancer, the impact of genetic testing many years after the initial cancer diagnosis and treatment was strongly influenced by their former experience of cancer [7]. Dorval hypothesized that after disclosure of the genetic test result, cancer patients may be more aware of their own risk developing a second primary tumour and be more conscious of the contribution of genetics to an increased risk of cancer in their offspring [60]. When genetic testing was offered to recently diagnosed colorectal cancer patients, the majority did not object to an active approach [61]. Individuals at high-risk for Lynch syndrome proved to know very little about microsatellite instability (MSI) testing, a hallmark for patients at risk for Lynch syndrome, but held positive attitudes towards MSI test utility [62].

This literature review also shows that most patients with colorectal cancer experience diminished physical, social and role functioning during the first 3 months after primary treatment. Decreased emotional and social functioning could persist for up to 1 year after treatment, especially in patients of younger than 60 years and in those with a stoma. Specific subgroups of patients with colorectal cancer appeared to be more vulnerable to genetic-testing-related distress, but their actual levels of distress did not generally reach clinical significance. Reduced emotional and social functioning may be related to the many taboos that still surround bowel dysfunction [63]. Especially the younger patients reported severe distress due to maladjustment to their colorectal cancer. Having a stoma can lead to feelings of stigmatisation and lead to withdrawal from social activities [64, 65]. Recurring themes in patients with colorectal cancer are loneliness and isolation [63]. It might be expected that disabilities after colorectal cancer treatment prevent the younger patients from going to work and contribute to their impaired social and role functioning, but it was found that most patients with colorectal cancer returned to work after treatment [64, 66]. An additional source of distress especially in younger male patients was the possible impact on sexual functioning [64, 67]. Studies have shown that after treatment for rectal cancer, sexual problems were common, inadequately discussed and/or treated by physicians [67]. Furthermore, the potential for impotence due to treatment for colorectal cancer was a serious concern especially in patients of younger than 60 years [64].

Conclusion

This review identifies the psychological impact of colorectal cancer during the first year after treatment and indicates specific subgroups of patients with colorectal cancer who could be vulnerable for genetic-testing-related distress. Most of the retrieved studies on diagnostic genetic testing for Lynch syndrome exclusively measured distress prior to genetic test disclosure and focused on patients who were diagnosed with colorectal cancer several years ago. Therefore, we are still unable to identify the psychological impact of genetic testing for Lynch syndrome in recently diagnosed patients with colorectal cancer.

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