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CICLO: XXXV

QUALITY OF LIFE, PSYCHOLOGICAL DISTRESS AND POST-TRAUMATIC GROWTH IN COLORECTAL CANCER PATIENTS: A PROSPECTIVE STUDY

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Non c’è nulla che vada come previsto,
è l’unica cosa che ci insegna il futuro
quando diventa passato.
(Daniel Pennac, “Diario di scuola”, 2007)

A tutti coloro che ci sono stati e continuano ad esserci,
ognuno a suo modo.
Alla me stessa di ieri e di oggi.
Grazie.

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Introduction

In research and clinical psychosomatic it is necessary to consider “at what levels and according to what dynamics in specific individuals which biological and which psychosocial factors are involved in the final outcome of onset, persistence and improvement of somatic symptoms” (Porcelli, 2014, p. 77). This should also be considered when we are in the presence of complex diseases such as oncological ones. Cancer has a unique place among chronic diseases and influences physical, social, psychological, and spiritual dimensions of life, causing numerous symptoms due to the disease process itself and treatments, as well as the meaning attributed to this experience by the patients (Okanli et al., 2018).

The interaction of genetic and environmental factors acts on carcinogenesis, producing various progressive and multiphasic molecular events causing DNA damage. The tissues most affected are those actively proliferating and particularly exposed to environmental carcinogens. Genetic cell modifications can be either acquired or inherited, but a second type of stimulus must intervene for that cell to progress to neoplastic transformation. Understanding which genetic and environmental factors contribute to carcinogenesis, with what role and how, is essential to enable the development of increasingly effective prevention and treatment programmes (Caligaris Cappio, 2015; AIOM & AIRTUM, 2018).

Of all types of cancer, colorectal cancer has high incidence rates worldwide (Boyle et al., 2013; Fidler et al., 2017; IARC-WHO, 2020; Reni, 2015; Sung et al., 2021; Zhang et al., 2023). In Italy, the estimated cancer cases for 2022 are 390700 of which 48100 new cases of colorectal cancer, representing one of the most frequent types of cancer in both sexes (AIOM et al., 2023; Pinto, 2023).

Colorectal cancer, its associated symptoms and treatments and their consequences can lead to major physical dysfunctions (e.g., bowel elimination, urinary and sexual dysfunctions) and high levels of psychological distress in patients, with a considerable impact on general well-being and Quality of Life (Buccafusca et al., 2019; Mosher et al., 2016; Haas et al., 2022; Peng et al., 2019; Towe et al., 2019; Wang et al., 2023a).

Over the years, researchers have become increasingly interested in the positive outcome of a traumatic event. A cancer diagnosis can represent a traumatic event with characteristics similar to other kinds of events that undermine the survival of the individual. It threatens physical health, causes profound psychological distress (e.g., anxiety and depression) and disrupt life “as usual” for a prolonged period (Buccafusca et al., 2019; Cordova, 2008; Cordova et al., 2017;

Threader & McCormack, 2016; Wang et al., 2023a). In general, living with a cancer diagnosis and coping with specific treatments can impair many aspects of daily life, including physical, emotional, social, and occupational functioning (Cordova et al., 2017; Wang et al., 2023a).

Cancer patients differ in their emotional reactions according to their perception of the disease and the meaning attributed to the diagnosis (Okanli et al., 2018). In order to explain the individual variability in the psychological and physical outcomes, it is necessary to identify the factors that influence this perception and the intercorrelation between these factors and outcomes. From a biopsychosocial perspective, longitudinal studies that consider several medical and psychosocial variables together are necessary to investigate their possible effects as risk or protective factors for patients' physical and psychological health. Medical variables include the impact of diagnosis, treatments and their consequences, adverse effects and cancer-specific symptoms on Quality of Life and mental health. Psychosocial factors include both personality and psychological characteristics that are structured from early life and through development that remain more or less stable over time (e.g., alexithymia and emotion dysregulation, psychological resilience and trait affectivity), and situational psychological variables related to the life moment being experienced (e.g., status affectivity, specific coping strategies and perceived social support).

The present dissertation aims to investigate the psychosomatic outcomes and components of colorectal cancer, attempting to explore and understand the interrelation between medical and psychosocial factors. The main aim of this study project was to investigate the change in Quality of Life, Post-Traumatic Growth and psychological distress in colorectal cancer patients, monitoring their trajectories from diagnosis to follow-up, through the different phases of the treatment pathway. Furthermore, this study aimed to explore the association between these variables and the medical and psychosocial factors that may contribute to physical and positive and negative psychological outcomes.

This thesis is structured in three chapters. The first chapter aims to provide general notions about colorectal cancer and psychosocial factors involved. The main characteristics of this specific gastrointestinal oncological disease will be described, from the epidemiological data to the possible causes, symptomatology, diagnosis and treatments. In addition, the constructs of Quality of Life, psychological distress, and Post-Traumatic Growth, which represent the main outcomes of oncological diseases, including colorectal cancer, will be described and discussed. Similarly, the psychophysical impact of specific treatments for colorectal cancer and psychosocial factors that have been shown in part to play a role on chronic and oncological disease outcomes will be introduced and described.

The second chapter is dedicated to the description of the extensive research project conducted on patients with colorectal cancer. The general objectives of this prospective observational cohort study were mentioned above: the theoretical and methodological details of the entire research project will be provided to clarify the work conducted over the years.

The third chapter will focus on two specific objectives of the larger project and describe the results obtained and their possible explanations and implications. The first part of the chapter will focus on presenting the theoretical background and objectives, while the second part will provide a brief description of the methodology, the results and the discussion for each objective. In particular, the first macro-objective will concern the assessment of changes in quality of life of colorectal cancer patients during the active treatment phase, from diagnosis to after surgery, and the exploration of possible physical and psychosocial predictors of quality of life in relation to the different treatment phases. The second macro-objective will concern the evaluation of changes in psychological distress and post-traumatic growth in patients with colorectal cancer during the treatment pathway from diagnosis to one year follow-up, and the exploration of the impact of certain medical and psychosocial variables on these two outcomes at follow-up.

Chapter 1.

Colorectal cancer: medical and psychological considerations

1.1 Oncological diseases of gastrointestinal tract

1.1.1 Anatomo-physiological hints of the digestive and gastrointestinal systems

The gastrointestinal system is connected to the outside through the cephalic (i.e., mouth) and the caudal extremities (i.e., anal orifice); its organs and glands occupy part of the head, the neck and a large portion of the torso (**Figure 1.1**) (Anastasi et al., 2010; Conti, 2010).

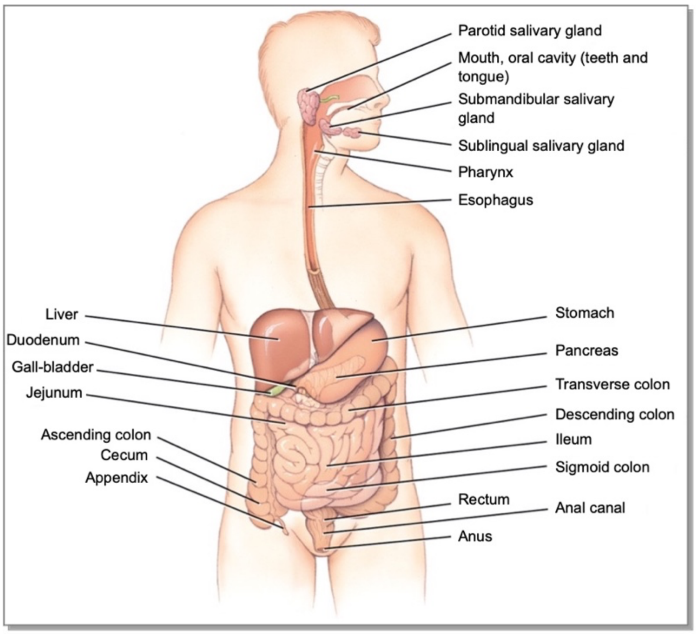

Figure 1.1. Overview of the digestive system.

The majority of the organs of the digestive system compose the gastrointestinal tract: the oesophagus has the function of conveying the bolus; the stomach contains the food material for a time, remixing and reducing it through the action of the gastric acid; and the intestine. The latter is subdivided into small intestine, which occupies the central portion of the abdomen and has three sections (duodenum, jejunum and ileum), and large intestine, in which there are three portions: cecum, colon (in which the ascending, transverse, descending, ileopelvic or sigmoid tracts are identified) and rectum. The large intestine is larger, but shorter and more fixed than the small intestine, and narrows considerably as it approaches the rectum and anal canal. The various intestinal sections also differ in terms of the physiological functions performed and the mechanisms involved in the transport of different substances: in the small intestine, the most important part of digestion takes place, i.e. the chemical breakdown of food, and the absorption of various basic substances (carbohydrates, proteins, lipids, water- and fat-soluble vitamins, minerals and trace elements, electrolytes and water); the large intestine is mainly responsible for the further absorption of electrolytes and water and the preparation of waste substances, which are eliminated with defecation (Anastasi et al., 2010; Conti, 2010).

1.1.2 Cancer types of the gastrointestinal tract

Given the extent and great involvement of organs and glands, there are many locations in the digestive system where malignant tumours can develop. There are several aspects that these tumours have in common: a severe prognosis, linked to the severity of the metabolic and physical imbalances they generate; often a late diagnosis of the diseases; the great invasive and metastasizing capacity, due to the proximity of the various organs in the abdominal cavity and the great vascular and lymphatic connection between them (Reni, 2015). In addition, carcinomas in this area often present initially asymptomatic and/or with various symptoms (depending on the organ tract affected), which are non-specific and common (such as diarrhoea, abdominal pain near meals, nausea), and become more severe with the progression of the disease (Reni, 2015).

The risk for these diseases increases significantly with advancing age and there are differences in geographical incidence both worldwide and in Italy. Although they have different impacts, common risk factors are: cigarette smoking, alcohol, a diet lacking in fruit and vegetables and rich in fats and processed meats, obesity, certain conditions of chronic inflammation (e.g., gastro-oesophageal reflux) or bacterial or viral infections (i.e., the relationship between Helicobacter pylori infection and gastric cancer or between hepatitis B or C and hepatocarcinoma is well-established), as well as a certain genetic and/or familial predisposition (Reni, 2015; AIOM et al., 2023).

Specifically, oesophageal cancer accounts for 5% of all types of cancer and is the third most frequent in the tract considered, as well as being among the top ten most common cancers worldwide, with a higher mortality (Reni, 2015). As for gastric cancers, cardias (about 40%) and stomach cancer have been distinguished and represent one of the most frequent causes of cancer death in Italy for both sexes, they are also one of the most common types of cancer of the gastrointestinal tract (De Vita, 2023). On the other hand, tumors of the small intestine are very rare and heterogeneous (1% of all digestive tract cancers and 0.3% of all forms), as well as carcinomas of the biliary tract (1% of all carcinomas), which affect the bile ducts or the gallbladder, with a different incidence for both sexes depending on the histotype. Primary liver cancer has a higher incidence in men and an age of occurrence around 40 years; this type of cancer is less frequent than secondary metastases in liver. Pancreatic carcinoma accounts for about 2% of all cancers and over the years its incidence has been increasing, especially in Western countries, accounting for 10% of cancers of the gastrointestinal tract (Reni, 2015). Finally, the most frequent neoplasm of the gastrointestinal tract is colorectal cancer (Dionigi, 2011; Fidler et al., 2017).

1.2 Colorectal cancer

Colorectal cancer (CRC) refers to all the different subtypes of cancer located in the tract between the ileo-caecal valve (located between the small and large intestine) and the anus (Reni, 2015). For medical and treatment reasons it would be appropriate to consider right colon, left colon and rectal cancers separately, but for epidemiological aspects it is more useful to treat them together (Dionigi, 2011).

Anatomically, the external surface of the colon is characterized by gibbosities, separated by furrows, and three laminae given by bundles of smooth muscle, while the internal surface has pockets (haustra) and ridges, also called semilunar folds. The rectum has transverse grooves in the external surface that are more or less deep and a series of variously oriented folds in the internal surface that allow the organ to distend (Anastasi et al., 2010). There are functional differences in the various tracts of which colorectum is composed: the transverse colon seems to be the section in which the main functions of the large intestine are mainly performed; the descending colon seems to perform essentially a conduction function; finally, the rectosigmoid is performed a storage function, the muscles and innervations provide the function of faecal continence and send signals on the need for emptying to the Central Nervous System (Conti, 2010).

1.2.1 Epidemiology

CRC has high geographical variability and incidence rates that fluctuate significantly, being higher in Western industrialised and developing countries, with rectal cancer alone contributing to more than 700,000 new cancer diagnoses each year, i.e. around 30% of the total (Boyle et al., 2013; Fidler et al., 2017; IARC-WHO, 2020; Reni, 2015; Sung et al., 2021; Zhang et al., 2023). In Italy, the estimated cancer cases (excluding skin cancers different from melanoma) for 2022 are 390700. In particular, from the latest Italian statistics, the most frequent types of cancer are: breast (55700 new cases, +0.5% compared to 2020), CRC (48100 new cases, +1.5% in men and +1.6% in women compared to 2020), lung (43900 new cases, +1.6% in men and +3.6% in women), prostate (40500 new cases, +1.5%), and bladder (29200 new cases, +1.7% in men and +1.0% in women). In terms of frequency, CRC represents the third most frequent type of cancer for men (26000 new cases) and the second for women (22100 cases), with an increase in the number of cases after the age of 50; in terms of prevalence, it is second in both sexes (AIOM et al., 2023; Pinto, 2023). Furthermore, rectal cancer contributes to approximately 30% of CRC diagnosis worldwide (Sung et al., 2021; Zhang et al., 2023).

Italian data on cancer mortality rank CRC second as a cause of death in proportion to total cancer deaths in both sexes, preceded only by lung cancer for men and breast cancer for women (AIOM & AIRTUM, 2018). However, CRC exhibits high survival rates, 65% in men and 66% in women after 5 years since diagnosis, influenced mainly by the time of diagnosis and the effectiveness of the therapies administered (Pinto, 2023; IARC-WHO, 2020; Sung et al., 2021; Zhang et al., 2023)

1.2.2 Risk factors

Risk factors for CRC are related to both lifestyle and familiarity.

Diet plays a significant role among the former. A dose-dependent association between alcohol consumption and increased risk, high consumption of red meat and preserved meats, high consumption of refined flours and sugars, obesity and reduced physical activity, cigarette smoking, low consumption of fruits, vegetables and carbohydrates, and insufficient intake of vitamin D and calcium are all significant risk factors for the development of CRC (Dionigi, 2011; Pinto, 2023).

Among the familial conditions were identified: the Familial Adenomatous Polyposis (FAP), characterized by the occurrence of a large number of adenomatous polyps (formations that are originally benign) by the age of 30, which in 100% of cases of FAP have malignant transformation if not early treated; the hereditary polyposis or Gardner's syndrome, which is similar to FAP but has a later onset and also spread to bone and soft tissue; the hereditary nonpolyposis colorectal cancer (HNCCP) or Lynch syndrome, which occurs most frequently in the right colon and has malignant transformation around the age of 43; the juvenile polyposis and the Peutz-Jeghers syndrome (Kumar et al., 2015; Reni, 2015). Approximately one-third of colorectal cancers have familial characteristics related to hereditary susceptibility and if a first-degree relative has been diagnosed with CRC, the risk of cancer increases almost twofold, compared to the general population, and more than threefold if the disease was diagnosed before the age of 50 (Pinto & AIRTUM Working Group, 2018, Reni, 2015).

Inflammatory bowel diseases, i.e. Crohn's disease and ulcerative rectocolitis, are also considered high-risk condition (Reni, 2015; Pinto, 2023). Finally, in the AIOM guidelines (2018), a person is further indicated as being 'at risk for rectal cancer' if they have at least one of the following characteristic: 40 to 60 years of age, with rectal bleeding associated with major changes in alvus persisting for at least 6 months; 60 or more years of age, with rectal bleeding and/or major changes in alvus persisting for at least 6 weeks; presence of palpable rectal mass, independently of age; men with particular parameters of anaemia not explained by other medical conditions; menopausal women with particular parameters of anaemia not explained in other ways; detection of faecal occult blood, independently of sex and age.

1.2.3 Symptomatology

The onset symptoms of CRC are non-specific and often underestimated by patients themselves (Dionigi, 2011; Rasmussen et al., 2015; Reni, 2015). Some symptoms are common to all sub-localizations of CRC: diffuse or localised abdominal pain, which can assume the characteristics of colic and be associated with borborigma and abdominal distension; transit disorders with changes in alvus (diarrhoea, constipation or mixed); mucorrhoea or pseudo-diarrhoea, which may mask a condition of intestinal obstruction; proctorrhagia and bleeding, which are most often revealed by chemical examination; anorexia; anaemia; asthenia; progressive weight loss (not justified); fever. According to the specific site of the cancer lesions, some symptoms are more prevalent: localised colic, diarrhoea, dyspepsia, asthenia, weight loss and fever are typical of right colon carcinomas; constipation and pseudodiarrhoea are characteristic of left colon tumours (with less frequent impairment of general condition); more marked bleeding (also independent of defecation) and tenesmus is more common in rectal tumours (Reni, 2015). The onset of disease with symptoms typical of advanced stage complications, i.e. occlusion due to mechanical ileus (more often seen in the left colon) or perforation of the intestinal wall (more often seen in the right colon), is significantly more uncommon (Dionigi, 2011).

1.2.4 Screening, diagnosis, and staging

Given the non-specific symptomatology of CRC, it is essential to implement screening programmes that facilitate the detection of risk conditions and early diagnosis.

Screening programmes for CRC have recently been implemented in both Europe and Italy. Specifically, the test offered every two years to the Italian resident population, aged between 50 and 69-74, is faecal occult blood detection with immunological testing, which when positive is followed by total colonoscopy (Ladabaum et al., 2020; Zhang et al., 2023; https://www.regione.piemonte.it/web/temi/sanita/prevenzione/screening-tumore-colon-retto).

The available screening tests by their nature can lead to low adherence by the population, as well as requiring a significant financial and structural cost, especially in the case of second-level endoscopic examinations (Ladabaum et al., 2020).

The diagnostic suspicion of CRC must be based on the clinical picture presented by the patient and characterised by the described symptoms.

Among the first examinations to be performed is the test that is also used in the screening phase, the search for faecal occult blood, in addition to laboratory tests, which can highlight anaemia, inflammation, electrolyte and liver function alterations. Of crucial importance is the endoscopic examination, the colonoscopy, which allows to determine the presence of lesions, perform tissue biopsies (to have histological confirmation). To obtain an exhaustive and complete staging of the disease, it is indicated to perform endorectal echo-endoscopy or magnetic resonance imaging, to assess wall infiltration and lymph node involvement, or abdominal ultrasound and thoraco-abdominal computed tomography, to detect distant metastases. Other instrumental examinations, such as bone scintigraphy, positron emission tomography and magnetic resonance imaging, should be used as appropriate to complete the diagnosis (AIOM, 2018, 2021a; Argilés et al., 2020; Mahmoud, 2022; Reni, 2015; Zhang et al., 2023).

In CRC, metastases primarily affect the peritoneum, regional lymph nodes, liver (especially in the case of colon cancer) and lungs (mainly in the case of rectal cancer). Given the presence of symptoms common to other intestinal diseases, the differential diagnosis must be posed with respect to Crohn’s disease, ulcerative rectocolitis, diverticulosis-diverticulitis, and benign neoplastic formations (Reni, 2015).

Therefore, the diagnosis of CRC must also take into account anatomo-pathological and histological characteristics of the lesion and the stage of the disease, as they have important implications for treatment and prognosis.

With regard to anatomo-pathological aspects, there are essentially four tumour forms: vegetating, which appears as an outgrowth with irregular margins; ulcerated, with characteristics typical of malignant ulcerations, with irregular and raised margins; infiltrating, with central ulceration and thickening of the intestinal wall, an evolution of the vegetating and ulcerated forms; annular-stenosing, involving the entire intestinal circumference and causing tract shrinkage and necrotic processes (Dionigi, 2011; Reni, 2015; Zhang et al., 2023).

Taking the histotype into account, in 85% of cases CRC is configured as an adenocarcinoma, while the remaining percentage of cases includes distinctly rarer and more unfavourable forms, such as mucinous adenocarcinoma, signet ring cell carcinoma, small-cell carcinoma, and medullary carcinoma (Reni, 2015; Kumar, Abbas, & Aster, 2015).

All these aspects contribute to determining the stage of the disease (**Table 1.1** and **Table 1.2**). Staging provides information on the extent of the disease and the most widely used system is the TNM, developed by the International Union against Cancer (UICC) and the American Joint Committee on Cancer (AJCC). It codifies the primary tumour according to three parameters: T – Tumour, size of the primary tumor (progressively from T1 to T4); N – Nodes, involvement of regional lymph nodes (N0 absent, N1 present); M – Metastasis, presence of distant metastases (M0 absent, M1 present). Their combination links the patient's condition to a precise stage (I to IV), at the increase of the latter the probability of recovery and survival of the subject decreases. Stage III represents a locally advanced disease, while stage IV denotes a metastatic disease (AIOM, 2021a; Brierley et al., 2016; Caligaris Cappio, 2015; Mahmoud, 2022). Approximately, 20% CRC cases are diagnosed at stage IV (Reni, 2015; AIOM, 2021a).

Table 1.1. TNM classification of CRC.

Classification	**Description**
TX	Undefinable primary tumour
T0	Undetectable primary tumour
Tis	Carcinoma in situ: intraepithelial or invasion of the lamina propria
T1	Tumour invading the submucosa
T2	Tumour invading muscle proper
T3	Tumour with invasion through the muscularis propria into the subserosa or pericyte and perirectal tissues not covered by peritoneum
T4	Tumour that directly invades other organs or structures and/or perforates the visceral peritoneum
T4a	Tumour perforating the visceral peritoneum
T4b	Tumour that directly invades other organs or structures
NX	Regional lymph nodes that cannot be evaluated
N0	Non-metastasis in regional lymph nodes
N1	Metastasis in 1-3 regional lymph nodes
N1a	Metastasis in 1 lymph node
N1b	Metastasis in 2-3 lymph nodes
N1c	Satellite tumor deposits in the subserosa or nonperitonealized jejunal and perirectal tissues without evidence of residual lymph node, vascular, or neural structures
N2	Metastasis in 4 or more regional lymph nodes

N2a	Metastasis in 4-6 lymph nodes
N2b	Metastasis in 7 or more lymph nodes
MX	Undetectable distant metastasis
M0	Absence of distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ (liver, lung, ovary, extra-regional lymph nodes)
M1b	Metastasis in more than one organ
M1c	Peritoneal metastasis with or without metastasis to one or more distant organs

T: Tumour; N: nodes; M: metastasis. Re-adapted from AIOM (2021a) and TNM (Brierley et al., 2016).

Table 1.2. Pathological subdivision into stages of CRC.

Stage	**Description**		
Stage 0	Tis N0M0		
Stage I	T1N0M0	T2N0M0	
Stage IIa	T3N0M0		
Stage IIb	T4aN0M0		
Stage IIc	T4bN0M0		
Stage IIIa	T1-2, N1a-c, M0	T1, N2a, M0	
Stage IIIb	T3, T4a, N1a-c, M0	T2-3, N2a, M0	T1-2, N2b, M0
Stage IIIc	T4a, N2a-b, M0	T3, N2b, M0	T4b, N1-2, M0
Stage IVa	All T, all N, M1a		
Stage IVb	All T, all N, M1b		
Stage IVc	All T, all N, M1c		

T: Tumour; N: nodes; M: metastasis. Re-adapted from AIOM (2021a) and TNM (Brierley et al., 2016).

1.2.5. Treatments and prognosis

Treatment choices are determined by the site, stage and operability of the tumour, but also by the patient’s general condition and characteristics such as age, other medical comorbidities, bowel obstruction, severity of symptoms (Abraha et al., 2018; AIOM, 2021a; Argilés et al., 2020; Mahmoud, 2022).

The chemotherapy, radiotherapy or their combination are defined as: neoadjuvant, when administered pre-operatively with the intent of downstaging, i.e. reducing the stage of the tumour, sometimes with the effect of reducing the tumour mass itself; adjuvant, when administered post-operatively (Dionigi, 2011). Pre-operative radiotherapy finds application specifically in rectal cancer, given its ability to prevent local recurrences. It is administered in a short-course or long-course regimen, indicating differences in dosage and fractioning in days, with cytoreductive effect. In combination with chemotherapy, pre-operative (chemo)radiotherapy has been shown to reduce the tumour mass and to increase the probability of a complete resection (Abraha et al., 2018; AIOM, 2021a; Argilés et al., 2020; Mahmoud, 2022). Furthermore, with similar results for the different modes of administration, long-term improvement in CRC-specific symptomatology and patients' well-being has been found. Notwithstanding, it may present adverse effects in some cases, with an impact on patients' physical and mental health, such as: drowsiness, skin erythema and/or dryness, scaling, hair loss, diarrhoea, proctitis, abdominal pain, frequent urination and dysuria, and early menopause (McLachlan, et al, 2016; Wiltink, et al., 2016),

Surgical resection appears to be the elective curative treatment for CRC, to be carried out with different timing depending on clinical characteristics, for example in rectal cancer surgery is indicated about 8-12 weeks after the end of pre-operative treatment. Surgery can be performed by lapascopy or laparotomy as appropriate, and the type of resection is differentiated according to the tumour characteristics: right haemicolectomy, for right colon cancers; transverse colon resection; left haemicolectomy, for tumours of the descending tract; sigmoidectomy; total mesorectal excision (TME), the standard technique for rectal cancers; abdominoperineal resection, used in tumours of the lower rectum, and also involves removal of the entire sphincter system (Abraha et al., 2018; AIOM, 2021a, 2021b; Argilés et al., 2020).

Connected to the surgical resection is the packing of an ostomy (distinguishable in colostomy or ileostomy, depending on the site of the tumour), i.e. the creation of an opening in the abdominal wall that connects a viscera with the outside. The ostomy may be temporary or permanent, depending on the radicality as well as the site of surgical resection (Abraha et al., 2018; AIOM, 2021a, 2021b; Argilés et al., 2020; Federazione delle Associazioni Incontinenti e Stomizzati, 2011).

Adjuvant treatment is essential to target and eradicate any micro-metastasis that may have disseminated. The use or not of such therapies depends on the pre-operative staging and the type of tumour. For colon cancer, the evidence does not support the systemic use of adjuvant chemotherapy in stage I and II, but it should be considered in the presence of adverse prognostic factors and/or particular risk conditions. At stage III, adjuvant chemotherapy has shown a 33% reduction in the relative risk of death, a statistically and clinically significant reduction in recurrences, and a 10-15% improvement in survival. With stage IV diagnosis, the use of chemotherapy may aim to prolong survival, delay disease progression and, in some cases, reduce the size of the tumour mass. For stage II and III rectal cancer, adjuvant chemotherapy is indicated (AIOM, 2021a, 2021b; Pinto, 2023).

Several factors affect the prognosis with a negative effect, starting with a delay in diagnosis. It is strongly correlated with the histotype and pathological stage of the disease at the diagnosis, and lymph node, metastatic and symptomatic progression. Additional adverse factors include:

the patient's age and the presence of serious diseases in comorbidity (AIOM, 2021a, 2021b; Pinto, 2023).

A recurrence of cancer occurs in a patient previously successfully treated. In the case of colon cancer, local recurrences are infrequent, whereas they are often located in liver, abdominal lymph nodes, peritoneum and lung. If the primary tumour is diagnosed at a stage that can be radically treated by surgery, the risk of recurrence is greatly reduced, with rates decreasing over time. In rectal cancer local recurrence is more frequent, probably due to the anatomical conformation of this tract. In the case of diagnosis in stage II-III, the risk of recurrence concerns about 20% of cases treated with surgery alone; a protective factor is represented by pre-operative radiotherapy treatments (AIOM, 2021a; Reni, 2015). The factors that may influence disease recurrence are various; the risk is higher in patients who smoke or are overweight and have unhealthy eating habits and inadequate vitamin D levels, which is a protective factor (AIOM, 2021a, 2021b; Pinto, 2023; Pullar et al., 2012).

The follow-up of patients with colorectal cancer involves the use of radiological and endoscopic investigations, the frequency and duration of which is complex to establish (usually scanned at 4-6 months for the first 3 years and every 6 months for the next two, up to the fifth year). Paying attention to the short- and long-term sequelae of the (chemo)radiotherapy, surgical resection and adjuvant treatment is crucial, as they affect the patient's life. Follow-up programmes and re-education of the cancer patient in more healthy lifestyles are two important factors that can positively influence recurrence prevention and health outcomes in general (AIOM, 2021a, 2021b).

1.3 Psychological aspect in cancer patients

The diagnosis of cancer involves a profound emotional and psychological disruption for the individual. Paying attention to the psychological aspects and outcomes related to mental well-being is fundamental for a comprehensive care of the cancer patient, from a biopsychosocial perspective. Indeed, psychosocial factors play an important role within the multicausal model of organic pathologies such as cancer, in which lifestyles and disease behaviours play an active and, in some cases, decisive role on the onset, progression and prognosis, together with biological and/or genetic (Amodeo & Torta, 2014; Antoni & Lutgendorf, 2007; Bolton & Gillett, 2019; Castelli et al., 2015). The development of studies in the field of psychoneuroendocrinoimmunology, which is linked to Selye's studies on the effects of stress, has highlighted interconnections and interdependencies between psychological factors (stress and mood disorders) and biological mechanisms involved in the pathogenesis and development of typically somatic diseases, according to a biomedical conception. The cognitive appraisal of an event as stressful and the prolonged occurrence of such stressful stimuli reactively activate numerous body systems (i.e., nervous, endocrine, immune, metabolic and circulatory systems), with problematic effects for the organism (Antoni & Lutgendorf, 2007; Bolton & Gillett, 2019; Bottaccioli, 2011).

For this reason, during the diagnostic and therapeutic pathway, it is crucial to involve the patient, taking into account not only the physical aspects but also the psychological ones, including mental adjustment to the disease condition, which is defined in terms of behavioural, cognitive and emotional responses to the stressful event (Amodeo & Torta, 2014; Castelli et al., 2015; Nicholls et al., 2014; Nordin & Glimelius, 1998). In fact, in one study, the patients evaluated as stressful also the psychological, social and daily aspects associated with the cancer condition, along with the somatic aspects of the disease (Wasteson et al., 2002).

1.3.1 Quality of Life

The World Health Organization – Quality of Life (WHO-QOL) group defined quality of life as "as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (The WHOQOL Group, 1995). It is a multidimensional construct concerning several areas of life: physical health, psychological health, independence, social relationships, living environment, spirituality, and personal beliefs (Delle Fave & Bassi, 2017).

A specific domain investigated over time is that of health-related QoL, which includes both physical-somatic manifestations and the perception of physical limitations caused by the disease and the assessment of self-reported health. When an individual is affected by a severe disease in some way disabling, the concepts of health-related QoL and general QoL become largely overlapping, as life is strongly affected by the disease (De Piccoli, 2014; Sitlinger & Zafar, 2018). In medicine, health-related QoL is considered to be a qualitative criterion in the assessment of the patient's living condition and the therapeutic intervention to which one is subjected. Accordingly, this construct provides an evaluation of "how" the patient will spend one's life, in addition to "how much" as an exclusively quantitative criterion, declined in terms of survival, and present for the longest time in clinical practice and research. The balance between quantity and quality of life takes on particular importance in oncology (Borasio et al., 2014). In cancer survivors, QoL is an index of their experience of treatments, changes in physical and psychosocial functions and disease burden (Ahn et al., 2017; Husson et al., 2015).

In research, the quality-of-life measure is used to predict possible adverse clinical outcomes (Ahn et al., 2017; Delle Fave & Bassi, 2017) and as an explanatory outcome of the individuals' condition. The studies often focus on measuring the impact of different clinical characteristics (such as tumour stage at diagnosis, presence of ostomy or faecal control problems) at different points in the disease history, or the impact of sociodemographic and psychosocial characteristics on patients' QoL levels in the short, medium and long term (Galić et al., 2014; Muzzatti et al., 2015; Sales et al., 2014).

Several factors appear to influence QoL levels in CRC patients as risk or protective factors. Although their interrelationships and influences remain to be defined, the psychological literature has highlighted the important role played by several psychosocial characteristics of individuals, such as personality traits and alexithymia, attachment styles, psychological resilience, emotional regulation skills, coping styles and perceptions of social support (Sales et al., 2014; Mosher et al., 2016).

1.3.2 Psychological distress and Post-Traumatic Growth

Various psychological factors not only contribute to determining QoL levels but also possible negative and positive psychological outcomes.

Psychological distress in cancer illness has been defined by the National Comprehensive Cancer Network (NCCN) 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." (Hess et al., 2015).

The term psychological distress is less stigmatising and opens the way to taking into account the needs of those who do not meet the nosographic criteria for defining mental disorders, but who nevertheless report suffering that goes beyond the purely physical distress associated with the illness (Hess et al., 2015).

In cancer patients, psychological distress has been recognised as the sixth vital parameter to monitor and treat (along with temperature, respiration, heart rate, blood pressure, and pain), as it affects perceived well-being and leads to negative outcomes through different biobehavioural pathways, such as poor adherence to treatment, adoption of an unhealthy lifestyle, and different symptom burden assessment (Sales et al., 2014)

It is important to consolidate early screening programmes for psychological distress, assessing it from the early stages of the disease and the early phases of treatments, as it may provide indications for the medium and long-term. For example, in a longitudinal study involving CRC survivors, high levels of psychological distress were recorded even five years after diagnosis (Dunn et al., 2013). The authors identified four subgroups of survivors on the basis of four trajectory patterns for psychological distress: about 19% of the participants showed a consistently low level ("Constant Low" model); almost 30% of participants, according to a "Medium Level" model, showed a U-shaped pattern (with an initial decrease in scores and a slight increase 4 years after diagnosis); 39% of survivors showed a constant increase ("Medium Increase" model) throughout the follow-up; finally, about 13% of participants showed a gradual decrease in scores, which were originally quite high ("High Decrease" model) (Dunn et al., 2013).

Different specifically medical aspects favour higher psychological distress in patients with CRC, such as the presence of medical comorbidities, bowel dysfunction and physical symptoms, especially in the first years after diagnosis (Mosher et al., 2016). However, events that may precede the diagnosis of CRC also have a negative influence on long-term psychological distress, such as the recourse to genetic testing (which would allow the early detection of familial forms or precursors of CRC) (Sales et al., 2014). Finally, fear of recidivism and a poor perception of self-reported health are recognised as specific risk factors for psychological distress (Ahn et al., 2017).

In patients with cancer pathology, it is often complex to frame the psychological condition using nosographic definitions and diagnostic criteria. However, evidence shows that diagnoses of depression, anxiety, adjustment and post-traumatic stress disorder are frequently reported. Even in cancer patients, depression and anxiety occurs with both psychological and somatic symptoms, which are difficult to differentiate from the more common and generic symptomatology that accompanies the onset and progression of cancer (e.g., insomnia, weight loss, fatigue) (Borio & Torta, 2014; Graça Pereira et al., 2012; Mosher et al., 2016; Peng et al., 2019; Sales et al., 2014; Wagner, et al., 2017). The importance of recognising not only the clinical but also the pre-clinical conditions of mental disorders in cancer patients is underlined by mortality data showing a 39% increase in those who meet the criteria for depression and a 25% increase in those with clinically relevant depressive symptoms (Wagner et al, 2017). In fact, psychological distress represents not only an outcome that can be influenced by various sociodemographic and psychosocial variables, but also a factor that affects QoL, often contributing to its reduction (Mosher et al., 2016; Ye et al., 2017).

However, positive psychological outcomes can also be found in cancer patients following the disease. Over the years, researchers have become increasingly interested in the positive outcome of a traumatic event. Particularly, Post-Traumatic Growth (PTG) is a psychological construct, developed by Tedeschi and Calhoun (1995) and defined as positive psychological change resulting from a struggle with traumatic life circumstances, that challenged beliefs about life. PTG indicates not a return to the baseline condition, before the traumatic event, but an improvement determined by cognitive processing and restructuring (Wang et al., 2023a). This subjective perception of positive change concerns different domains of the individual's life: change in priorities and new possibilities, appreciation of life, spiritual dimension, interpersonal relationships, and sense of life (Calhoun & Tedeschi, 2006; Tedeschi & Calhoun, 2004).

PTG indicates both the cognitive process of change and its outcome. The models that attempt to explain its occurrence assume that the traumatic event violates the individual's beliefs about self and world and, consequently, activates a process to reconstruct beliefs and goals, resulting in personal growth (Ben-Zur et al., 2015). The socio-cognitive processing model, for example, emphasises the importance of cognitive elaboration of the traumatic event in determining growth (Dong et al., 2017). Post-traumatic growth is considered a universal phenomenon, which is influenced by cultural variables (Ben-Zur et al., 2015; Tedeschi & Calhoun, 2004).

A cancer diagnosis can be considered as a traumatic event, and certain characteristics of cancer may provide opportunities for PTG. For example, patients may experience uncertainty about the possibility of recurrence, but this same feeling may lead them to try to live their life as best they can, with a new appreciation. In addition, a cancer diagnosis can be a circumstance that also drastically changes the organisation of the individual’s life, which begins to be marked by “medical time”, and from which may arise a desire to find a new balance. Finally, cancer confronts the individuals with their own mortality and finiteness, leading them to re-evaluate their beliefs, values and, in general, their own spirituality (Cordova, 2008). In cancer survivors of an Italian study, for example, these positive aspects were more present than worry, uncertainty and dissatisfaction with their lives (Muzzatti et al., 2015).

However, the relationship between psychological distress and post-traumatic growth appears still unclear, due to the limited number of studies and the heterogeneity of methodologies and instruments used. Some research has pointed out that these two conditions may co-occur, suggesting that they are not mutually exclusive (Casellas-Grau et al., 2016; Cordova et al., 2017; Romeo et al., 2017b).

Besides factors strictly related to the type of cancer, research has highlighted that different psychological aspects are associated with PTG in cancer patients (Casellas-Grau et al., 2016; Cordova, 2008; Cordova et al., 2017; Romeo et al., 2019; Tedeschi et al., 2018; Wang et al., 2023a).

Socio-demographic and psychosocial variables that are often significantly associated with PTG following a cancer diagnosis (also in CRC) include: young age, being in a significant relationship, being employed and having a higher level of education; a greater perception of social support and cognitive and personality factors, such as the use of more active coping styles and optimism; a stronger perception of a threat to life, especially evident in more severe stages, and more intentional attempts to process the event (Cordova, 2008; Dong et al., 2017; Schmidt et al., 2012; Wang et al., 2023a).

To date, there have been few studies examining the changes and predictors in psychological distress and PTG in CRC longitudinally, and most of them focused on survivors, disregarding the early stages of cancer treatment from the time of diagnosis communication (Occhipinti et al., 2015; Qaderi et al., 2021; Song et al., 2022; Wang et al., 2023a).

1.4 Impact of treatments and psychosocial factors

1.4.1 Impact of colorectal cancer treatments

The psychological reactions of the cancer patient are also closely related to the stage of the tumour, the phase of the diagnostic and treatment pathway, the therapies, and their sequelae.

In the treatment of CRC, there are several treatments indicated by the guidelines and each one presents a stressful condition for the patient physically and mentally, due to the characteristics of the treatment itself and the possible adverse effects it may involve.

Radiotherapy, pre-operative in the case of rectal cancer treatment, often appears to be the cancer intervention of which patients have the least knowledge and understanding about functioning. This attitude undermines the benefits derived from being an active part of their own treatment process (Smith et al., 2017) and can lead to high levels of anxiety and depression (Mackenzie et al., 2015). Although more than 60% of cancer patients receive radiotherapy (Hernández Blázquez & Cruzado, 2016) and 22-35% of them report clinically relevant psychological distress (Riedi et al., 2018), only few studies have focused on the psychological distress before starting radiotherapy (Rades et al., 2023) and subsequent impact of this treatment specifically in CRC patients (Acquati et al., 2022).

In the literature, the estimated need of psychosocial support for radiotherapy patients is around 14%–50% (Kirchheiner et al., 2013), frequently not including some variables that could further influence this need of support: the type of cancer, the therapies previously received, the degree of cultural openness to the request of psychological support, and intrinsic characteristics of the individual. At the same time, it appears that between 13% and 41% of patients receiving radiotherapy accept being sent to a psychology service if it is actively suggested to them by medical staff, and that the request comes from the patients themselves in cases of high levels of pain, reduced independence, need for help in daily life and decreased functional status (Riedi et al., 2018).

Similarly, it is important to understand the impact that resection surgery can have on patients, especially in the case of ostomy packing. Living with an ostomy involves numerous physical changes and a significant psychological impact, due to the loss of significant bodily functions (such as evacuation control, sexual and urinary dysfunction) and the alteration of body image, which can often result in low self-esteem, social withdrawal, depression and suicidal ideation in patients (Alenezi et al., 2021; De Luca et al., 2018; Dong et al., 2017; McLachlan et al., 2016). The patient, potentially candidate for ostomy, should be informed of this possibility prior to surgery, providing support and guidance in dealing with the difficulties of ostomy management and what it can involve on a nutritional and psychological perspective (AIOM, 2021a, 2021b).

Different treatments for CRC have several effects on QoL. One study compared the outcomes of “watch-and-wait” treatment, in which patients receive (chemo)radiotherapy alone, with the outcomes of treatment including surgery. The former showed better outcomes in most dimensions of QoL, possibly because patients did not experience the physical and psychological consequences of surgery, although according to the authors, these patients may have felt more insecure due to more frequent follow-ups (Hupkens et al., 2017).

In the specific case of patients with rectal cancer, comparing the effects on QoL of two types of pre-operative treatment, short-course radiotherapy or long-course (chemo)radiotherapy (both of which reduce the risk of recurrence), no significant differences were found between the two treatments (McLachlan et al., 2016; Wiltink et al., 2016). This finding was consistent with a previous literature review that highlighted the need to wait for assessment three months after surgery to see an improvement in patient QoL (Sales et al., 2014).

Treatments and their consequences also show a significant impact on psychological distress. The optimal frequency of psychological distress assessment during treatments is still unclear, and it is important to understand this so as to monitor changes during therapies and provide timely support to the patient. In CRC patients also undergoing radiotherapy, evaluations conducted at one-week intervals had shown that psychological distress levels were high at the beginning of therapy, probably due to patients not knowing what to expect from this type of treatment. However, the psychological distress levels decreased after a few sessions of therapy, and rised again after a few weeks, when the first side effects and symptoms of the treatment appeared (Hess et al., 2015; Sales et al., 2014). In a longitudinal study with assessments before starting radiotherapy, at the end of the treatment and one month after the end, almost 47 % of the participants had experienced mental disorders at some time during the study, with a higher frequency of anxiety disorders at each assessment points, in accordance with the results of previous studies. Also in this case, a higher frequency of anxiety disorders at the end of radiotherapy was shown (Hernández Blázquez & Cruzado, 2016). Studies on different types of cancer had found the presence of clinically relevant anxiety symptoms between 5% and 21% of patients undergoing radiotherapy, and clinically relevant depressive symptoms between 13% and 24% (Frick et al., 2007; Hervouet et al., 2005; Kelly et al., 2007; Maher et al., 1996; Mckenzie et al., 2013; Neilson et al., 2013).

Regarding the impact of surgical resection, an impact is evident not only on negative but also on positive psychological outcomes. In fact, living with ostomy is also recognised as a specific risk factor for psychological distress in CRC patients (Alenezi et al., 2021; De Luca et al., 2018; Sales et al., 2014).

However, several studies found that subjects undergoing more onerous treatments also experienced greater personal growth (Jansen et al., 2011; Romeo et al., 2017).

Dong and colleagues (2017), in fact, found higher levels of PTG in CRC patients with permanent ostomy, compared to patients who had not required permanent ostomy in another study.

The limitations in scientific knowledge in this field that still persist are related to methodological aspects and also to the choice of sample.

Patients with rectal cancer and those with colon cancer present peculiarities with regard to both the psychological impact of planned treatments and individual needs (Rivard et al., 2022), but are often considered together in studies focusing on psychosocial aspects.

Several psychosocial aspects play a role in determining adaptation to the disease and treatments and represent risk and/or protective factors not only for the physical but also for the mental well-being of patients diagnosed with CRC.

1.4.2 Personality traits

In the field of studies on personality and role played by different traits in particular populations, there are several configurations that have interested researchers who have investigated in patients with cancer diseases.

Over time, individuals with certain personality traits may be more vulnerable to chronic stress situations and consequent physiological alterations and biological reactions, which are implicated in the multicausal processes of pathogenesis.

In 1996, type-D personality (or distressed type personality) was first described based on studies among patients with cardiovascular diseases. Type-D personality was described as the tendency to simultaneously experience negative emotions and inhibition of emotion expression and social relationships. In early studies, it was associated with high levels of depression and social alienation in patients (Denollet et al., 1996). High levels of negative affectivity and social inhibition are the distinctive traits of this personality pattern. Negative affectivity is defined as the tendency to experience negative emotions over time and in different situations, with an increased frequency of dysphoric feelings, anxiety, irritability, and negative views of self and future. Social inhibition is the tendency to repress emotions and their expression in social interactions, showing up nervous and insecure, for fear of the reaction or disapproval of others. Individuals exhibiting these traits are more vulnerable to developing chronic illnesses, depression, anxiety and irritability, post-traumatic stress symptoms, and increased risk of physiological hyperreactivity, low levels of subjective and psychological well-being and positive affect, and adverse outcomes in terms of both morbidity and mortality (Denollet, 2005). Type-D personality predicts significant impairments in QoL and cancer patients with these traits report an increased number of somatic symptoms and a lower degree of adjustment to their disease condition. Finally, it is associated with greater dissatisfaction with the care and the doctor-patient relationship, the perception of receiving insufficient information about one's illness, and greater utilisation of health services (Mols et al., 2012).

In more recent years, type-D personality has been increasingly studied in CRC patients. Approximately 19% of CRC survivors report these traits, similar to findings in studies on patients with different types of cancer. CRC patients with type-D personalities reported more severe and prolonged cancer-related consequences, appeared more anxious about their disease, and more often indicated psychological distress as a causal factor of disease, compared to those without such traits. They also reported worse levels of health-related QoL, cognitive and emotional functioning, and more physical symptoms, such as insomnia, diarrhoea and/or constipation, problems with ostomy, sexual difficulties and a worse perception of body image, higher levels of anxiety and depression, and worse predictions for the future (Husson et al., 2015; Mols et al., 2012; Zhang et al., 2016), with a further deterioration at 6 months post-diagnosis, probably due to the tendency for increased negativity (Zhang et al., 2016).

CRC patients with these personality traits are also at risk of a lower probability of complying with guidelines on physical activity and alcohol consumption, with a negative effect on health behaviours and mortality risk (Husson et al., 2017; Schoormans et al., 2017).

With respect to the possible implications of type-D personality on personal growth, there are still few studies available, especially in the CRC. However, several studies have reported conflicting results on the role of personality in promoting or not PTG in these patients (Knauer et al., 2022).

1.4.3 Attachment styles

In the early theorisations on attachment, Bowlby wanted to provide a biological structure to aspects of the individual's psychological development and an explanation of the relationships of closeness and care (Bowlby, 1969; Romeo et al., 2017a). The attachment style determines the way of being in a relationship with the other, in terms of defining the image of self and the image of the other (Bowlby, 1969). Starting with theorisations on attachment in childhood (Ainsworth et al., 1978; Bowlby, 1969), different approaches have been proposed to define adult attachment styles. The models of self are related to the perception of self and of being worthy of support, while models of other affect expectations of receiving care and the trust that should be placed in the other. These models are independently positive or negative and, as proposed by Bartholomew and Horowitz (1991), when combined they provide a description of four prototypical styles of attachment, one on the security side and the other three on the insecurity one. Each style defined in this way has been matched with different illness behaviours, characterised by different levels of symptom perception and health care recourse (Porcelli, 2022; Romeo et al., 2017a).

The secure style is found in adults who had, presumably, available caregivers. These adults perceive themselves as worthy of support, accept appropriate levels of dependency in relationships and are able to ask for, receive and provide assistance and care, exhibiting low levels of somatic symptoms perception and normal use of services.

Among the insecure attachment styles are the dismissive style that originates from relationships with unavailable and inadequate caregivers, so that the individual has learnt to rely highly on oneself and resents being dependent on others and trusting in others (which is also evident with health care figures), having an altered perception of physical symptoms and making a limited use of health care services. In contrast, the preoccupied style characterises individuals whose caregivers have been available discontinuously and unpredictably. they are individuals who are emotionally dependent on the approval of others, they have low self-esteem and tend to focus on negative emotions, demand excessive care, and show a high perception of symptoms and use of services. Finally, the fearful style concerns individuals who had openly rejecting or rigid caregivers. As a result, these individuals have developed a negative self-model, characterised by low trust and self-esteem; they manifest a desire for closeness but inhibited by fear of rejection, and report a high perception of symptoms, with low use of health services (Bartholomew & Horowitz, 1991; Porcelli, 2022; Romeo et al., 2017a).

Attachment styles are considered significant predictors of psychological adjustment in individuals with chronic conditions (Hamama-Raz & Solomon, 2006; Turner-Cobb et al., 2002) and it is known that insecure attachment makes individuals more vulnerable to negative post-traumatic outcomes, whereas secure attachment plays a protective role (Woodhouse et al., 2015).

It is not yet clear how attachment styles influence adaptation to illness and consequently physical and mental health outcomes. However, there is evidence of a higher proportion of insecure attachment in cancer patients, compared to the general population, associated with poor adaptation to illness and high levels of catastrophising pain experiences, supporting the idea that individuals with anxious attachment experience a more severe condition due to hypervigilance over symptoms (Nicholls et al., 2014).

Furthermore, the insecure style exposes patients with metastatic cancer to an even greater risk of experiencing more severe depressive symptoms, associating with other psychosocial risk factors (Lo et al., 2010). In an Italian study, it was found that patients with an anxious style showed greater hopelessness and worry about the disease (Cicero et al., 2009).

A number of studies have focused on analysing the relationship between different attachment styles and the development of post-traumatic psychopathological symptoms, emphasising the protective value of a secure attachment, which entails a greater possibility of experiencing positive changes. In a study among survivors of different types of cancer, secure attachment was correlated with higher PTG (Schmidt et al., 2012).

1.4.4 Psychological resilience

Resilience, in physics, indicates the characteristic of certain materials and objects, which are able to resist shocks and strain without suffering any effects on their integrity, later returning to their original form. Similarly, the concept of psychological resilience indicates the ability of an individual to display appropriate levels of competence following exposure to significantly adverse events, referring to the positive psychosocial adaptation behaviours that are enacted when physical and/or psychological integrity is at risk. Resilience is a positive psychological trait that promotes positive adaptation to stressors and adversity, including medical illness (Gouzman et al., 2015; Inguglia & Lo Coco, 2013; Sihvola et al., 2022; Wang et al., 2023a). Resilient individuals are particularly able to adaptively use both internal and external available resources and thus employ more adaptive coping strategies (Gouzman et al., 2015; Sihvola et al., 2022).

Resilience would act through the processes of reducing the impact of risk factors and negative chain reactions, maintaining self-esteem and self-efficacy and being open to opportunities. Resilient individuals, even in situations of stress related to chronic diseases (including cancer), are shown to be more focused on positive emotions and able to cope with events with flexibility (Ye et al., 2017).

Moreover, research showed that high levels of resilience were associated with better physical health outcomes and more positive psychological conditions, consequently contributing to higher levels of adaptation to illness and QoL (Dong et al., 2017; Gouzman et al., 2015; Ye et al., 2017).

This construct is affected by sociocultural aspects. Resilience and QoL levels appeared generally significantly lower in the Chinese cancer patient population, compared to Western patients, probably due to the different meaning attributed to the request for support at a cultural level, as well as by the individual. In this population, the high levels of resilience were associated with a reduction in the risk of experiencing anxiety, depression and psychological distress, by 64%, 70% and 90%, respectively. This had a consequent positive effect on the study participants' perceived QoL levels, confirming across cultures this finding (Ye et al., 2017).

Identifying cancer patients with poor resilience, from the time of diagnosis, would enable to provide them with earlier psychosocial support, in the medical treatment pathway and follow-up, for an improved long-term adjustment (Gouzman et al., 2015). A pilot study of patients with metastatic CRC (advanced or terminal stage of disease) showed an association between levels of resilience and hope at the end of life (Solano et al., 2016).

Resilience appears to play a role in the development of PTG. Specifically, in patients with digestive cancer, a positive association was found between resilience, positive affectivity, and PTG (Gouzman et al., 2015). Also, in a study on CRC patients with permanent ostomy emerged an association between high levels of resilience and high levels of PTG (Dong et al., 2017).

1.4.5 Alexithymia and emotion dysregulation

In the context of studies on the bidirectional interaction between mind and body, the interest in the psychoneurobiological mechanisms of affective regulation and the role of social interactions has developed (Taylor, 2005). Emotional response involves three types of interrelated processes: neurophysiological, motor or behavioural/expressive and cognitive/experiential (i.e., awareness and ability to express emotional states). Generally, the process of emotional regulation depends on the integration of these processes with the environment (Porcelli & Todarello, 2005; Epifanio et al., 2014).

Thus, social interactions require the regulation of emotions, using a range of processes, depending on the goals, to alter their duration or intensity. However, some individuals present a chronic inability in their modulation, which generates psychological, psychopathological, relational problems and a reduction in physical well-being (Sighinolfi et al., 2010).

Taylor proposed a reading of the construct of alexithymia that could explain emotional regulation disorder, in which there is a deficit in the cognitive-experiential domain (Epifanio et al., 2014; Luminet et al., 2019).

The term alexithymia derives from ancient Greek and, literally, means a "lack of words for emotions". It was first introduced in the psychosomatic field in 1973 by Nemiah and Sifneos, based on behavioural observations of patients with "classical psychosomatic illnesses", of which it appeared to be a characteristic (Caretti et al., 2005; De Vries et al., 2012; Luminet et al., 2019; Porcelli, 2022; Sales et al., 2014).

The nature of alexithymia has long been debated as to be considered a stable personality trait (or primary alexithymia) or a momentary pathological state consequent to disease (or secondary alexithymia). Today increasing evidence intends it as a transnosographic clinical dimension, to be seen along a continuum from normal to pathological, not as an "all-or-nothing" phenomenon of general inability of recognition and expression of emotions (Caretti et al., 2005; Epifanio et al., 2014; Luminet et al., 2019; Messina et al., 2014).

Characteristics of alexithymia include: difficulty in identifying emotions and distinguishing between subjective emotional states and somatic components of emotional activation, so that the expression of emotion occurs more through the physiological component; difficulty in describing emotions, with low awareness of the emotional states experienced, intense emotional manifestations, unrelated to the specific situations from which they originate; externally oriented thinking, with a preponderance of rational thought, resulting almost devoid of emotional participation and empathy; finally, poverty of fantasy and of the functions related to it, also found in the scarce dream activity characterised, for the most part, by the reproduction of daytime events (Luminet et al., 2019; Porcelli, 2022).

With regard to the development of alexithymia, several theorists have considered the impact of relationships with unresponsive primary caregivers and insecure attachment styles as crucial. Therefore, a difficulty in mentalising one's own internal states emerges, which leads to regulation through acting out behaviours; there is also a greater disposition to undifferentiated negative affective states and a poor capacity to experience positive ones (Caretti et al., 2005; Luminet et al., 2019).

Alexithymia plays a role in the onset and maintenance of symptoms of psychiatric and physical conditions, such as substance abuse, pathological gambling, eating and somatoform disorders, chronic pain, stress disorders, asthma, myocardial infarction, hypertension, diabetes, HIV, inflammatory bowel disease and cancer (Benfante & Romeo, 2023; Carrozzino & Porcelli, 2018; De Vries et al, 2012; Di Tella et al., 2023; Martino et al., 2020; Porcelli, 2022) Furthermore, it appears to be associated with impaired immune function in both clinical and healthy populations, psychosocial maladjustment, high recourse to medical care, and poor treatment adherence (Porcelli, 2022).

Research in psycho-oncology has usually analysed the correlation of this construct with variables such as somatisation, depressive symptoms, psychological distress, pain, coping styles and QoL. The most common feature in alexithymic patients was found to be externally oriented thinking that results in more negative perceptions of the illness, along with negative beliefs about its control and tractability and more intense negative feelings towards the disease condition (Okanli et al., 2018).

Many studies have been conducted on women with breast cancer, demonstrating a higher proportion of alexithymic patients among them compared to healthy subjects. For example, in an Italian study among women had not yet undergone clinical examination, in the absence of signs and symptoms of disease, the rates of alexithymia were 20.5% in the subgroup with a subsequent positive diagnosis of neoplasia, compared to 4.5% in the subgroup negative for any breast pathology (Epifanio et al., 2005). Similarly, in a study that evaluated alexithymia prior to the endoscopic screening examination, a significantly higher frequency of alexithymic subjects was found among those who were subsequently diagnosed with a colon disease (adenoma or adenocarcinoma) (Lauriola et al., 2011). A review pointed out, already from the few studies examined, the presence of controversial outcomes, probably also due to the still open debate on the possibility of distinguishing between primary and secondary (i.e., trait or state) alexithymia; despite this, it is important to consider its negative effects on symptom recognition, treatment adherence, and physical and psychological outcomes (De Vries et al., 2012).

Only few studies have examined the association between alexithymia and PTG, suggesting that alexithymia prevents the development of PTG (Cakmak et al., 2021; Orejuela-Dávila et al., 2017).

1.4.6 Trait and state affectivity

Positive and negative affectivity are the dimensions that describe affective experience and emotional components of subjective well-being. This construct was developed mainly from the studies of Ed Diener, who defined it as an evaluation that the individual gives of one's own life, consisting of a cognitive and an emotional component, the perception of life satisfaction and positive and negative affectivity, respectively. They refer both to a particular period or event (i.e., state affectivity) and to the whole life (i.e., trait affectivity) (De Piccoli, 2014; Hart & Charles, 2013; Sales et al., 2014; Voogt et al., 2005). Distress, unpleasant involvement, anger, disgust, guilt, fear are included in negative affectivity, while positive affectivity is defined by pleasant emotional states, being active, alert, enthusiastic and promotes psychosocial adjustment to cancer (Hart & Charles, 2013; Sales et al., 2014; Voogt et al., 2005).

Studies on cancer patients had found low levels of positive affectivity and an association between levels of negative affectivity and poorer physical functioning and fatigue (Sales et al., 2014). In patients with gastrointestinal cancer, the reactions to diagnosis and the outcomes of surgery represent two factors that correlate strongly with their subjective and emotional well-being (Nordin & Glimelius, 1998).

Both positive and negative affectivity seem to be associated with PTG, however only a few studies are specifically on CRC patients (Ben-Zur et al., 2015; Gouzman et al., 2015; Yu et al., 2014). In particular, PTG appears to be positively associated with positive affectivity, even in patients with CRC as in women with breast cancer. Conversely, it does not appear to be negatively related to negative affectivity, in contrast to studies showing a concomitant decrease in psychological distress, which is often accompanied by a negative emotional state. The results of this study show that PTG may also act as a personal psychosocial resource, limiting the effects that the illness event has on well-being (Ben-Zuret al., 2015). However, further studies are needed in this specific population.

1.4.7 Cancer-related coping styles

Psychological adjustment to illness is determined, in addition to the individual's trait characteristics, by various situational factors (such as the impact of treatments and their consequences) and the modalities in which an individual copes with a stressful condition such as the disease. These strategies are partly elicited by past experiences and closely related to resilience levels.

The term coping refers to those cognitive, behavioural, and emotional strategies that an individual implements to cope with a stressful situation. Lazarus and Folkman (1987) define coping as an effort to manage external and/or internal demands that exceed the individual's resources, thus as a process that can change over time and depending on the situation (Galić et al., 2014; Nordin & Glimelius, 1998; Wasteson et al., 2002). From their studies on cognitive appraisal of stressors and the mediation of appraisal on the responses enacted, two groups of strategies are identified: those problem-focused, in which the situation appears to be addressable, focusing on cognitive resolution and restructuring of the event and minimisation of the effects (Delle Fave & Bassi, 2017; Galić et al., 2014); those emotion-focused, of which are identified passive forms, which focus on elicited distressing emotions and of which avoidance is an example, and active forms (such as that identified in emotional approach coping), which cope with the situation through the recognition and verbal/non-verbal expression of emotions related to the event (Reese et al., 2017).

In CRC patients, it was found that the latter coping approach had psychological benefits, with less depressive symptoms (Reese et al., 2017). Furthermore, there would appear to be gender-related differences in these coping strategies in CRC patients. In fact, women employed them more often, showing to perceive greater benefits than men (Rinaldis et al., 2010).

In addition to the broader distinction between problem-focused, emotion-focused and meaning-focused coping strategies, several cancer-specific coping styles have been identified.

Greer and colleagues (1987, 1991) recognised five possible emotional responses to the diagnosis of cancer and their manifestations:

- Fighting spirit, in which an attitude of optimistic confidence in the ability to fight and defeat the disease is found.
- Denial, in which there is a tendency to minimise the event and an attitude of indifference.
- Fatalistic attitude, in which a tendency towards passive resignation to the disease and a lack of opposition prevail.

- Anxious preoccupation, which presents with reactions of alarm and distress with respect to the disease and its consequences, with a committed search for information that maintains or increases the state of tension.

These responses largely overlap and are integrated with the four coping styles identified by Burgess and colleagues (1988), distinguished on the basis of the differences in the depression and anxiety levels, in the type of locus of control (i.e., perception of causality of life events) and in the behavioural and coping responses implemented:

- Hopelessness/Helplessness, presenting high levels of anxiety and depression, absence of strategies aimed at acceptance of the diagnosis, external locus of control regarding the disease.
- Fighting spirit, characterised by moderate levels of anxiety and depression, confrontational behaviour, internal locus of control.
- Denial/Avoidance, presents absence of anxiety and depression, absence of cognitive strategies, internal and external locus of control.
- Stoic acceptance, characterised by low levels of anxiety and depression, absence of confrontation behaviour, fatalism attitude and external locus of control (Scalabrino & Malabaila, 2014).

These coping strategies were also investigated in patients with gastrointestinal cancer, although only in a few cases a cancer-specific model was used. The main findings were the presence of similar patterns between patients with treatable and untreatable cancer, and the association between high scores in the Fighting Spirit and the Fatalism styles and higher QoL scores (Nordin & Glimelius, 1998).

Besides the criteria used to identify the styles, there is agreement that coping strategies, which promote a more active and differentiated strategies of dealing with disease-related issues, are found to facilitate disease adjustment and improve patients' QoL and levels of perceived psychological distress. This also partly contributes to promote increased levels of PTG, especially in survivors (Casellas-Grau et al., 2016; Cakmak et al., 2021; Galić et al., 2014; Knauer et al., 2022; Scalabrino & Malabaila, 2014; Schmidt et al., 2012; Wang et al., 2023a).

More generally, it has been shown that passive coping strategies are associated with excessive activation of the hypothalamic-pituitary-adrenal axis and low stimulation of the sympathetic-adrenal system, resulting in an immunosuppressive effect and an increased risk of developing chronic diseases, including oncological ones (Galić et al., 2014; Sales et al., 2014)

In certain conditions, such as those of cancer patients, the recourse to external resources such as support provided in interpersonal relationships can also broadly function as a manner of coping with stress.

1.4.8 Perceived social support

Interpersonal relationships affect the promotion of health both directly and indirectly, as sources of well-being and positive emotions, and support in stressful conditions. Biological mechanisms involved in the production of various neurochemical substances, which facilitate relaxation and sedation, and are traced in the development of attachment and affiliative behaviour, such as oxytocin and endogenous opioids, contribute to the development of interpersonal relationships and their positive effects on the individual (Delle Fave & Bassi, 2017). Endogenous opioids are also produced in the hormonal reaction to stress mediated by activation of the hypothalamic-pituitary-adrenal axis, modifications of which have also been found in various psychopathological disorders (Amodeo & Torta, 2014).

The construct of social support is complex and multidimensional, with cross-cultural effects. It represents an important external resource for those coping with a serious illness condition and influences the cognitive process of adaptation, which is facilitated in individuals with high levels of support (Binaschi et al., 2014; Mosher et al, 2016; Dong et al., 2017).

An Italian study had highlighted the predictive role of social support on the levels of adjustment to cancer disease and patients' psychosocial well-being. In addition to partner support, the contribution of other family members and friends was also important. The support received from the others seemed to be associated with the patient's tendency to view cancer as a challenge, to take a more active role in treatment, and with less resignation and passive acceptance of the situation (Cicero et al., 2009). Probably being in relationships based on trust, closeness, with high emotional intimacy, could facilitate the processing of thoughts and emotions related to the stressful event (Reese et al., 2017). Moreover, in CRC survivors a positive association between high levels of social support and psychological growth, consequent to the disease considered as a traumatic event, has been found (Binaschi et al., 2014; Mosher et al., 2016; Dong et al., 2017).

In contrast, oncology patients with poor perceived social support show higher levels of psychological distress and worse QoL (Dunn et al., 2013; Galić et al., 2014).

The study by Rieti et al. (2018) on patients undergoing radiotherapy had shown that a poor perception of social support affected the perceived need to ask for psychological support and, consequently, the lack of recognition of one’s suffering.

All these aspects should be investigated together to understand their interrelation and specific implications in CRC patients. In this way, patient-tailored screening and intervention programmes could be structured for a more integrated care.

Chapter 2.

Research project – An exploratory prospective observational cohort study

2.1 Introduction

Receiving a cancer diagnosis can be an extremely stressful traumatic event. This event is a source of great disruption in the life of the individual, pervading the sense attributed to the experience of self and one's life, including its future quality. The cancer patient experiences changes affecting physical as well as psychological and social dimensions.

With respect to the physical dimension, the change concerns the body in a disabling way. While, regarding the psychological dimension, this change refers to assuming a new idea of oneself as a "patient" and to the "existential threat" intrinsic to oncological pathology. Finally, the change relating to the social dimension involves interference with one's social roles, both from a family and relational perspective (Torta & Mussa, 2007).

Therefore, cancer patients may experience multiple psychosocial problems, which contribute to increase psychological distress and impair QoL. The incidence of clinically relevant levels of psychosocial distress has been reported in 20-35% of cancer patients (Kendal et al., 2011). On one hand, the diagnosis of cancer can trigger a series of negative psychological consequences, ranging from anxiety and depressive symptoms to the development of psychopathological disorders; on the other hand, it can also be a stimulus for a psychological growth process referred to as PTG (Tedeschi et al., 1998; Tedeschi & Calhoun, 2004). The possibility that psychological distress and PTG are not mutually exclusive can be understood in light of multidimensional models of emotional well-being, which would suggest that adaptation to illness is not exclusively dichotomised into positive and negative (Cordova, 2008). PTG is defined as the tendency, following trauma, to report positive change characterised by increased levels of appreciation for life, intimacy in relationships, personal strength, recognition of new possibilities, and spiritual growth (Tedeschi et al., 1998; Tedeschi & Calhoun, 2004). The term PTG refers both to the cognitive process of change, which begins when one is confronted with events of high traumatic potential, and to the outcome of this process itself. Although the literature suggests that PTG is associated with clinical and socio-demographic variables, such as the time since diagnosis, the patient's age, the presence of an adequate social support and the use of appropriate coping strategies, which promote a positive re-elaboration of the event (Cordova, 2008; Schmidt et al., 2012; Dong, et al., 2017), to date, there are no definitive conclusions about this aspect. Therefore, it is necessary to conduct further studies on which medical-clinical, socio-demographic and psychological elements, influencing the re-elaboration and acceptance of the disease condition, may influence the psychological and QoL outcomes, eventually promoting PTG.

In particular, it was chosen to focus the study on CRC, that is the most frequent malignant neoplasm of the gastrointestinal tract (Reni, 2015; Fidler et al., 2017). According to Italian epidemiological data of 2018, excluding skin cancers (non-melanomas), CRC was the second most frequent neoplasm for both sexes, and it was among the top five neoplasms in order of frequency, in all three age groups considered (<50 years, 50-70 years, >70 years). The survival rates at 5 and 10 years after diagnosis were 66% and 64% of colon cancer patients and 62% and 58% of rectal cancer patients respectively (Associazione Italiana Oncologia Medica & Associazione Italiana Registri Tumori, 2017). Surgical resection appears to be the treatment of choice for CRC. A pre-operative (neoadjuvant) (chemo)radiotherapy treatment aimed at downstaging, i.e. reducing the stage of the tumour, may also be included in the treatment pathway to improve local control of the tumour and, in general, the curative outcome for these patients. In some cases, adjuvant chemotherapy may also be indicated, with a survival advantage (Pinto & AIRTUM Working Group, 2018). Radio/chemotherapy and surgical treatments can lead to important physiological changes, some of which may persist even after recovery, with important consequences on the personal and social life of patients. For example, the changes in habits and lifestyle faced by an ostomy patient, or the repercussions on the emotional life of the sexual dysfunctions, that often result from such treatments (Mosher et al., 2016; Sales et al., 2014).

The ability to cope with the stress related to the entire treatment pathway and to re-elaborate the traumatic experience, translating it into a stimulus for psychological growth, has an important impact on adjustment to the disease and, consequently, on the QoL and psychological well-being of CRC patients.

2.2 Objectives

The main aim of this exploratory prospective observational cohort study was to investigate the change in PTG, psychological distress, and QoL in CRC patients, monitoring their trajectories from the diagnosis to follow-up, through the different phases of the treatment pathway. Moreover, this study aimed to identify, through an initial baseline assessment of certain stable personality and psychosocial characteristics (i.e., Type-D personality, alexithymia, attachment style, trait affectivity, resilience, emotion dysregulation) and the periodic detection of medico-clinical and psychosocial variables (coping strategies, perceived social support, state affectivity), which of these factors might contribute to the QoL and positive and negative psychological outcomes. In particular, emphasis was placed on two specific focuses:

I. to evaluate the changes in QoL during the active treatment phase and to explore which physical and psychosocial factors could predict QoL at each timepoints, with a focus on assessing the impact of each treatment and of previous one. In fact, this early phase of the treatment pathway and the impact of a specific treatment such as (chemo)radiotherapy have been poorly investigated.
II. to evaluate the changes in psychological distress and PTG from diagnosis to follow up and to explore which physical and psychosocial factors could predict the extent of psychological distress and PTG at follow-up. Few studies have examined these aspects longitudinally in CRC patients, not considering together the variables addressed in the present study and following the treatments from the beginning of the planned course.

In the first instance, the exploratory hypotheses that will be tested in relation to these two specific objectives will concern only certain times, as indicated by the lack of psychological literature on these stages specifically, and only certain variables that will be considered of primary interest given the limited literature available for the specific population of CRC patients and the numerous findings that have emerged for other oncological populations. Furthermore, no studies were found that examined these variables in combination and in relation with treatment phases in CRC patients, or in other cancer populations.

1.1 There is a change in the patient’s QoL, which can be negative due to the treatments and their consequences and the associated psychological distress.

1.2 Certain factors, such as specific CRC symptoms, psychological distress, coping styles, affectivity, alexithymia and perceived social support, influence general QoL differently at different times.

2.1 There is a change in the patient’s psychological distress and PTG. Changes in PTG could be positive, given the longitudinal literature on other types of cancer. On the other hand, the evidence for psychological distress is very inconsistent.

2.2 Certain factors, such as specific CRC symptoms, QoL, coping styles, affectivity, alexithymia and resilience, might influence psychological distress and PTG at follow-up, one year after surgery.

The identification of predictive factors will make it possible to structure targeted therapeutic interventions, in order to promote the PTG and reduce the risk of psychological distress in the long term, with a consequent improvement in QoL.

2.3 Study population

This exploratory prospective observational cohort study was carried out through the collaboration between the Department of Psychology of the University of Turin and the S.C. Radiotherapy U. department (Dir. Prof. Umberto Ricardi) of the A.O.U. Città della Salute e della Scienza of Turin, a ward that had been treating cancer patients through radiotherapy for many years. The research project was aimed at patients who had been diagnosed with CRC and were undergoing treatment at this structure. The treatment pathway usually consisted of pre-operative radiotherapy, often combined with chemotherapy with parallel oral administration, followed a few weeks later by surgical resection and, as appropriate, by adjuvant chemotherapy treatment.

2.4 Materials and Methods

2.4.1 Study design

The present study had a longitudinal design, specifically it was an exploratory prospective observational cohort study.

The study was approved by the Institutional Review Board of the Hospital Ethics Committee (protocol number 0017109, procedure number CS2/1118).

This study was conducted in accordance with the principles of the Declaration of Helsinki (2013) and the EU General Data Protection Regulation (GDPR, Regulation EU 2016/679; 2018). Participants were assured of data confidentiality and made aware that participation in the study was voluntary, without compensation and would not change the expected treatment pathway for patients with the specific medical condition. Participants were also informed that they could withdraw their consent to participate and/or use the data at any time. Finally, the participants were informed about the frequency of the appointments for the fulfilment of the questionnaires for the research and the time required for each of them. All participants gave informed consent before the start of the study (see **Supplementary Material** for complete informed consent forms).

2.4.2 Inclusion and exclusion criteria for participants

Patients were recruited at the S.C. Radiotherapy U. Department (Director Prof. Umberto Ricardi) of the A.O.U. “Città della Salute e della Scienza” of Turin. The study was proposed only to newly diagnosed CRC patients awaiting pre-operative radiotherapy and who met the inclusion criteria.

Inclusion criteria included the following:

- have been diagnosed with CRC for the first time;
- have had an indication for pre-operative radiotherapy and surgical resection;
- be over 18 years of age;
- have a good knowledge of written and spoken Italian;
- not suffer from severe psychopathological and/or cognitive disorders, as reported in the patient’s medical record. These may include for example: schizophrenic spectrum disorders and other psychotic disorders, bipolar disorders, depressive and anxiety disorders, personality disorders, neurocognitive disorders.

Conversely, the following exclusion criteria were established:

- being diagnosed with recurrence of CRC;
- have had an indication for different treatment pathway;
- be under 18 years old;
- not have a good knowledge of written and spoken Italian;
- suffer from severe psychopathological and/or cognitive disorders, as reported in the patient’s medical records, based on official diagnosis.

2.4.3 Procedure

The meetings for the administration of the questionnaires were scheduled to coincide with five standard medical appointments. The assessments were planned as follows:

- T0: baseline evaluation, carried out following enrolment, at the time of radiation oncologists’ appointment, during which patients received indication for pre-operative radiotherapy and subsequent treatments (i.e., before the starting pre-operative treatment).
- T1: performed at least one month after the end of pre-operative (chemo)radiotherapy, during the pre-surgical appointment.
- T2: performed approximately at least one month after surgical rection.
- T3a: performed at least six months after surgery (for patients with permanent ostomy or without).
- T3b: performed pre-operatively for patients with temporary ostomy.

- T4: follow-up assessment performed at least one year after surgery and at least 3 months after recanalization surgery (i.e., approximately at least 18 months after diagnosis).

The study covered a total duration of approximately 18 months for each patient, from initial recruitment to final follow-up (T4).

2.4.4 Measures

The data collected included sociodemographic and medical-clinical information, and different psychological variables investigated using the following instruments, in accordance with the temporal scheme presented in **Table 2.1**.

The sociodemographic and medical-clinical information were collected with two anamnestic forms: one for gender, age, years of education, marital status, employment status, and one for data related to cancer condition, comorbid illnesses and details on medical treatment, oncological pathology, any comorbid illnesses, and the medical treatments carried out.

The symptomatology and impact of cancer were investigated through QoL questionnaires specific for oncological diseases. The other outcome variables examined were the presence of psychological distress (i.e., anxiety and depressive symptoms) and PTG.

The personological and psychological variables investigated were: type-D personality, attachment styles, psychological resilience, alexithymia and emotional dysregulation, positive and negative affectivity (trait and state), perceived social support, and cancer-specific coping styles.

The instruments were administered with the intention of not eliciting emotional responses, that might have biased the answers given in the subsequent questionnaire. Hence, at T0 the order of administration was: QoL, alexithymia, resilience, affectivity trait and state, type-D personality, emotion dysregulation, attachment styles, social support, coping strategy, psychological distress. Some questionnaires were removed from T1, the order of the others was maintained and the PTG instrument was added at the end.

Table 2.1 *- Summary of longitudinal evaluations and instruments used.*

	T0	T1	T2	T3a/b	T4
Sociodemographic data	X				
Clinical data	X	X	X	X	X
Psychosocial variables					
Type-D Personality (DS-14)	X				
Attachment Style (RQ)	X				
Resilience (RS)	X				
Alexithymia (TAS-20)	X				X
Emotion Dysregulation (DERS-16)	X				X
Trait Affectivity (PANAS-Trait)	X				
State Affectivity (PANAS-State)	X	X	X	X	X
Social Support (MSPSS)	X	X	X	X	X
Coping Style (Mini-MAC)	X	X	X	X	X
Outcome variables					
Quality of Life (EORTC QLQ C30 & CR-29)	X	X	X	X	X
Psychological distress (HADS)	X	X	X	X	X
Post-Traumatic Growth (PTGI)		X	X	X	X

DS-14: Type-D Scale; RQ: Relationship Questionnaire; RS: Resilience Scale; TAS-20: Toronto Alexithymia Scale; DERS-16: Difficulties in Emotion Regulation Scale; PANAS: Positive and Negative Affect Scale; MSPSS: Multidimensional Scale of Perceived Social Support; Mini-MAC: Mini-Mental Adjustment to Cancer Scale; EORTC QLQ-C30 & CR29: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; HADS: Hospital Anxiety and Depression Scale; PTGI: Post- Traumatic Growth Inventory.

European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30 and QLQ-CR29)

The EORTC QLQ-C30, version 3, is a cancer specific self-report to assess QoL and health-related QoL, developed by Aaronson and colleagues (1993) and was then translated and validated also in Italian by Apolone and colleagues (1998). The Italian version was used in this study. It consists of 30 items divided into: five functional scales (physical, role, emotional, cognitive, social functioning); three symptom scales (fatigue, pain, nausea/vomiting); one global health status/QoL scale; six individual items for additional symptoms (dyspnea, insomnia, loss of appetite, constipation, diarrhea) and financial difficulties. It has a 4-points response scale (1 “not at all” – 4 “very much”), except for the health status scale with a 7-points response scale (1 “very poor” – 7 “excellent”). It provides a general score for health-related QoL and the raw scores were transformed into a linear rating scale ranging from 0 to 100, where higher scores represented more favourable outcome. In the original version, this scale demonstrates good internal consistency with Cronbach's α >.70 (from .54 to .86; Aaronson et al., 1993). Also, the Italian version has a good consistency with Cronbach's from .64 to .90 (Apolone et al., 1998).

The EORTC QLQ-CR29 is a supplementary cancer-specific questionnaire, developed by Whistance and colleagues (2009). The Italian version was developed by the EORTC team and is available on request. It consists of 4 functional subscale (Body Image, Anxiety, Weight, Sexual Interest in men and women) and 18 symptoms scale (urinary frequency, blood and mucus in stool, stool frequency, urinary incontinence, dysuria, abdominal pain, buttock pain, bloating, dry mouth, hair loss, taste, flatulence, faecal incontinence, sore skin, embarrassment, stoma care problems, impotence, dyspareunia). Scoring is similar to those of the EORTC QLQ-C30. Higher scores represented more favorable outcome for functioning scale and a greater symptom burden for the symptom scales. EORTC QLQ-CR29 has also a good internal consistency, with Cronbach's α ranging between .70 and .84 (Whistance et al., 2009). However, the consistency data of the Italian version are not available.

Hospital Anxiety and Depression Scale (HADS)

The HADS was developed by Zigmond and Snaith (1983) and was then translated and validated also in Italian by Costantini and colleagues (1999). The Italian version was used in this study. evaluates anxiety and depressive symptoms in patients with medical condition. In fact, it does not investigate the somatic symptoms included in the nosographic criteria, which in patients with medical conditions could be closely related to the disease itself. It is a self-report of 14 items (7 for anxiety and 7 for depressive symptoms) and a 4-point scale is used for responses, with 0 meaning "never" and 3 meaning "often right". HADS has two subscales' scores with a range of 0-21 and a cut-off of 8, that indicate clinically relevant symptoms. It also has a total score for psychological distress, ranging from 0 to 42 and a cut-off of 15, with high scores indicating a higher level of psychological distress. Original version of HADS has a good internal consistency, with Cronbach's α of .82 and .90 (Bjelland et al., 2002; Zigmond & Snaith, 1983). Similarly, in the Italian version the Cronbach's α of .89 and .88 (Costantini et al., 1999).

Post-Traumatic Growth Inventory (PTGI)

The PTGI is a self-report instrument used to assess positive psychological changes after a traumatic experience, developed by Tedeschi and Calhoun (1996) and was then translated and validated also in Italian by Prati and Pietrantoni (2014). The Italian version was used in this study. It includes five subscales: relating to others, new possibilities, personal strength, spirituality, and appreciation of life. It consists of 21 items with a 6-point Likert type-scale ranging from 0 (no change) to 5 (high change). The PTG total score ranges from 0 to 105, with higher scores indicating a greater positive growth. Original version of PTGI had an excellent total internal reliability, with a Cronbach's α of .90 (Tedeschi & Calhoun, 1996); also, Italian version had a Cronbach's α of .93 (Prati & Pietrantoni, 2014).

Type-D Scale (DS-14)

The DS-14 is a self-report that investigates distressed personality traits (type-D), developed by Denollet (2005) and was then translated and validated also in Italian by Gremigni and Sommaruga (2013). The Italian version was used in this study. It consists of 14 items divided into two sub-scales, one for negative affectivity (NA), which measures dysphoria, worry and irritability, and one for social inhibition (SI), which concerns discomfort in social interactions, reticence and lack of social stability. It provides a response scale from 0 (false) to 4 (true). Scores above the cut-off ≥10 on both subscales determine the presence of type D personality. The scale has good internal reliability, with a Cronbach's α of .88 for NA and .86 for SI in the original version (Denollet 2005), Cronbach's α of .82 for NA and .80 for SI in the Italian version (Gremigni & Sommaruga, 2013).

Relationship Questionnaire (RQ)

The RQ is an instrument developed to detect the attachment style of adults. It was developed by Bartholomew and Horowitz (1991), an Italian adaptation was used in this study. Through four brief descriptions it identifies four attachment prototypes (secure, distancing, preoccupied and fearful), defined using the combination of the "image of self" (positive or negative) with the "image of others" (positive or negative). It presents the possibility of using two types of response: categorical, allowing individuals to be classified according to the attachment style perceived as most similar to their own; dimensional, providing a more complete profile of the individual's attachment and relationship styles, using a scale from 1 (strongly disagree) to 7 (strongly agree) for each description. It is also possible to calculate a score for the "model of self", concerning conceptions of one's own image, as well as a score for the "model of others" dimension (Bartholomew & Horowitz, 1991).

Wagnild and Young Resilience Scale (RS)

The RS was developed by Wagnild and Young (1993) and was then translated and validated also in Italian by Girtler and colleagues (2010). The Italian version was used in this study. It is an instrument for evaluating resilience, defined by 6 dimensions, such as meaningfulness, perseverance, independence, existential loneliness and two aspects of equanimity. It includes 24 items, with response on a 7-point scale (from completely disagree to completely agree). It provides a total score ranging from a minimum of 24 to a maximum of 168. The results indicate low resilience for scores <116, medium resilience for scores between 116 and 141, high resilience for values >141(Wagnild & Young, 1993). The Italian version of RS has good internal consistency with Cronbach's α .84 (Girtler et al., 2010).

Toronto Alexithymia Scale (TAS-20)

The TAS-20 is a self-report scale to evaluate alexithymia trait; it was first created by Bagby and colleagues (1994) and then validated in its Italian version by Bressi and colleagues (1996). It consists of 20 items on a 5-point Likert scale (ranging from strongly agree, to strongly disagree) that assesses the three theoretical aspects of the alexithymia construct: difficulty in identifying feelings (DIF), difficulty in describing feelings (DDF), and externally oriented thinking (EOT). The total score ranges from 20 to 100, with a cut-off as follows: < 51 non-alexithymic, 51-60 borderline, > 61 alexithymic. This scale has good internal consistency with Cronbach's α ≥.70 for original version and .82 for Italian version in clinical population (Bagby et al., 1994; Bressi et al., 1996; Taylor et al., 2003).

The TAS-20 was validated in the Italian version both on healthy individuals and on patients with physical and psychiatric illnesses, confirming the characteristics already found in the original version. Considering the literature in some cases discordant on theoretical aspects of definition of the construct of alexithymia (i.e., alexithymia as a stable personality trait vs. temporary pathological state, or primary alexithymia vs. secondary alexithymia), in the present study it was decided to proceed with the use of TAS-20 both at baseline and at follow-up (T4) to observe the trend of the scores (Caretti et al., 2005; Messina et al., 2014).

Difficulties in Emotion Regulation Scale-16 (DERS-16)

The DERS is a self-report scale, which measures clinically relevant difficulties in the regulation of negative emotions. The DERS was developed by Gratz and Roemer (2004) and the italian version was validated by Sighinolfi and colleagues (2010). The questionnaire consists of five subscales, each investigating one dimension of the emotional regulation construct: clarity, indicating lack of emotional clarity; goals, concerning difficulties in adopting goal-oriented behaviour; impulses, related to difficulties in controlling impulses; strategies, concerning limited access to emotional regulation strategies; and non-acceptance of emotional responses. It consists of 16 items, chosen from the original 36, answered on a 5-point Likert scale (where

1 almost never and 5 always). Scores can range from 16 to 80 and high scores indicate the presence of severe difficulties in emotional regulation. The DERS-16 appears to possess the same psychometric qualities as the extended version, with excellent internal consistency with Cronbach's α of .92 for original version and .90 for Italian version (Bjureberg et al., 2016; Sighinolfi et al., 2010).

Given the association between the constructs of alexithymia and emotional dysregulation, it was chosen in this study to also obtain a baseline and a follow-up (T4) assessment for the DERS-16, so as to check for any change over time.

Positive and Negative Affect Schedule (PANAS)

The PANAS is a self-report instrument to assess the dimensions of affective experience, the two emotional components of subjective well-being. The PANAS was first developed by Watson and colleagues (1988) and then validated by Terracciano and colleagues (2003) in Italian language. It consists of 20 words: 10 for positive affect (PA) and 10 for negative affect (NA). Participants indicate the extent to which they experience the various feelings and emotions, on a scale of 1 (very slightly) to 5 (extremely). PANAS has two versions, for trait (PANAS-PAtr and PANAS-NAtr) and state (PANAS-PAst and PANAS-NAst) affectivity, by changing the temporal specification. In the original version Cronbach's α was .89 for PA and .85 for NA state scales, and .88 for PA and .87 for NA trait scales (Crawford & Henry, 2004; Watson et al., 1988). For the Italian version, Cronbach's alpha was .72 for PA and .80 for NA using the state time instruction, and .72 for PA and .83 for NA using the trait time instruction (Terracciano et al., 2003).

Multidimensional Scale of Perceived Social Support (MSPSS)

The MSPSS was developed by Zimet and colleagues (1990) and then validated by Prezza and Principato (2002). It is a self-report that evaluates perceived support from family, friends and a significant person. It has 12 item and seven-point Likert-type scale (1 – completely false, 7 – completely true). Range score from 12 to 84, with high scores indicate a greater perception of support. Both original and Italian version of MSPSS has a good internal consistency. The original version has a Cronbach's α for each domain ranged from .81 to .98, while for the Italian version Cronbach's α for each domain ranged from .92 to .96 (De Maria et al., 2018; Prezza & Principato, 2002; Zimet et al., 1990)

Mini-Mental Adjustment to Cancer Scale (Mini-MAC)

The Mini-MAC is a 29 item self-report to evaluate coping styles specific for cancer. It was developed by Watson and colleagues (1994) and the Italian version was validated by Grassi and colleagues (2005). Generally, it analyses three adaptive coping strategies (Cognitive Avoidance, Fighting Spirit, and Fatalism), and two maladaptive ones (Helplessness/Hopelessness and Anxious Preoccupation). The Cognitive Avoidance style indicates the tendency to avoid direct confrontation with disease-related problems; the Fighting Spirit represents the tendency to confront and face the disease in active way; and the Fatalism style concerns the tendency to have a resigned and fatalistic attitude towards the disease, with a stoic acceptance of one's condition. Indeed, the Helplessness/Hopelessness style indicates the tendency to adopt a pessimistic attitude about the disease, and the Anxious Preoccupation concerns the tendency to experience the disease as an event source of marked anxiety and tension. A 4-point scale is used for responses, from 1 (definitely does not apply to me) to 4 (definitely applies to me). Cronbach’s α coefficients for each domain ranged from .62 to .88 for the original version and from .55 to .80 for Italian version (Watson et al., 1994; Grassi et al., 2005).

2.5 Data analysis planned

In order to carry out a proper statistical analysis of the data, it was planned to calculate the kurtosis and skewness values of the continuous variables and to use the Kolmogorov-Smirnov statistical test to verify the normal distribution of these variables. With regard to descriptive analyses, it was planned to calculate percentage frequencies and mean scores, with their standard deviation, depending on the type of variable considered.

Given the exploratory nature and the prospective design of the study, to evaluate the change of the outcomes’ variables over time, it was planned to use repeated-measures ANOVAs, to compare the scores obtained on the questionnaires at the different timepoints considered, in order to highlight the presence of statistically significant differences in the scores. When the sphericity was violated according to the Mauchly test, the Greenhouse-Geisser correction would be used. When the main effect of time was significant, it was planned to conduct post-hoc contrasts with Bonferroni correction to assess the differences between each timepoint and the previous timepoint. In this way, it will be possible to understand the differences between the pre-post timepoint pairs of the different specific treatments. Due to the exploratory nature of the study α will be not correct.

Given the paucity of available literature and the exploratory nature of the study, Pearson's or Spearman's bivariate correlations, on the other hand, were planned to investigate the relationships between demographic, clinical and psychological variables and psychological and QoL outcomes measures.

Subsequently, in order to investigate which factors might have the greatest influence on the outcome measures (i.e., PTG, psychological distress, QoL), starting with the results of Pearson's or Spearman's bivariate correlations, it was planned to analyse the relationships with the demographic, clinical and psychological variables. It was planned to include the variables, which were found to be statistically significant correlated with the criterion variables, as independent variables in multiple hierarchical regression models. In this way, it is possible to identify which demographic, clinical, psychological and personological variables contribute in a statistically significant manner to predict outcomes. In the specific case of QoL, interest in the impact of treatments such as radiotherapy, which are not widely studied, led to the decision to investigate predictors for each of the times considered. It was planned to verify the normality of the distribution of the residuals of the regression.

All analyses are carried out with the software "Statistical Package for Social Sciences – SPSS", version 26 or later.

2.5.1 Estimated sample size

The sample size was calculated using the program G*Power 3 (Franz et al., 2007) on the basis of the planned analyses and the literature of references.

With reference to the first macro-objective, a sample size of 47 participants or more was estimated to explore the change of QoL over time using repeated measures ANOVA (3 longitudinal evaluations): with effect size *d*: 0.25 (mean; Cohen, 1988); α probability: 0.0038 (Bonferroni correction); power: 0.80.

Moreover, a sample size of 160 participants or more was estimated to assess possible predictors using regression analysis with QoL as dependent variables; 21 independent variables (e.g., CRC symptoms and functional status, psychological distress, state and trait affectivity, alexithymia, coping styles, perceived social support); effect size F^2: 0.15 (mean; Cohen, 1988); α probability: 0.05; Power: 0.80.

With reference to the second macro-objective, sample size of 39 and 47 participants or more were estimated to explore the change of psychological distress and PTG over time using repeated measures ANOVA, respectively (4 longitudinal evaluations for psychological distress and 3 for PTG): with effect size *d*: 0.25 (mean; Cohen, 1988); α probability: 0.0038 (Bonferroni correction); power: 0.80.

A sample size of 160 participants or more was estimated to assess possible predictors using regression analysis with psychological distress or PTG as dependent variables; 21 independent variables (e.g., QoL, CRC symptoms and functional status, state and trait affectivity, alexithymia, coping styles, resilience); effect size F^2: 0.15 (mean; Cohen, 1988); α probability: 0.05; Power: 0.80.

Given the indications of sample size and a possible drop-out rate of 15%, it was considered to enrol a sample of 185 patients at T0.

2.6 Expected results

Investigating which factors contribute to PTG in cancer patients is of primary importance from a preventive perspective, in order to structure interventions aimed at early assessment and enhancement of these factors. Supportive interventions, if carried out after the oncological diagnosis, could reduce the risk of psychological distress in the long term, improving patients' psychological adjustment to the disease and promoting the psychological growth process. The results of this study were supposed to confirm the importance of integrating a psychological assessment into the complex care pathway of CRC patients, with the aim of implementing specific psychological interventions that take into account the individual's personal and social resources. An early and specific psychological screening and, consequently, an individualized psychological therapy could promote, according to the various phases of the treatment pathway, the increase of protective factors to develop psycho-physical well-being of the patient, with important implications on the QoL and the socio-familial context of the patients.

Finally, based on the results of this study, it was planned to evaluate the application of the proposed protocol to other oncological pathologies, adapting it to the respective treatment and follow-up pathways in clinical practice. The aim would be the evaluation of possible experiences related to the different oncological diseases, by identifying the factors that promote a better QoL and PTG in each of them.

2.7 Timing of research

The project was scheduled to 48 months, structured according to the following timetable:

a) Month 1-4: final drafting and presentation to the Ethics Committee; organisational meetings; preparation of the paper-based test material and definition of the final operational aspects.

b) Month 5: starting of progressive patient recruitment, with initial assessment (T0).

c) Months 6-42: continuation of progressive recruitment and starting of re-evaluations at T1, T2, T3a/b and T4 assessments.

d) Month 43: statistical processing of data for the preparation and publication of a scientific article in an international journal and the presentation of results at congresses specific to the field.

Chapter 3.

Trajectories and predictors of Quality of Life, psychological distress and Post-Traumatic Growth

3.1 Introduction

According to the latest available data, CRC ranks third in incidence and second in prevalence and mortality for both sexes worldwide (IARC-WHO, 2020; Sung et al., 2021; Zhang et al., 2023). In recent years, however, screening programs and early detection have increased survival rates (Salvatore et al., 2020; Zhang et al., 2023). The tumor site and the extent of the lesion determine the type of surgical resection, which remains the treatment of choice, and its potential consequences, such as the need for a temporary or permanent ostomy (Buccafusca et al., 2019; Haas et al., 2023; Mahmoud, 2022; Salvatore et al., 2020; Simillis et al., 2023). Nonetheless, over the years, scientific evidence has incorporated pre-operative (chemo)radiotherapy and, in some cases, adjuvant chemotherapy into the treatment course for CRC patients to improve oncologic outcomes and tumor regression (Abaha et al., 2018; Buccafusca et al., 2019; Pape et al., 2021; Salvatore et al., 2020; Simillis et al., 2023; Wo et al., 2021).

CRC, its associated symptoms, and the consequences of treatment can lead to significant physical dysfunction (e.g., bowel, urinary and sexual dysfunction, permanent stoma) and high psychological distress in patients, with significant impact on overall well-being (Buccafusca et al., 2019; Haas et al., 2022; Pape et al., 2021; Peng et al., 2019; Wang et al., 2023a). It is also undeniable that the diagnosis and treatment of CRC can negatively affect patients' QoL (Buccafusca et al., 2019; Haas et al., 2023; Murata et al., 2008; Pachler & Wille-Jørgensen, 2012; Sales et al., 2014; Waddell et al., 2023). Health-related QoL is a multidimensional concept that includes physical, emotional, cognitive, and social aspects involving various environmental and personal factors (Bours et al., 2016).

Psychological distress is associated with poorer QoL outcomes in all age groups and in both sexes (Pape et al., 2021; Sales et al., 2014; Waddell et al., 2023). CRC can lead to changes in body image and self-representation, fears about treatment outcomes, and disease recurrence, which can increase psychological distress such as anxiety and depressive symptoms (Graça Pereira et al., 2012; Sales et al., 2014; Waddell et al., 2023).

After years of focusing on the possible psychopathology resulting from a traumatic event, in recent years researchers have become increasingly interested in the positive psychological consequences of a traumatic event. PTG is a psychological construct developed by Tedeschi and Calhoun (1995) and defined as positive psychological change resulting from struggling with traumatic life circumstances that challenge beliefs about life. This subjectively perceived positive change affects different areas of life: change in priorities and new possibilities, appreciation of life, spiritual dimension, interpersonal relationships, and sense of life (Calhoun & Tedeschi, 2006; Tedeschi & Calhoun, 2004). PTG does not imply a return to the baseline state prior to the traumatic event, but rather an improvement determined by cognitive processing and restructuring (Wang et al., 2023a).

The occurrence of psychopathology and PTG are not opposing and mutually exclusive outcomes of a traumatic event. In fact, the presence of PTG does not preclude the person from simultaneously experiencing high levels of psychological distress (Tedeschi & Calhoun, 2004; Dekel et al., 2012).

The concurrent presence of PTG and psychological distress has also been observed in cancer patients (Casellas-Grau et al., 2016; Cordova et al., 2017). A cancer diagnosis is an event that threatens an individual's survival and affect many aspects of daily life: it undermines physical health, causes profound psychological distress (e.g., anxiety and depression), and disrupts "normal" functioning for an extended period (Buccafusca et al., 2019; Cordova, 2008; Cordova et al., 2017; Threader & McCormack, 2016; Wang et al., 2023a).

3.2 Objectives of the study

3.2.1 Objectives I: QoL during active treatment phases

Some personal aspects may influence QoL in CRC patients, such as affective experience and emotion recognition (De Vries et al., 2012; Sales et al., 2014). Positive (e.g., pleasant emotional states, being active, alert, and enthusiastic) and negative (e.g., unpleasant involvement, distress, disgust, guilt) affectivity describe affective experience and the emotional components of subjective well-being. High levels of positive affectivity promote psychological well-being and psychosocial adjustment in cancer patients, as well as better QoL (Sales et al., 2014; Voogt et al., 2005). In terms of emotion recognition, alexithymia, characterized by difficulties in identifying and describing subjective feelings and bodily sensations, as well as externally oriented thinking, has been associated with poorer health and QoL outcomes in populations affected by various medical conditions, including cancer (De Vries et al., 2012; Di Tella et al., 2023; Sales et al., 2014; Taylor et al., 1997).

Coping is a process of self-regulation that involves behavioral and cognitive strategies aimed at managing external and/or internal demands that exceed the individual's resources, such as cancer-related illness (Lashbrook et al., 2018; Lazarus & Folkman, 1987). Cancer patients who choose adaptive styles tend to have better physical health, fewer psychological problems and a better QoL (Kang & Son, 2019; Lashbrook et al., 2018; Sales et al., 2014).

Social support is an important external resource for the individual that positively influences the cognitive adjustment process, with low perception of social support being associated with poorer QoL in patients (Bours et al., 2016; Cicero et al., 2009; Haviland et al., 2017).

Although previous studies have identified several factors that influence the QoL of CRC patients, most of these studies have analysed them separately, and little attention has been paid to the relationship between these factors and the different phases of CRC treatment, particularly regarding the early stages of the treatment process, i.e., medical appointments immediately after communication of diagnosis and pre-operative therapy. Indeed, each medical treatment can have profound and specific effects on physical and psychological well-being.

For these reasons, Objectives I of this exploratory prospective study were to evaluate the changes in health-related QoL of CRC patients from diagnosis to after surgical resection and to explore which physical and psychosocial factors better predict health-related QoL at different phases of CRC treatment, i.e., radiation oncologists' appointment, during which patients received indication for cancer treatments (T0 - diagnosis), after pre-operative (chemo)radiotherapy (T1), and after surgical resection (T2). Attempting to understand the reciprocal role that physical and psychosocial factors play on health-related QoL from the diagnosis and during subsequent medical treatments could improve screening programs for early detection of negative prognostic factors for patients' health-related QoL.

3.2.2 Objectives II: psychological distress and PTG from diagnosis to follow-up

Besides factors strictly related to the type of cancer, research has highlighted that different psychological aspects are associated with PTG in cancer patients (Casellas-Grau et al., 2016; Cordova, 2008; Cordova et al., 2017; Romeo et al., 2017b, 2019; Tedeschi et al., 2018; Wang et al., 2023a).

Resilience is a positive psychological trait that promotes positive adaptation to stressors and adversity, including medical illness, and appears to play a role in the development of PTG (Gouzman et al., 2015; Sihvola et al., 2022; Wang et al., 2023a). Resilient individuals are particularly able to adaptively use both internal and external available resources and thus employ more adaptive coping strategies (Gouzman et al., 2015; Sihvola et al., 2022).

Coping, defined as a process of cognitive and behavioral change in response to external and/or internal demands that exceed a person's resources, is another crucial aspect of adaptation to oncologic disease (Lazarus & Folkman, 1987). The various coping strategies play a role not only in dealing with psychological distress, but also in the development of PTG (Casellas-Grau et al., 2016; Knauer et al., 2022; Wang et al., 2023a), as positive, action-oriented coping strategies are often associated with higher levels of PTG in longitudinal studies (Cakmak et al., 2021; Knauer et al., 2022).

Finally, affective experience and emotion recognition may influence both psychological distress and PTG in cancer patients (Cakmak et al., 2021; Orejuela-Dávila et al., 2017; Yu et al., 2014). Positive (such as pleasant emotional states, being active and enthusiastic) and negative (such as anger, disgust, fear) affectivity are the dimensions that describe affective experience and emotional components of subjective well-being. Positive affectivity promotes psychosocial adjustment to cancer (Hart & Charles, 2013; Sales et al., 2014; Voogt et al., 2005) and appears to be associated with PTG.

Regarding emotion recognition, the inability to recognize and elaborate one's emotional reactions is detrimental to positively coping with a highly stressful experience. Indeed, the presence of alexithymia, i.e., difficulty identifying and describing one's emotions, and externally oriented thinking, was found to be associated with poorer physical and mental health outcomes in several chronic conditions (Taylor et al., 1997; De Vries et al., 2012; Benfante & Romeo, 2023; Di Tella et al., 2023; Martino et al., 2020). Few studies have examined the association between alexithymia and PTG, suggesting that alexithymia prevents the development of PTG (Cakmak et al., 2021; Orejuela-Dávila et al., 2017).

To date, there have been few studies examining the trajectory of psychological distress and PTG in CRC longitudinally, and most of them have focused on CRC survival, disregarding the early stages of cancer treatment from the time of diagnosis communication (Occhipinti et al., 2015; Qaderi et al., 2021; Song et al., 2022; Wang et al., 2023).

Considering all these premises, Objectives II of this exploratory prospective study were to evaluate the changes in psychological distress and PTG in CRC patients, following the successive treatment phases, from diagnosis to follow-up, and to explore which factors could significantly predict the extent of psychological distress and PTG at follow-up. Treatment phases included: radiation oncologists' appointment, during which patients received indication for cancer treatments (T0 - diagnosis), pre-operative (chemo)radiotherapy (T1), surgical resection (T2) and one year after surgery (T3 - follow-up).

3.3 Materials and Methods I

3.3.1 Study design and participants

Participants were recruited from April 2019 to April 2021 at the Radiation Oncology Department of the "Città della Salute e della Scienza" University Hospital in Turin, Italy.

Sociodemographic and clinical information as well as psychological and health-related QoL questionnaires were completed at the time of radiation oncologists' appointment, during which patients received indication for pre-operative radiotherapy and subsequent treatments (baseline assessment, T0 - diagnosis). Psychological and health-related QoL questionnaires were then repeated at least one month after the end of pre-operative treatment (T1, on average 3 months after diagnosis) and at least one month after surgical resection (T2, on average 6 months after diagnosis). Trait variables, such as alexithymia and trait affectivity, were only assessed at T0.

The current data were acquired as part of a larger project investigating QoL and positive and negative psychological outcomes and their psychosocial predictors in CRC patients from diagnosis to one years after surgery follow-up.

Only those questionnaires that were of interest for the specific Objectives I have briefly mentioned. All detailed information of the study is available in Chapter 2 of the present dissertation.

3.3.2 Measures

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) C30 (QLQ-C30), version 3, is a cancer-specific self-report with 30 items that examine health-related QoL. The final score ranges from 0 to 100, with high scores indicating better health-related QoL (Aaronson et al., 1993). In study's sample, Cronbach's α was .77.

The EORTC QLQ-CR29 (QLQ-CR29) is a supplementary disease-specific questionnaire. It consists of 4 functional subscales (Body Image (BI), Anxiety (Anx), Weight (Wei), Sexual interest (SexInt)) and 18 symptoms scales, which were grouped according to the affected area/body function: Urinary Symptoms (UrSy), Intestinal Symptoms (InSy), Pain Symptoms (PainSy), Mouth Symptoms (MoSy), Sexual Symptoms (SexSy). High scores mean a favorable outcome on the functional scale, but a greater symptom burden on the symptom scales (Whistance et al., 2009). In study's sample, Cronbach's α ranged from .33 to .71.

The Hospital Anxiety and Depression Scale (HADS) is a 14 item self-report instrument for assessing psychological distress symptoms in patients with organic diseases. The HADS total score ranges from 0 to 42, with a cut-off score of 15, with high scores indicating a high level of psychological distress (Bjelland et al., 2002; Zigmond & Snaith, 1983). In study's sample, Cronbach's α ranged from .59 to .78.

The Positive and Negative Affect Scale (PANAS) is a self-report instrument with two 10 item scales for positive affect (PA) and negative affect (NA). Participants rate the extent to which they experience various emotions and feelings for both the trait (PANAS_PAtr and PANAS_NAtr) and state (PANAS_PAst and PANAS_NAst) versions (Watson et al., 1988). In study's sample, Cronbach's α was .82 for PA and NA trait scales, and .80 for PA and .86 for NA state scales.

The Toronto Alexithymia Scale (TAS-20) is a 20 item self-report instrument. The TAS-Total score ranges from 20 to 100 with a cut-off point ≥ 61 indicating the presence of alexithymia (Taylor et al., 2003). In study's sample, Cronbach's α was .70 for TAS-Total.

The 29-item Mini-Mental Adjustment to Cancer Scale (Mini-MAC) assesses cancer-specific coping styles: three adaptive (cognitive avoidance: CA, fighting spirit: FS and fatalism: F) and two maladaptive (helplessness/hopelessness: HH and anxious preoccupation: AP) (Watson et al., 1994). In study's sample, Cronbach's α was .56 for F and FS, .78 for CA, .72 for HH, .81 for AP.

The Multidimensional Scale of Perceived Social Support Scale (MSPSS) assesses perceived support with 12 items. Scores range from 12 to 84, with high scores indicating a greater perception of support (Zimet et al., 1990). In study's sample, Cronbach's α was .87.

3.3.3 Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences - 28.0 (IBM SPSS Statistics for Macintosh, Armonk, NY, USA: IBM Corp.).

Descriptive statistics were used to summarise the variables collected for the three different time points. The normality assumption (absolute values for skewness and kurtosis below 3.0 and 8.0 respectively) was met for all variables. The Mann–Whitney U test and Fisher's Exact Test were used for within-group baseline comparisons between patients who completed the study and patients who dropped out.

Linear repeated-measures model analyses were used to assess changes in variables over time, applying the Greenhouse-Geisser correction when the assumption of sphericity was violated. In case of significant main effects, post-hoc analyses with Bonferroni correction were performed to assess differences between T1 and T0 and between T2 and T1. Due to the exploratory nature of the study α was not correct.

Explorative hierarchical multiple regression analyses were performed to investigate which variables better predicted health-related QoL (QLQ-C30) at the different time points (T0, T1 and T2). Only variables that correlated significantly with the outcome variables (Pearson or Spearman bivariate correlations) were included in the regression models, stepwise in the order of 1) clinical symptoms (QLQ-CR29 subscales); 2) psychological symptoms (TAS-20, PANAS, HADS, Mini-MAC, MSPSS) and in chronological order (first T0, then T1 and then T2). Collinearity was assessed using the statistical factors of tolerance and Variance Inflaction Factor (VIF). The distribution of the residuals of the regressions had been evaluated and all were normal.

3.4 Results I

3.4.1 Demographic and clinical characteristics

At baseline, 43 CRC patients (two-thirds men) with a mean age of approximately 62 years (range 34-84 years) were enrolled in the study (**Table 3.1**).

Most patients were diagnosed as T3N2M0 according to the 8th edition of the TNM staging system (2016) and all but one patient received pre-operative chemotherapy in addition to radiotherapy. After surgery, 38 patients (86.5%) had an ostomy (permanent in 11 patients and temporary in 21 patients) and 17 (39.5%) patients received adjuvant chemotherapy.

Of the 43 patients enrolled in the study, 3 patients dropped out at T1, and 3 patients dropped out at T2 for medical and personal reasons. However, the between-group comparisons of sociodemographic, clinical and psychological variables at T0 of the completers and dropouts showed no differences between the two groups.

Table 3.1. Sociodemographic and clinical characteristics at diagnosis.

		Mean (SD)	N (%)
Age		61.6 (12.6)	
Gender			
Male			29 (67.4)
Female			14 (32.6)
Educational level (years)		11.35 (4.3)	
Primary School			5 (11.6)
Middle School			12 (27.9)
High School			15 (34.9)
Graduate			11 (25.6)
Marital status			
Single/Divorced/Widow(er)			11 (25.6)
Married/ Cohabiting			32 (74.4)
Work status			
Employed			24 (55.8)
Housewife/houseman			2 (4.7)
Retired			17 (39.5)
TNM Stage of cancer			
Tumor extent:	T3		41 (95.3)
	T4		2 (4.7)
Lymph nodes:	N0		3 (7)
	N1		9 (20.9)
	N2		31 (72.1)
Metastasis:	M0		43 (100)
ECOG_PS			
0			39 (90.7)
1			4 (9.3)

ECOG_PS: Eastern Cooperative Oncology Group Performance Status.

3.4.2 QoL, clinical symptoms and psychological variables trajectories

Table 3.2 summarises the data collected at T0 (N=43), T1 (N=40) and T2 (N=37) and the results of the repeated measures ANOVA assessing the main effect of time for each variable. The QLQ-C30 data confirmed an overall preserved health-related QoL but decreasing over time (p = .002). Indeed, contrasts showed a statistically significant decrease in scores between T1 and T2 (F(1,36) = 8.86, p = .005).

The functional subscales of the QLQ-CR29 revealed a statistically significant change in the QLQ-CR29_BI and QLQ-CR29_SexInt scales, with contrasts showing a greater impairment of body image between T0 and T1 (F(1,36) = 6.58, p = .015) and between T1 and T2 (F(1,36) = 6, p = .019) as well as a decrease in sexual interest between T1 and T2 (F(1,36) = 18.37, p < .001). Repeated measures ANOVA for the QLQ-CR29_Anx showed an improvement over time, with contrasts showing a significant decrease in health anxiety between T0 and T1 (F(1,36) = 14.31, p < .001).

The symptoms subscales of the QLQ-CR29 revealed an overall low level of symptoms, with intestinal (QLQ-CR29_InSy) and pain (QLQ-CR29_PainSy) symptoms showing no statistically significant changes over time. However, symptoms related to the urinary system, the mouth area and sexual symptoms increased over time, with post-hoc contrasts showing a significant change in QLQ-CR29_UrSy between T0 and T1 (F(1,36) = 8.27, $p = .007$).

In terms of psychological traits, the sample showed a low level of alexithymia, with only 6 (14%) patients scoring above the TAS-20 cut-off, and a low tendency to experience a negative affectivity (PANAS_NAtr). The PANAS_PAst did not change over time, while a statistically significant decrease was found in the PANAS_NAst, with the contrast confirming the statistically significant decrease in negative affectivity experienced between T0 and T1 (F(1,36) = 4.71, $p = .037$).

The HADS showed a less linear course of psychological distress symptoms, with the contrasts showing a statistically significant decrease between T0 and T1 (F(1,36) = 12.38, $p < .001$), followed by a renewed increase between T1 and T2 (F(1,36) = 9.79, $p = .003$).

The MSPSS indicates a very high level of perceived social support at all the assessment times.

The Mini-MAC showed that Fighting Spirit and Helplessness/Hopelessness were the most and least utilised coping styles, respectively, while Anxious Preoccupation changed statistically over time, with contrasts confirming a significant decrease between T0 and T1 (F(1,36) = 6.31, $p = .017$) and between T1 and T2 (F(1,36) = 6.56, $p = .015$).

Results of variables that show significant changes over time and contrasts are standardized and presented for visual inspection in **Figure 3.1**.

Table 3.2. Repeated measures ANOVAs on health-related Quality of Life (QLQ-C30) and data collected at diagnosis (T0), after neoadjuvant treatments (T1) and after the surgery (T2).

	T0	**T1**	**T2**		
	N = 43	**N = 40**	**N = 37**	**F(df1,df2)**	***p***
QLQ-C30	86.89 (8.9)	87.20 (12.3)	80.52 (12.8)	F(1.5,54)=8.56	.002
QLQ-CR29					
QLQ-CR29_BI	92.51 (12.8)	86.11 (14.8)	78.38 (19.4)	F(2,72)=10.75	<.001
QLQ-CR29_Anx	46.51 (28.3)	65 (25)	68.47 (26)	F(2,72)=10.8	<.001
QLQ-CR29_Wei	89.15 (21.5)	85.83 (19.8)	84.68 (21.7)	F(2,72)=0.67	.514
QLQ-CR29_SexInt	25.58 (28)	30.83 (26.6)	13.51 (22.9)	F(2,72)=12.15	<.001
QLQ-CR29_SexSy	10.08 (18.6)	19.66 (30.3)	26.13 (36.1)	F(1.46,51.2)=4.1	.033
QLQ-CR29_UrSy	9.82 (13)	13.19 (15)	16.97 (16.6)	F(2,72)=9.60	<.001
QLQ-CR29_InSy	17.21 (13.8)	11.75 (12.7)	14.96 (13.2)	F(1.65,59.5)=2.29	.119
QLQ-CR29_PainSy	19.38 (16.9)	14.58 (14)	20.27 (13.8)	F(1.69,60.94)=2.68	.085
QLQ-CR29_MoSy	9.69 (13.2)	12.08 (16.9)	17.12 (20.2)	F(2,72)=4.45	.015
TAS-20	44.81 (10.5)				
PANAS					
PANAS_PAtr	36.98 (6.2)				
PANAS_NAtr	18.93 (5.8)				
PANAS_PAst	31.86 (6.4)	31.8 (6.1)	30.89 (5.9)	F(2,72)=1.19	.310
PANAS_NAst	18.38 (6.3)	16.22 (5.8)	15.89 (5.7)	F(1.7,61.3)=3.74	.036
HADS	10.07 (5.3)	7.67 (5.3)	9.81 (6.2)	F(1.66,59.8)=5.78	.008
MSPSS	73.23 (10.7)	73.08 (9.3)	71.46 (12.1)	F(2,72)=0.89	.416
Mini-MAC					
Mini-MAC_F	2.93 (0.62)	2.96 (0.6)	2.96 (0.6)	F(2,72)=0.12	.887
Mini-MAC_FS	3.38 (0.44)	3.39 (0.5)	3.3 (0.4)	F(2,72)=0.58	.561
Mini-MAC_HH	1.56 (0.44)	1.54 (0.5)	1.54 (0.5)	F(2,72)=0.06	.942
Mini-MAC_AP	2.63 (0.61)	2.39 (0.6)	2.15 (0.6)	F(2,72)=12.04	<.001
Mini-MAC_CA	2.78 (0.76)	2.76 (0.7)	2.7 (0.8)	F(1.67,60)=0.33	.680

QLQ-CR29: EORTC colorectal cancer module: _BI: Body Image; _Anx: Anxiety; _Wei: Weight; _SexInt: Sexual Interest, functional scales; _SexSy: Sexual Symptoms; _UrSy: Urinary Symptoms, _InSy: Intestinal Symptoms, _PainSy: Pain Symptoms, _MoSy: Mouth Symptoms, subcales; TAS-20: Toronto Alexithymia Scale; PANAS: Positive and Negative Affect Scale, _PAtr: Positive Affect Trait; _NAst: Negative Affect Trait; _PAst: Positive Affect State; _NAst: Negative Affect State; HADS: Hospital Anxiety and Depression Scale; MSPSS: Multidimensional Scale of Perceived Social Support; Mini-MAC: Mini-Mental Adjustment to Cancer scales, _F: Fatalism; _FS: Fighting Spirit; _HH: Helplessness/Hopelessness; _AP: Anxious Preoccupation; _CA: Cognitive Avoidance.

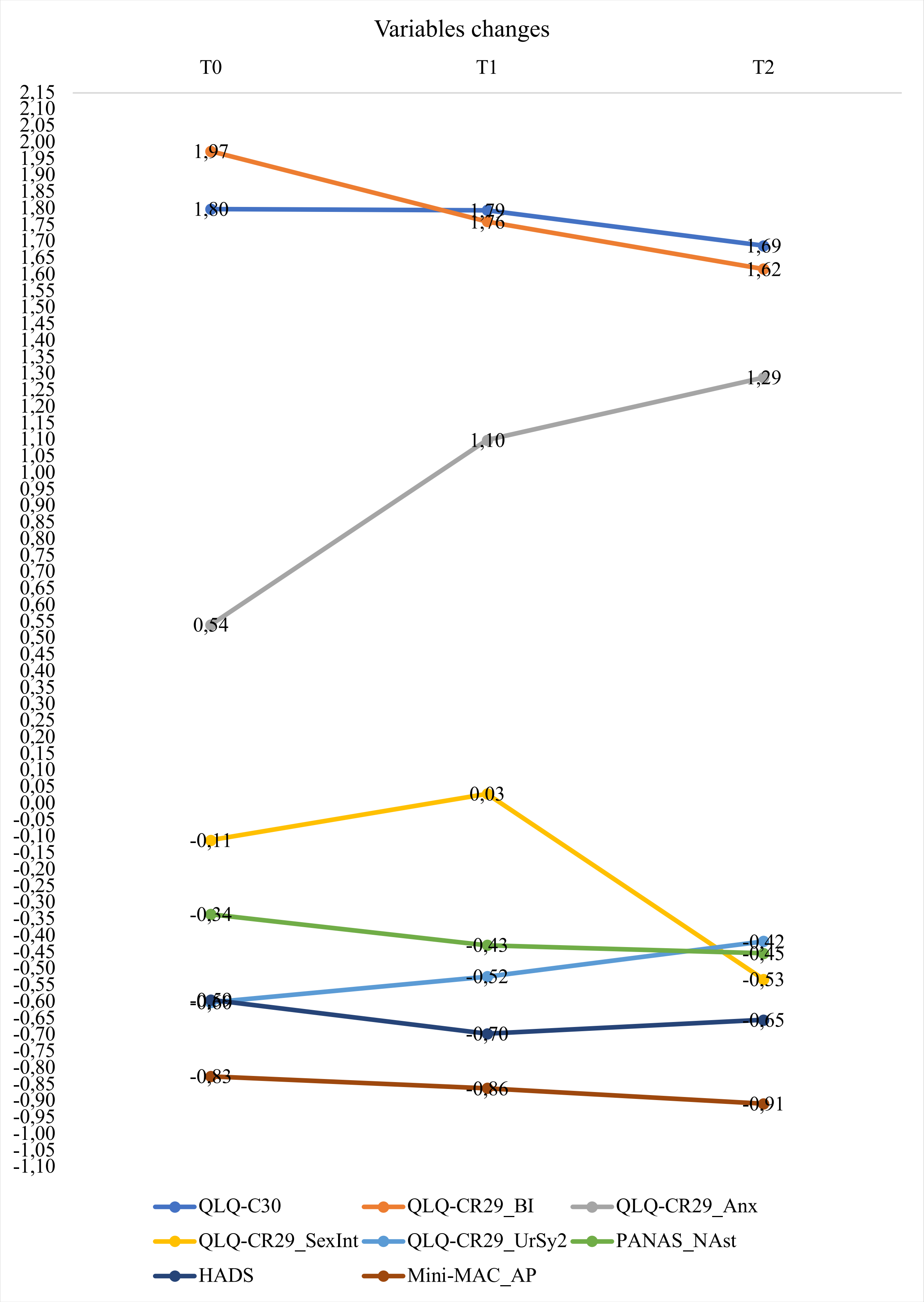

Figure 3.1. Standardized means of variables that changes significantly over time.

3.4.3 Explorative regression analysis

Explorative hierarchical multiple regression analyses were conducted to examine which variables better predicted health-related QoL (QLQ-C30) at the different time points. Correlation analyses between QoL at T0, T1 and T2 and all other variables were performed to identify the variables to be included in the models (**Table 3.3**).

Table 3.3. Pearson correlations among health-related Quality of life (QLQ-C30) at the different time points (T0. T1 and T2) and all other variables.

	QLQ-C30_T0 N=43	**QLQ-C30_T1 N=40**		**QLQ-C30_T2 N=37**		
Variable	**T0**	**T0**	**T1**	**T0**	**T1**	**T2**
Age	.118	.027	/	.105	/	/
Gender[1]	-.164	-.191	/	-.076	/	/
Years of education	.159	.297	/	-.053	/	/
QLQ-CR29						
QLQ-CR29_BI	.366*	.529***	.618***	.230	.256	.289
QLQ-CR29_Anx	.401**	.263	.381*	.099	.173	.578***
QLQ-CR29_Wei	.197	.309	.267	.019	.023	.312
QLQ-CR29_SexInt	.057	.175	.279	.158	.100	.093
QLQ-CR29_SexSy	-.024	.051	-.235	-.064	-.142	-.125
QLQ-CR29_UrSy	-.499***	-.600***	-.643***	-.251	-.434**	-.294
QLQ-CR29_InSy	-.734***	-.668***	-.777***	-.184	-.182	-.372*
QLQ-CR29_PainSy	-.633***	-.738***	-.575***	-.246	-.494**	-.420**
QLQ-CR29_MoSy	-.544***	-.402*	-.497***	-.241	-.435**	-.664***
TAS-20	-.207	-.297	/	-.419**	/	/
PANAS						
PANAS_PAtr	.102	.014	/	.387*	/	/
PANAS_NAtr	-.389**	-.252	/	-.189	/	/
PANAS_PAst	.114	.242	.432**	.258	.311	.541***
PANAS_NAst	-.236	-.069	-.372*	-.374*	-.325	-.388*
HADS	-.581***	-.402*	-.631***	-.306	-.384*	-.743***
MSPSS	.098	.233	.140	.208	.162	.220
Mini-MAC						
Mini-MAC_F	<.001	-.205	-.110	.121	.347*	.310
Mini-MAC_FS	.029	-.222	-.024	-.042	.316	.386*
Mini-MAC_HH	-.132	-.156	-.562***	-.036	-.101	-.487**
Mini-MAC_AP	-.239	-.223	-.631***	-.259	-.256	-.461**
Mini-MAC_CA	-.023	-.270	-.401*	-.106	.003	-.027

*p-value < .05; **p-value < .01; ***p-value < .001; [1]Spearman' rho coefficients.

QLQ-C30: EORTC quality of life questionnaire; QLQ-CR29: EORTC colorectal cancer module: _BI: Body Image; _Anx: Anxiety; _Wei: Weight; _SexInt: Sexual Interest, functional scales; _SexSy: Sexual Symptoms; _UrSy: Urinary Symptoms; _InSy: Intestinal Symptoms; _PainSy: Pain Symptoms; _MoSy: Mouth Symptoms, subcales; TAS-20: Toronto Alexithymia Scale; PANAS: Positive and Negative Affect Scale; _PAtr: Positive Affect trait; _NAtr: Negative Affect trait; _PAst: Positive Affect state; _NAst: Negative Affect state; HADS: Hospital Anxiety and Depression Scale; MSPSS: Multidimensional Scale of Perceived Social Support; Mini-MAC: Mini-

Mental Adjustment to Cancer Scales. _F: Fatalism; _FS: Fighting Spirit; _HH: Helplessness/Hopelessness; _AP: Anxious Preoccupation; _CA: Cognitive Avoidance.

The full regression models are presented in **Table 3.4** for QLQ-C30_T0, in **Table 3.5** for QLQ-C30_T1, and in **Table 3.6** for QLQ-C30_T2.

The QLQ-CR29_InSy at T0 (β = -0.581, *t*(38) = -5.67, *p* < .001) and tendency toward negative affectivity (PANAS_NAtr_T0: β = -0.215, *t*(38) = -2.25, *p* = .03) were the only statistically and negatively significant predictive factors of the QLQ-C30 at T0, with the final model explaining 68% of the variance of the QLQ-C30_T0 (F(4,38) = 23.3, *p* < .001) (**Table 3.4**).

Table 3.4. Hierarchical multiple regression with health-related Quality of Life (QLQ-C30) at T0 as dependent variable (N=43).

	Predictor	**R^2**	**Adj R^2**	**F**	**F-ΔR^2**	**B**	**SE B**	**β**	***p***
1	*(Constant)*	0.54	0.53	47.78***	47.78***	*95.07*	*1.51*		*<.001*
	QLQ-CR29_InSy_T0					-0.48	0.069	-0.734	<.001
2	*(Constant)*	0.63	0.61	33.77***	9.66**	*96.65*	*1.462*		*<.001*
	QLQ-CR29_InSy_T0					-0.36	0.073	-0.555	<.001
	QLQ-CR29_PainSy_T0					-0.18	0.059	-0.349	.003
3	*(Constant)*	0.67	0.65	26.65***	5.25*	*92.69*	*2.218*		*<.001*
	QLQ-CR29_InSy_T0					-0.36	0.069	-0.552	<.001
	QLQ-CR29_PainSy_T0					-0.15	0.058	-0.282	.015
	QLQ-CR29_Anx_T0					0.07	0.030	0.221	.027
4	*(Constant)*	0.71	0.68	23.33***	5.05*	*98.93*	*3.49*		*<.001*
	QLQ-CR29_InSy_T0					-0.38	0.07	-0.581	<.001
	QLQ-CR29_PainSy_T0					-0.11	0.06	-0.199	.082
	QLQ-CR29_Anx_T0					0.06	0.03	0.185	.054
	PANAS_NAtr_T0					-0.33	0.15	-0.215	.030

**p-value < .05; **p-value < .01; ***p-value < .001*

QLQ-C30: EORTC quality of life questionnaire; QLQ-CR29: EORTC colorectal cancer module: _InSy: Intestinal Symptoms; _PainSy: Pain Symptoms; _Anx: Anxiety, subscales; PANAS_NAtr: Positive and Negative Affect Scale_Negative Affect trait.

The QLQ-CR29_PainSy at T0 (β = -0.458, *t*(35) = -5.31, *p* < .001), QLQ-CR29_InSy at T1 (β = -0.322, *t*(35) = -3.25, *p* = .003) and QLQ-CR29_UrSy at T1 (β = -0.306, *t*(35) = -2.75, *p* = .009) were the statistically significant predictive factors of the QLQ-C30 at T1, with the final model explaining 80% of the variance of QLQ-C30_T1 (F(4,35) = 40.93, *p* < .001) (**Table 3.5**).

Table 3.5. Hierarchical multiple regression with health-related Quality of Life (QLQ-C30) at T1 as dependent variable (N=40).

	Predictor	**R^2**	**Adj R^2**	**F**	**F-ΔR^2**	**B**	**SE B**	**β**	**p**
1	*(Constant)*	0.55	0.53	45.49***	45.49***	*97.57*	*2.03*		*<.001*
	QLQ-CR29_PainSy_T0					-0.53	0.08	-0.738	<.001
2	*(Constant)*	0.70	0.68	43.24***	19.20**	*99.47*	*1.73*		*<.001*
	QLQ-CR29_PainSy_T0					-0.44	0.07	-0.613	<.001
	QLQ-CR29_UrSy_T0					-0.39	0.09	-0.414	<.001
3	*(Constant)*	0.79	0.77	44***	14.33***	*100.13*	*1.49*		*<.001*
	QLQ-CR29_PainSy_T0					-0.31	0.07	-0.436	<.001
	QLQ-CR29_UrSy_T0					-0.25	0.09	-0.262	.006
	QLQ-CR29_InSy_T1					-0.38	0.10	-0.395	<.001
4	*(Constant)*	0.82	0.80	40.93***	7.58**	*101.17*	*1.42*		*<.001*
	QLQ-CR29_PainSy_T0					-0.33	0.06	-0.458	<.001
	QLQ-CR29_UrSy_T0					-0.06	0.11	-0.063	.569
	QLQ-CR29_InSy_T1					-0.31	0.10	-0.322	.003
	QLQ-CR29_UrSy_T1					-0.25	0.09	-0.306	.009

***p-value < .01; ***p-value < .001*

QLQ-C30: EORTC quality of life questionnaire; QLQ-CR29: EORTC colorectal cancer module: _PainSy: Pain Symptoms; _UrSy: Urinary Symptoms; _InSy: Intestinal Symptoms.

With respect to T2 (**Table 3.6**), the final model explained 71% of the variance of the QLQ-C30_T2 (F(5,31)=18.97, p<.001). Psychological distress at T2 (HADS_T2: β=-0.394, t(31)=-3.26, p=.003) was the strongest negative contributor, followed by QLQ-CR29_MoSy at T2 (β=-0.369, t(31)=-3.56, p=.001) and the Mini-MAC_F at T1 (β=0.040, t(31)=2.65, p=.013). The latter was the only positive predictive factor: the more the patients adopted a fatalistic coping style at T1, the better their health-related QoL at T2.

Table 3.6. Hierarchical multiple regression with health-related Quality of Life (QLQ-C30) at T2 as dependent variable (N=37).

	Predictor	**R^2**	**Adj R^2**	**F**	**F- ΔR^2**	**B**	**SE B**	***β***	***p***
1	*(Constant)*	0.18	0.15	7.44**	7.44*	103.41	8.61		*<.001*
	TAS-20					-0.52	0.19	-.419	.010
2	*(Constant)*	0.34	0.30	8.56***	8.15**	119.46	9.66		*<.001*
	TAS-20					-0.55	0.17	-.442	.003
	PANAS_NAst_T0					-0.81	0.28	-.400	.007
3	*(Constant)*	0.45	0.40	9.10***	7.11*	97.63	12.09		*<.001*
	TAS-20					-0.55	0.16	-.446	.002
	PANAS_NAst_T0					-0.79	0.26	-.393	.005
	Mini-MAC_F_T1					7.36	2.76	.343	.012
4	*(Constant)*	0.67	0.63	16.17***	20.92***	95.84	9.55		*<.001*
	TAS-20					-0.36	0.13	-.286	.012
	PANAS_NAst_T0					-0.65	0.21	-.323	.004
	Mini-MAC_F_T1					5.97	2.20	.279	.011
	QLQ-CR29_MoSy_T2					-0.32	0.07	-.500	<.001
5	*(Constant)*	0.75	0.71	18.97***	10.65**	92.21	8.45		*<.001*
	TAS-20					-0.18	0.13	-.143	.181
	PANAS_NAst_T0					-0.39	0.20	-.195	.056
	Mini-MAC_F_T1					5.15	1.95	.240	.013
	QLQ-CR29_MoSy_T2					-0.23	0.07	-.369	.001
	HADS_T2					-0.81	0.25	-.394	.003

**p-value < .05; **p-value < .01; ***p-value < .001*

QLQ-C30: EORTC quality of life questionnaire; TAS-20: Toronto Alexithymia Scale; PANAS_NAst: Positive and Negative Affect Scale_Negative Affect state; QLQ-CR29: EORTC colorectal cancer module: _MoSy: Mouth Symptoms, subscale; Mini-MAC_F: Mini-Mental Adjustment to Cancer Scales_Fatalism; HADS: Hospital Anxiety and Depressive

3.5 Discussion I

The present exploratory prospective study aimed to assess the QoL of CRC patients in the early stages of cancer treatment, i.e., immediately after diagnosis communication, after pre-operative (chemo)radiotherapy and after surgical resection, to investigate the progression of changes and to evaluate which physical and psychosocial factors better predict health-related QoL at the different stages of CRC treatment. Understanding these aspects could allow early identification of negative prognostic factors for patients' QoL to plan psychosocial interventions in time.

An early psychological screening program should include patients from the time of diagnosis. However, previous research studies have not always examined patients in the early phase of cancer treatment (Acquata et al., 2022; Haviland et al., 2017; Orive et al., 2022; Sales et al., 2014; Waddell et al., 2023). Therefore, we recruited 43 CRC patients who had just received the diagnosis and treatment program and performed the T0 assessment before starting pre-operative treatment.

Consistent with two recent studies (Orive et al., 2022; Qaderi et al., 2021), overall health-related QoL (QLQ-C30) was preserved, and patients had limited physical symptoms (QLQ-CR29) at baseline. Major symptoms included intestinal and pain symptoms such as blood and mucus in the stool, flatulence, high stool frequency and buttock pain, which were directly associated with the local advanced CRC (Mahmoud, 2022; Salvatore et al., 2020). Until a few years ago, CRC patients and survivors reported poorer health-related QoL, as shown in a 10-year-old review (Sales et al., 2014). The introduction of increasingly early screening procedures for CRC diagnosis may explain the low physical symptoms and overall preserved health-related QoL found in the more recent studies (Mahmoud, 2022).

However, overall preserved QoL at baseline was associated with moderate levels of psychological distress, with approximately one-fifth of patients reporting clinically significant distress on the HADS. Considering that the patients had just received the diagnosis, these data are not surprising and are confirmed by the results of the QLQ-CR29_Anx, which indicate high levels of health anxiety. The diagnosis of CRC is a traumatic event that can lead to health anxiety and psychological symptoms, with literature estimating the prevalence of depressive symptoms at 2% to 57% and anxiety at 1% to 47% (Graça Pereira et al., 2012; Peng et al., 2019; Sales et al., 2014).

Of the physical and psychosocial factors examined, exploratory regression showed that only intestinal symptoms and the tendency to experience negative affectivity negatively predicted health-related QoL at baseline. Thus, our data suggest that cancer-related physical symptoms and a personality predisposition to experience high levels of negative emotions are the factors that may influence QoL immediately after diagnosis.

Most recent studies that have examined QoL in CRC patients longitudinally have enrolled patients who had already undergone major cancer treatment, i.e. surgery (Orive et al., 2022; Qaderi et al., 2021; Wang et al., 2023), so their baseline assessment can be equated to our T2. While these studies found an improvement in QoL over time, the results of our study showed that patients experienced a significant decline in QoL during the early treatment process, particularly at surgery. The only study we are aware of that compared QoL before and after surgery found a similar deterioration four weeks after surgery but confirmed a subsequent improvement after one year (Reudink et al., 2021).

Over the course of treatments, our patients experienced a functional deterioration in body image and a general worsening of physical symptoms, particularly related to the urinary system, the mouth area and sexual symptoms (QLQ-CR29). In particular, urinary symptoms increased after pre-operative treatments as a possible side effect of radiotherapy, while sexual interest worsened after surgery, probably due to the resection complications (Haas et al., 2023; Murata et al., 2008; Towe et al., 2019; Waddell et al., 2023).

Regression analysis showed that pain symptoms at baseline and intestinal and urinary symptoms after pre-operative treatment were the only factors that predicted worse health-related QoL at T1, while worse mouth symptoms at T2 significantly explained QoL at T2, confirming the literature reporting a strong impact of physical symptoms on patients' QoL (Murata et al., 2008; Reudink et al., 2021; Waddell et al., 2023).

Although physical symptoms increased, health anxiety improved over time, significantly decreasing after pre-operative treatment, similar to psychological distress and negative affectivity. The high levels of health anxiety and negative emotions and their decrease after pre-operative treatments could be due to the initial burden of the cancer diagnosis and worry about the effects of radiotherapy, which patients are least aware of (Hernández-Blázquez & Cruzado, 2016; Stiegelis et al., 2004). Psychological distress increased again at T2, probably due to adjustment to postoperative conditions (e.g., ostomy management) or possible adjuvant therapy (Qaderi et al., 2021; Wang et al., 2023), with regression analysis showing that psychological distress at T2 significantly predicted QoL.

The QLQ-C30 at T2 was also positively predicted by the use of Fatalism at T1. This tendency toward a resigned and stoic attitude toward the disease and an external locus of control before surgery could be an indicator of greater acceptance and confidence in treatment, which could then translate into a future better QoL (Kang & Son, 2019; Lashbrook et al., 2018; Sales et al., 2014). Fatalism, and Fighting Spirit, were also the most frequently used adaptive coping styles at all assessment times, which is consistent with previous studies of cancer patients (Kang & Son, 2019; Lashbrook et al., 2018; Sales et al., 2014), while Anxious Preoccupation was the only one that decreased over time, paralleling the decrease in health anxiety.

3.5.1 Study limitations

The main limitation of the present study is the small sample size, which reduces the power of the analyses. The COVID-19 pandemic not only hindered the recruitment and subsequent reassessment of patients, but also made access to cancer screening more difficult, leading to a decrease in new diagnoses. Moreover, this study did not take into account information on any psychological treatment of patients, which might have an effect on the psychological state variables under investigation. Finally, the use of self-report instruments only, which may have introduced biases due to social desirability effects, casual responses, and potential lack of awareness of participants.

Future longitudinal studies are needed to improve and confirm the results obtained with a larger and more heterogeneous sample of CRC patients to further assess the impact of the disease and the different treatments on patients' QoL.

3.5.2 Clinical implications

From a clinical perspective, our results emphasise that several physical and psychological factors play a role in both the rapid changes in patients' QoL in response to cancer diagnosis and subsequent treatments and in the medium-term follow-up, pointing to the need for a biopsychosocial assessment of CRC patients since the diagnosis and in all subsequent phases of the treatment process, each of which includes physical and psychological specificities. Based on these specificities, support services should be tailored to both the individual patient and the treatment phase, in particular through the implementation of multidisciplinary and multimodal preventive and pre-habilitation interventions not only before surgery, but even better immediately after diagnosis, in order to improve QoL and psychological health in the medium and long term.[38,39]

In fact, we found a general deterioration in QoL in CRC patients from the time of diagnosis until one month after surgical resection. In addition to surgery, pre-operative radiotherapy seemed to be a crucial step from both a psychological and physical point of view. This is because not only the side effects, especially those related to the urinary system, are among the symptoms that significantly worsen the QoL one month after the end of pre-operative treatment, but it is also the treatment that worries patients the most and contributes to increased health anxiety and psychological distress after diagnosis. Psychological distress should then be monitored, as at the end of the main cancer treatments, psychological adjustment to the CRC diagnosis seems to explain QoL more than physical symptoms. In this context, psychological programmes should also promote the early adoption of active coping styles, such as fatalism, which seem to positively predict mid-term QoL.

3.6 Materials and Methods II

3.6.1 Study design and participants

Participants were recruited from April 2019 to April 2021 at the Radiation Oncology Department of the "Città della Salute e della Scienza" University Hospital in Turin, Italy.

The study included four evaluation points, following the subsequent treatment phases: radiation oncologists' appointment, during which patients received indication for pre-operative radiotherapy and subsequent treatments (T0 - diagnosis), at least one month after the end of pre-operative treatment (T1, on average 3 months after diagnosis), at least one month after surgical resection (T2, on average 6 months after diagnosis), and at the follow-up of at least one year after surgical resection (T3, on average 18 months after diagnosis). Sociodemographic and clinical information, as well as psychological and QoL questionnaires, were completed at T0 and then repeated at all time points. Trait variables (alexithymia, trait affectivity, and resilience) were completed only at T0, whereas PTG was evaluated from T1 to T3.

The current data were acquired as part of a larger project investigating QoL and positive and negative psychological outcomes and their psychosocial predictors in CRC patients from diagnosis to one years after surgery follow-up.

Only those questionnaires that are of interest for the specific Objectives II have briefly mentioned. All detailed information of the study is available in Chapter 2 of the present dissertation.

3.6.2 Measures

The Hospital Anxiety and Depression Scale (HADS) is a brief self-report measure that assesses anxiety and depression symptoms in patients with medical conditions. The subscale scores (HADS-A: anxiety symptoms; HADS-D: depressive symptoms) range from 0 to 21, with a cut-off score of 8 indicating the presence of clinically relevant symptoms. The total psychological distress score (HADS-Tot) ranges from 0 to 42, with a cut-off of 15 (Bjelland et al., 2002; Zigmond & Snaith, 1983). In study's sample, Cronbach's α ranged from .59 to .78.

The Post-Traumatic Growth Inventory (PTGI) is a self-report instrument designed to assess positive psychological changes following a traumatic experience. It consists of 21 items divided into five subscales: relating to others (RtO), new possibilities (NP), personal strength (PS), spiritual change (SC), and appreciation of life (AoL). The total PTG score ranges from 0 to 105, with higher scores indicating greater psychological growth (Tedeschi & Calhoun, 1996). In study's sample, Cronbach's α was .89 for RtO, .84 for NP, .86 for PS, .76 for SC, .78 for AoL, and .95 for total.

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) C30 is a cancer-specific self-report measure of QoL. The final score ranges from 0 to 100, with higher scores representing a more favorable outcome for global health status/QoL (Aaronson et al., 1993). In study's sample, Cronbach's α was .77.

The EORTC QLQ-CR29 is the supplementary disease-specific module for colorectal cancer. It consists of 4 functional subscales (Body Image (BI), Anxiety (Anx), Weight (Wei), Sexual Interest (SexIn – sexual interest), and 18 symptom scales that we grouped by affected site/body function in: Urinary Symptoms (UrSy), Intestinal Symptoms (InSy), Pain Symptoms (PainSy), Mouth Symptoms (MoSy), and Sexual Symptoms (SexSy). Higher scores represent a more favorable outcome on the functional scale and a higher symptom burden on the symptom scales (Whistance et al., 2009). In study's sample, Cronbach's α ranged from .33 to .71.

The Mini-Mental Adjustment to Cancer Scale (Mini- MAC) is a 29-item self-report assessment of cancer-specific coping styles. It analyses three adaptive coping strategies (Cognitive Avoidance – CA, Fighting Spirit – FS, and Fatalism – F), and two maladaptive ones (Helplessness/Hopelessness – HH, and Anxious Preoccupation – AP) (Watson et al., 1994). In study's sample, Cronbach's α ranged from .56 to .81.

The Positive and Negative Affect Scale (PANAS) is a self-report instrument with 20 items: 10 for positive affect (PA) and 10 for negative affect (NA). Participants indicate the extent to which they experience the various feelings and emotions for trait (PANAS-PAtr and PANAS-NAtr) and state (PANAS-PAst and PANAS-NAst) affectivity (Watson et al., 1988). In study's sample, Cronbach's α ranged from .80 to .86.

The Resilience Scale (RS) by Wagnild and Young (1993) is a 24-item self-report scale that assesses personal resilience. The score ranges from 24 to 168, divided into: < 116 low resilience; 116-141 medium resilience; > 141 high resilience (Wagnild & Young, 1993). In study's sample, Cronbach's α was .86.

The Toronto Alexithymia Scale (TAS -20) consists of 20 items that assesses: difficulty in identifying feelings (DIF), difficulty in describing feelings (DDF), and externally oriented thinking (EOT). The TAS-Total score ranges from 20 to 100, with a cut-off as follows: < 51 non-alexithymic, 51-60 borderline, > 61 alexithymic (Taylor et al., 2003). In study's sample, Cronbach's α was .70.

3.6.3 Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Sciences - 28.0 (IBM SPSS Statistics for Macintosh, Armonk, NY, USA: IBM Corp.).

Descriptive statistics were used to summarize the patients' clinical and psychological variables for the different time points. The normality assumption was tested and met for all variables (all absolute values for skewness and kurtosis were less than 3.0 and 8.0, respectively) (Kline, 2005). For within-group comparisons of sociodemographic and clinical characteristics of completers and dropouts, the Mann–Whitney U test and Fisher's exact test were used.

Repeated-measures linear model analyses were performed to assess the changes in psychological distress and PTG. When sphericity was violated according to the Mauchly test, the Greenhouse-Geisser correction was used. When the main effect of time was significant, post-hoc contrasts with Bonferroni correction were planned to assess the differences between each time point and the previous one (i.e., T0 vs T1, T1 vs T2, T2 vs T3). Due to the exploratory nature of the study α was not correct.

Pearson and Spearman bivariate correlations were used to analyse the relationship between the variables. Two exploratory hierarchical multiple regression analyses were then performed to examine which variables better predicted the psychological distress (HADS) and Post-Traumatic Growth (PTGI) at follow-up (T3). Only the variables observed as significantly correlated with the outcome variables were included in the regression models, stepwise, in chronological order, following the sequence: clinical symptoms first and then psychological symptoms, so: 1) clinical symptoms at T0; 2) psychological symptoms at T0; 3) clinical symptoms at T1; 4) psychological symptoms at T1 and so on.

Collinearity was assessed using the statistical factors of tolerance and Variance Inflaction Factor (VIF). The distribution of the residuals of the regressions had been evaluated and all were normal.

3.7 Results II

3.7.1 Demographic and clinical characteristics

Sociodemographic and cancer-related variables of 43 patients are reported in **Table 3.7**. Most of the patients were diagnosed as T3N2M0 according to the 8th edition of the TNM staging system (2016). While receiving oncological surgery, 21 (56.8%) and 11 (29.7%) patients had a temporary or permanent ostomy, respectively, and 17 (39.5%) patients received adjuvant chemotherapy.

Table 3.7. Sociodemographic and clinical characteristics of patients (N=43) at diagnosis (T0).

	Mean (SD)	**N (%)**
Age	61.6 (12.6)	
Gender		
Male		29 (67.4)
Female		14 (32.6)
Educational level (years)	11.35 (4.3)	
Primary School		5 (11.6)
Middle School		12 (27.9)
High School		15 (34.9)
Graduate		11 (25.6)
Marital status		
Single/Divorced/Widow(er)		11 (25.6)
Married/ Cohabiting		32 (74.4)
Work status		
Employed		24 (55.8)
Housewife/houseman		2 (4.7)
Retired		17 (39.5)
TNM Stage of cancer		
Tumor extent: T3		41 (95.3)
T4		2 (4.7)
Lymph nodes: N0		3 (7)
N1		9 (20.9)
N2		31 (72.1)
Metastasis: M0		43 (100)
ECOG_PS		
0		39 (90.7)
1		4 (9.3)
Pre-operative Chemotherapy		
No		1 (2.3%)
Yes		42 (97.7%)
Adjuvant Chemotherapy		
No		26 (60.5%)
Yes		17 (39.5%)
Stoma at T2		
No stoma		5 (13.5%)
Temporary stoma		21 (56.8%)
Permanent stoma		11 (29.7)
Stoma at T3		
No stoma		26 (70.3%)
Permanent stoma		11 (29.7)
Outcome at T3		
NED		36 (83.7%)
AWD		6 (14%)
DOD		1 (2.3%)

ECOG_PS: Eastern Cooperative Oncology Group Performance Status; NED: no evidence of disease; AWD: alive with disease; DOD: died of disease.

Of the 43 patients assessed at T0, 3 patients drop-out at T1, 3 patients at T2, and 6 patients at T3 for personal or clinical reasons. However, the between-group comparisons of the sociodemographic, clinical, and psychological variables at T0 of completers and drop-outs showed no baseline differences between the two groups (all the p value for the Mann–Whitney U tests and Fisher's Exact Tests were >.05).

Data regarding QoL, clinical symptoms and psychological variables at the different time points are reported in the **Table 3.8**.

Table 3.8. Data regarding physical and psychological variables and health-related quality of life after diagnosis (T0; N=43), after pre-operative treatment (T1; N=40), after surgical resection (T2; N=37) and at follow-up (T3; N=31).

	T0	**T1**	**T2**	**T3**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
QLQ-C30	**86.89 (8.9)**	87.20 (12.3)	80.52 (12.8)	**87.25 (10.5)**
QLQ-CR29				
QLQ-CR29_BI	92.51 (12.8)	86.11 (14.8)	78.38 (19.4)	78.85 (21.9)
QLQ-CR29_Anx	46.51 (28.3)	65 (25)	68.47 (26)	69.89 (24.9)
QLQ-CR29_Wei	89.15 (21.5)	85.83 (19.8)	84.68 (21.7)	86.02 (22.4)
QLQ-CR29_SexIn	25.58 (28)	30.83 (26.6)	13.51 (22.9)	22.58 (26.4)
QLQ-CR29_SexSy	10.08 (18.6)	19.66 (30.3)	26.13 (36.1)	29.03 (37.3)
QLQ-CR29_UrSy	9.82 (13)	13.19 (15)	16.97 (16.6)	8.78 (11.5)
QLQ-CR29_InSy	17.21 (13.8)	11.75 (12.7)	14.96 (13.2)	14.62 (13.7)
QLQ-CR29_PainSy	19.38 (16.9)	14.58 (14)	20.27 (13.8)	16.4 (12.1)
QLQ-CR29_MoSy	9.69 (13.2)	12.08 (16.9)	17.12 (20.2)	9.68 (15.4)
RS	**145.51 (14.2)**			
High resilience (>141) N(%)	*27 (62.8%)*			
Medium resilience (116-141) N(%)	*16 (37.2%)*			
TAS-20_Tot	**44.81 (10.5)**			**46.10 (13.2)**
TAS-20_DIF	13.42 (5.6)			13.61 (5.8)
TAS-20_DDF	12.02 (4)			11.97 (4.3)
TAS-20_EOT	19.37 (5.2)			20.52 (5.5)
Alexithymia (≥ 61) N(%)	*6 (14%)*			*4 (12.9%)*
Borderline (52-60) N(%)	*7 (16.3%)*			*8 (25.8%)*
PANAS				
PANAS_PAtr	36.98 (6.2)			
PANAS_NAtr	18.93 (5.8)			
PANAS_PAst	31.86 (6.4)	31.8 (6.1)	30.89 (5.9)	34.58 (6.7)
PANAS_NAst	18.38 (6.3)	16.22 (5.8)	15.89 (5.7)	16.32 (6.5)
Mini-MAC				
Mini-MAC_F	2.93 (0.62)	2.96 (0.6)	2.96 (0.6)	3 (0.47)
Mini-MAC_FS	3.38 (0.44)	3.39 (0.5)	3.3 (0.4)	3.14 (0.35)
Mini-MAC_HH	1.56 (0.44)	1.54 (0.5)	1.54 (0.5)	1.51 (0.39)
Mini-MAC_AP	2.63 (0.61)	2.39 (0.6)	2.15 (0.6)	2.25 (0.53)
Mini-MAC_CA	2.78 (0.76)	2.76 (0.7)	2.7 (0.8)	2.77 (0.61)

QLQ-C30: EORTC quality of life questionnaire; QLQ-CR29: EORTC colorectal cancer module: _BI: Body Image, _Anx: Anxiety, _Wei: Weight, _SexInt: Sexual Interest Functional Scales; _SexSy: Sexual Symptoms;

_UrSy: Urinary Symptoms, _InSy: Intestinal Symptoms, _PainSy: Pain Symptoms, _MoSy: Mouth Symptoms Subcales; RS: Resilience Scale; TAS-20_Tot: Toronto Alexithymia Scale – total score, DIF: difficulty identifying feelings, DDF: difficulty describing feeling, EOT: externally oriented thinking subscale; PANAS: Positive and Negative Affect Scale, _PAtr: Positive Affect Trait; _NAst: Negative Affect Trait; _PAst: Positive Affect State; _NAst: Negative Affect State; Mini-MAC: Mini-Mental Adjustment to Cancer Scales, _F: Fatalism, _FS: Fighting Spirit, _HH: Helpless/Hopeless, _AP: Anxious Preoccupation, _CA: Cognitive Avoidance.

3.7.2 Psychological distress and PTG trajectories

Table 3.9 shows the levels of psychological distress and PTG at the different assessments and the results of the repeated measures ANOVA which evaluate the main effect of time for each variable.

Although on average patients showed moderate mean levels of psychological distress, the HADS scores showed statistically significant changes over time, in particular relating to the anxiety symptoms. Indeed, contrasts revealed a statistical significant reduction between T0 and T1 (F(1,30) = 16.45, p <.001) in the HADS-A score, which however increased again between T1 and T2 (F(1,30) = 4.25, p = .048). Specifically, 13 (30.2%), 2 (5%), 9 (24.3%) and 5 (16.1%) patients reported the presence of clinically relevant anxiety symptoms at T0, T1, T2 and T3, respectively, as suggested by a HADS-A score above the cut-off. No statistically significant changes emerged on the HADS-D subscale.

Regarding PTG, data highlighted a progressive increase over time, with the repeated measures ANOVAs showing statistically significant changes in the total score of the PTGI and in all its subscales. Planned contrast, in particular, showed the presence of a statistically significant increase in the scores between T2 and T3 (PTGI_Tot: F(1,30) = 20.78, p < .001; PTGI_RtO: F(1,30) = 8.07, p = .008; PTGI_NP: F(1,30) = 23.47, p < .001; PTGI_PS: F(1,30) = 8.35, p = .007; PTGI_SC: F(1,30) = 6.14, p = .019; PTGI_AoL: F(1,30) = 21.65, p < .001).

Results of variables that show significant changes over time and contrasts are standardized and presented for visual inspection in **Figure 3.2**.

Table 3.9. Trajectories of psychological distress (HADS) and Post-Traumatic Growth (PTGI) after diagnosis (T0), after pre-operative treatment (T1), after surgical resection (T2) and at follow-up (T3).

	T0	**T1**	**T2**	**T3**	**F(df1,df2)**	***p***
	N = 43	**N = 40**	**N = 37**	**N = 31**		
HADS_Tot	10.07 (5.3)	7.67 (5.3)	9.81 (6.2)	8.45 (5.9)	F(2.47,74)=3.14	.039
Clinically relevant psychological distress	*9 (20.9%)*	*4 (10%)*	*10 (27%)*	*7 (22.6%)*		
HADS-D	4.23 (3.1)	3.73 (3.1)	5.11 (3.9)	4.23 (3.4)	F(3,90)=2.39	.074
Clinically relevant depression	*6 (14%)*	*4 (10%)*	*7 (18.9%)*	*6 (19.4%)*		
HADS-A	5.84 (2.8)	3.95 (2.7)	4.70 (3.3)	4.23 (3)	F(3,90)=4.77	.004
Clinically relevant anxiety	*13 (30.2%)*	*2 (5%)*	*9 (24.3%)*	*5 (16.1%)*		
PTGI_Tot		36.7 (24.5)	40.3 (25)	56.10 (20)	F(2,60)=16.35	<.001
PTGI_RtO		12.95 (9)	13.86 (8.7)	18.29 (8)	F(2,60)=6.64	.002
PTGI_NP		6.23 (6)	7.16 (6.6)	11.42 (6)	F(2,60)=20.45	<.001
PTGI_PS		8.13 (5.6)	9.05 (5.9)	11.84 (4.7)	F(2,60)=7.15	.002
PTGI_SC		2.65 (3)	3.46 (3.4)	5 (3.5)	F(2,60)=8.82	<.001
PTGI_AoL		6.75 (4.3)	6.76 (4.3)	9.55 (3.1)	F(2,60)=11.88	<.001

HADS: Hospital Anxiety (HADS-A) and Depression (HADS-D) Scale; PTGI: Post-Traumatic Growth Inventory; _RtO: Relating to others; _NP: New possibilities; _PS: Personal strength; _SC: Spiritual change; _AoL: Appreciation of life.

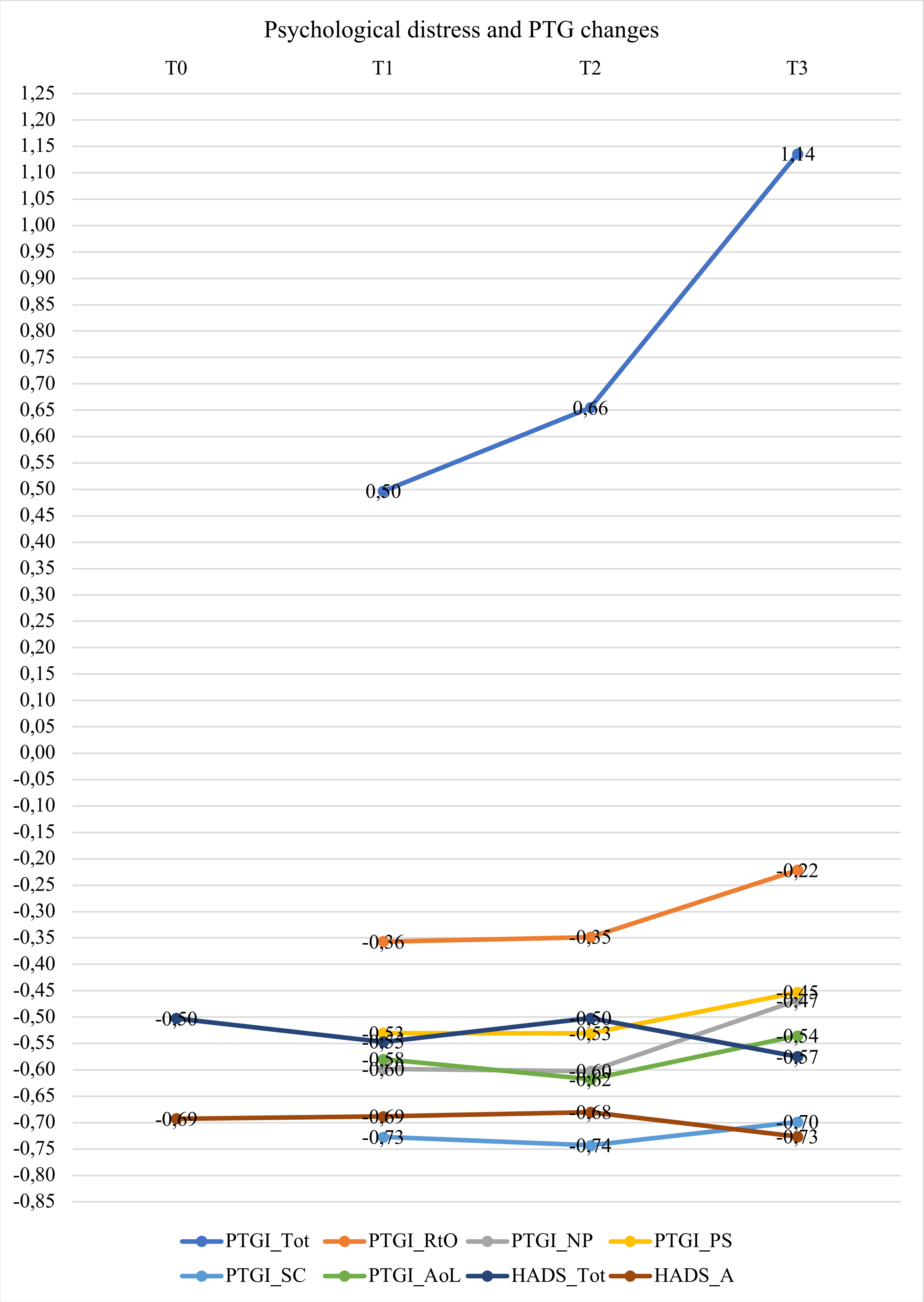

Figure 3.2. Standardized means of variables that changes significantly over time.

3.7.3 Explorative regression analyses

Explorative hierarchical multiple regression analyses were performed to evaluate which variables better predicted the psychological distress (HADS_Tot) and the Post-Traumatic Growth (PTGI) at follow-up. To identify the variables to be included in the models, correlation analyses between the criterions (HADS_Tot_T3 and PTGI_T3) and all the other variables were performed (**Table 3.10**).

Table 3.10. Pearson correlations with psychological distress (HADS_Tot) and Post-Traumatic Growth (PTGI_Tot) at follow-up (T3) (N=31).

	HADS_Tot_T3				**PTGI_Tot_T3**			
Variable	**T0**	**T1**	**T2**	**T3**	**T0**	**T1**	**T2**	**T3**
Age	.036	/	/	/	-.047	/	/	/
Gender[1]	.326	/	/	/	-.272	/	/	/
Education–year	-.152	/	/	/	-.171	/	/	/
QLQ-C30	-.460**	-.484**	-.120	-.615***	.145	-.008	.195	.255
QLQ-CR29								
QLQ-CR29_BI	-.357*	-.394*	-.392*	-.320	-.247	.096	.398*	.246
QLQ-CR29_Anx	-.435*	-.537**	-.322	-.572***	-.130	-.090	.209	-.200
QLQ-CR29_Wei	-.182	-.238	-.408*	.041	-.174	-.116	.253	-.056
QLQ-CR29_Sex	-.351	-.339	-.282	-.312	.213	.219	.199	.143
QLQ-CR29_UrSy	.133	.202	-.086	.134	-.159	-.207	-.304	-.250
QLQ-CR29_InSy	.518**	.508**	.159	.134	-.210	.022	-.353	.059
QLQ-CR29_PainSy	.491**	.147	.041	.487**	.130	-.105	-.217	-.191
QLQ-CR29_MoSy	.482**	.278	.163	.024	-.145	-.179	-.233	-.189
TAS-20								
TAS-20_Tot	.100	/	/	.439*	-.059	/	/	.105
TAS-20_DIF	.201	/	/	.550***	-.068	/	/	.220
TAS-20_DDF	.134	/	/	.419*	-.093	/	/	.299
TAS-20_EOF	-.114	/	/	.147	.025	/	/	-.212
RS	-.208	/	/	/	.285	/	/	/
PANAS								
PANAS_PAtr	-.068	/	/	/	.329	/	/	/
PANAS_NAtr	-.032	/	/	/	.283	/	/	/
PANAS_PAst	-.176	-.560***	-.314	-.425*	.104	.321	.420*	.371*
PANAS_NAst	-.150	.462**	.279	.543**	.169	.359*	.151	.256
Mini-MAC								
Mini-MAC_F	.369*	.050	.176	.204	.245	.440*	.214	.159
Mini-MAC_FS	.063	-.273	-.318	-.387*	.465**	.287	.373*	.029
Mini-MAC_HH	.255	.455*	.366*	.458**	-.110	.056	-.062	.113
Mini-MAC_AP	.295	.589***	.392*	.594***	.252	.319	-.114	.143
Mini-MAC_CA	.203	.170	.362*	.344	.093	.317	-.026	-.019
HADS_Tot	.374*	.639***	.390*	-	.118	.182	-.123	.014
PTGI_Tot	/	-.088	-.170	.014	/	.689***	.740***	-

**p-value < .05; **p-value < .01; ***p-value =< .001; [1]Spearman' rho coefficients*

HADS_Tot: Hospital Anxiety and Depression Scale, total score; PTGI_Tot: Post-Traumatic Growth, total score; QLQ-C30: EORTC quality of life questionnaire; QLQ-CR29: EORTC colorectal cancer module: _BI: Body Image, _Anx: Anxiety, _Wei: Weight, _SexInt: Sexual Interest Functional Scales; _SexSy: Sexual Symptoms; _UrSy: Urinary Symptoms, _InSy: Intestinal Symptoms, _PainSy: Pain Symptoms, _MoSy: Mouth Symptoms Subcales; TAS-20_Tot: Toronto Alexithymia Scale – total score, DIF: difficulty identifying feelings, DDF: difficulty describing feeling, EOT: externally oriented thinking subscale; RS: Resilience Scale; PANAS: Positive and Negative Affect Scale, _PAtr: Positive Affect Trait; _NAst: Negative Affect Trait; _PAst: Positive Affect State; _NAst: Negative Affect State; Mini-MAC: Mini-Mental Adjustment to Cancer Scales, _F: Fatalism, _FS: Fighting Spirit, _HH: Helpless/Hopeless, _AP: Anxious Preoccupation, _CA: Cognitive Affective.

The results of the regression analysis on the psychological distress at follow-up are shown in **Table 3.11**. The final model explained a significant proportion (72%) of the variance of the HADS_Tot_T3 (F(6,24) = 13.52, $p < .001$). Positive affectivity (PANAS_PAst_T1: $\beta = -0.379$, $t(24) = -3.13$, $p = .005$) and health anxiety (QLQ-CR29_Anx_T1: $\beta = -0.310$, $t(24) = -2.93$, $p = .007$) at T1 were found to be statistically significant contributing factors. The negative association means that the higher the level of positive affectivity and the higher the score on the QLQ-CR29_Anx subscale (suggesting a better functioning and thus a low level of health anxiety) at T1, the lower were the levels of psychological distress at T3. Also the negative affectivity measured at T3 showed to be statistically significant (PANAS_NAst_T3: $\beta = 0.326$, $t(24) = 2.71$, $p = .012$), with high score at the negative affectivity predicting high levels of psychological distress.

Table 3.11. Hierarchical multiple regression with psychological distress (HADS_Tot) at follow-up (T3) as dependent variable (N=31).

	Predictor	**R^2**	**Adj R^2**	**F**	**F-ΔR^2**	**B**	**SE B**	***β***	***p***
1	*(Constant)*	0.27	0.24	10.63**	10.63**	*4.40*	*1.55*		*.008*
	QLQ-CR29_InSy_T0					0.24	0.07	0.518	.003
2	*(Constant)*	0.40	0.36	9.35***	6.17*	*8.76*	*2.26*		*<.001*
	QLQ-CR29_InSy_T0					0.21	0.07	0.464	.004
	QLQ-CR29_Anx_T0					-0.09	0.03	-0.368	.019
3	*(Constant)*	0.56	0.51	11.23***	9.39**	*13.98*	*2.61*		*<.001*
	QLQ-CR29_InSy_T0					0.19	0.06	0.426	.003
	QLQ-CR29_Anx_T0					-0.06	0.03	-0.262	.062
	QLQ-CR29_Anx_T1					-0.09	0.03	-0.410	.005
4	*(Constant)*	0.65	0.59	11.97***	6.88*	*25.36*	*4.94*		*<.001*
	QLQ-CR29_InSy_T0					0.11	0.06	0.249	.079
	QLQ-CR29_Anx_T0					-0.06	0.03	-0.262	.041
	QLQ-CR29_Anx_T1					-0.09	0.03	-0.383	.004
	PANAS_PAst_T1					-0.33	0.13	-0.356	.014
5	*(Constant)*	0.70	0.64	11.75***	4.48*	*25.94*	*4.65*		*<.001*
	QLQ-CR29_InSy_T0					0.12	0.06	0.264	.050
	QLQ-CR29_Anx_T0					-0.04	0.03	-0.175	.162
	QLQ-CR29_Anx_T1					-0.07	0.03	-0.317	.013
	PANAS_PAst_T1					-0.27	0.12	-0.292	.035
	QLQ-CR29_Anx_T3					-0.06	0.03	-0.271	.045
6	*(Constant)*	0.77	0.72	13.52***	7.37*	*21.66*	*4.44*		*<.001*
	QLQ-CR29_InSy_T0					0.07	0.06	.153	.220
	QLQ-CR29_Anx_T0					-0.04	0.03	-0.178	.114
	QLQ-CR29_Anx_T1					-0.07	0.02	-0.310	.007
	PANAS_PAst_T1					-0.36	0.11	-0.379	.005
	QLQ-CR29_Anx_T3					-0.02	0.03	-0.102	.441
	PANAS_NAst_T3					0.30	0.11	0.326	.012

**p-value < .05; **p-value < .01; ***p-value < .001*

HADS_Tot: Hospital Anxiety and Depression Scale, Total Score; QLQ-CR29: EORTC colorectal cancer module: _InSy: Intestinal Symptoms, _Anx: Anxiety; PANAS: Positive and Negative Affect Scale, _PAst: Positive Affect State, _NAst: Negative Affect state scale.

The results of the regression analysis on the PTGI are shown in **Table 3.12**. The final model explained a significant proportion (59%) of the variance (F(3, 27)=15.5, p<.001). The PTG at T1 appeared to be the strongest positive contributors (PTGI_Tot_T1: β=0.509, t(27)=3.96, p<.001), followed by the Fighting Spirit coping style at T0 (Mini-MAC_FS_T0: β=0.340, t(27)=2.8, p=.009) and the Fatalism coping style at T1 (Mini-MAC_F_T1: β=0.283, t(27)=2.28, p=.031).

Table 3.12. Hierarchical multiple regression with Post-Traumatic Growth (PTGI) at follow-up (T3) as dependent variable (N=31).

	Predictor	**R^2**	**Adj R^2**	**F**	**F- ΔR^2**	**B**	**SE B**	***β***	***p***
1	*(Constant)*	0.22	0.19	8.00**	8.00**	-20.45	27.25		*.459*
	Mini-MAC_FS_T0					22.82	8.07	0.465	.008
2	*(Constant)*	0.42	0.38	10.14***	9.83**	-65.75	27.89		*.026*
	Mini-MAC_FS_T0					23.37	7.06	0.476	.003
	Mini-MAC_F_T1					14.58	4.65	0.451	.004
3	*(Constant)*	0.63	0.59	15.52***	15.66***	-43.24	23.30		*.074*
	Mini-MAC_FS_T0					16.69	5.97	0.340	.009
	Mini-MAC_F_T1					9.14	4.01	0.283	.031
	PTGI_Tot_T1					0.42	0.11	0.509	<.001

**p-value < .05; **p-value < .01; ***p-value < .001*

PTGI: Post-Traumatic Growth Inventory, _Tot: Total score; Mini-MAC_FS: Mini Mental Adjustment Scale, Fighting Spirits subscale; Mini-MAC_F: Mini Mental Adjustment Scale, Fatalism subscale.

3.8 Discussion II

The present exploratory prospective study aimed at investigating psychological distress and PTG trajectories following the subsequent treatment phases in CRC patients from diagnosis to follow-up, and to explore which factors may predict the extent of these changes at follow-up.

Previous studies on the prevalence of anxiety and depression symptoms indicated a moderate mean level of psychological distress in CRC (Peng et al., 2019; Qaderi et al., 2021). Furthermore, longitudinal studies suggested a linear decreasing trend in psychological distress, with higher levels of anxiety after surgery, likely due to adjustment to postoperative conditions (e.g., ostomy management) and communication about histologic results and thus possible adjuvant chemotherapy, which then decreased over time (Qaderi et al., 2021; Song et al., 2022; Wang et al., 2023). To the best of our knowledge, only few studies investigated levels of emotional and psychological distress in rectal cancer patients prior to receiving (chemo)radiotherapy, finding low to moderate levels of symptoms (Rades et al., 2023; Acquati et al., 2022). Moreover, Acquati and colleagues (2022) highlighted a decrease in psychological distress during the treatment pathway.

Our data confirmed the low-to-moderate prevalence of psychological distress, ranging from 10% after pre-operative treatment to 27% after surgical resection, with significant changes over time. However, in contrast to previous studies, we found a fluctuating trajectory, particularly in anxiety symptoms, which were high at diagnosis, decreased after pre-operative treatment and then increased after surgery, before starting to decrease again at follow-up. The results of a fluctuating instead of a linear trend may be related to the different design we adopted compared to previous longitudinal studies, which rarely included assessment of psychological distress between diagnosis and surgical resection. The only other study we are aware of that longitudinally assessed psychological distress in rectal cancer patients before the start of pre-operative treatment using the Emotion Thermometer reported a general decrease in psychological distress over time, although visual inspection of mean psychological distress scores over time seems to confirm our fluctuating trend (Acquati et al., 2022).

The high level of anxiety symptoms at diagnosis and their decrease after pre-operative (chemo)radiotherapy may be due not only to the initial burden of cancer diagnosis but also to anxiety about subsequent treatment. Indeed, radiotherapy still appears to be the treatment about which patients know the least (i.e., how it works and possible adverse effects). Studies that have specifically investigated the effect of this treatment in other cancer types have shown that anxiety levels decrease within a few days after the start and after the end of radiotherapy, and that it is important to provide information before and during treatment (Hernández-Blázquez & Cruzado, 2016; Hess et al., 2015; Stiegelis et al., 2004). To the best of our knowledge, only one retrospective study investigated levels of emotional distress in rectal cancer patients immediately prior to receiving (chemo)radiotherapy, finding low to moderate levels (Rades et al., 2023).

That pre-operative treatment could be a crucial phase of the CRC treatment from a psychological perspective is also confirmed by the results of the exploratory regression analyses. High levels of health anxiety and low levels of positive affectivity after pre-operative therapy significantly contributed to predicting higher levels of psychological distress at follow-up, which was also associated with the concurrent experience of higher levels of negative affectivity.

From a clinical perspective, these data sustain the importance of monitoring psychological distress in CRC patients throughout all the course of the disease, since diagnosis, in order to promptly identify patterns of increasing psychological distress symptoms and perform tailored and well-timed psychological intervention (Hess et al., 2015; Peng et al., 2019). In particular, psychological monitoring should focus on the emotional and affective reactions to the different phases of treatment, especially to the pre-operative therapy. Indeed, high symptoms of health anxiety and a low experience of pleasant emotional states after pre-operative (chemo)radiotherapy could be suggestive of a difficult adjustment to the CRC and could interfere with the patient's ability to cope with surgical resection and its sequelae from both a physical and psychological perspective, with a medium- to long-term negative impact even at follow-up (Hart & Charles, 2013; Sales et al., 2014; Voogt et al., 2005).

To date, there has only been one study that tracked longitudinally PTG in CRC patients with several assessment points, from five months post-diagnosis (which corresponds on average to our T2 assessment) to five years after (Occhipinti et al., 2015). In line with this study, in which variation in individual scores suggested an underlying linear growth (Occhipinti et al., 2015), we found a progressive increase in PTG over time in all its different domains. Indeed, our data suggested that the PTG process develops early in CRC patients, starting from pre-operative (chemo)radiotherapy (a phase that is often understudied form a psychological perspective), with an initial gradual progression followed by a steeper and statistically significant increase between the post-surgery assessment and the follow-up.

At follow-up, we found an overall low-to-moderate PTG level, consistently with the results of a recent review (Wang et al., 2023a). PTG results from struggling with traumatic life circumstances that challenge beliefs about life, and the subjective evaluation of the event as traumatic is crucial for its development (Calhoun & Tedeschi, 2006; Groleau et al., 2013). The limited psychological growth found in CRC patients compared to other types of cancer patients may be related to the fact that CRC is increasingly diagnosed with a localized disease, when symptoms are still absent or mild and has a greater curative possibility, factors that may influence the subjective evaluation of the event (Calhoun & Tedeschi, 2006; Casellas-Grau et al., 2017; Groleau et al., 2013).

The finding of an onset of the PTG process in the early phases of CRC treatment is a novel finding that is even more important when considering the results of the exploratory regression analysis, which showed that PTG after pre-operative treatment is the strongest predictive factor for a higher PTG outcome at follow-up. From a clinical perspective, the important role of PTG levels in the early phases of cancer treatment in predicting PTG at follow-up points to the need for a prompt assessment after a cancer diagnosis so that targeted interventions can be taken to promote early onset of this psychological growth process (Capaldi et al., 2023; Wang et al., 2023b).

Early assessment and intervention should also be focused on coping strategies. Although a limited number of studies investigated coping strategies specifically in CRC and few longitudinal studies have examined PTG and coping styles together in CRC patients using a specific instrument to assess cancer-related coping styles, such as the Mini-MAC (Czerw et al., 2016; Kang & Son, 2019; Knauer et al., 2022; Nordin & Glimelius, 1998), literature reports an association between the use of adaptive, positive, proactive coping styles and PTG in different types of cancer (Knauer et al., 2022; Wang et al., 2023a). In line, our data show the important prognostic role of the coping styles adopted since the diagnosis, with the use of Fighting Spirit at diagnosis and Fatalism after pre-operative treatment being significant predictors for PTG at follow-up. From a longitudinal perspective, using Fighting Spirit coping style (characterized by an optimistic attitude of confidence in being able to fight the disease) after the diagnosis might lead to facing the following treatment pathway with a better adjustment and a greater predisposition to positive psychological changes. Similarly, the use of a Fatalism coping style (described as a tendency to a resigned attitude and stoic acceptance of the disease, and an external locus of control) prior to the surgery might be an indication of a greater acceptance of the disease and reliance on treatment, which is then reflected in an impulse to the PTG.

None of the clinical (physical symptoms or cancer related variables) and sociodemographic variables proved to be significant predictors of PTG outcome at follow-up, nor was resilience, which has previously been found to be positively associated with PTG in CRC (Sihvola et al., 2022; Wang et al, 2023a). However, our patients reported very high levels of resilience, with more than 60% of them falling into the "high resilience" range, likely resulting in a ceiling effect for this variable.

3.8.1 Study limitations

Our results need further investigation and should be considered with caution, even considering the limitations of the present study. The most important limitation concerns the small sample size of this exploratory study, which made the regression analyses underpowered. Unfortunately, recruitment procedures were severely affected by the COVID-19 pandemic, although all necessary measures were taken to continue the longitudinal assessment of recruited patients and to reduce the number of dropouts. Moreover, this study did not take into account information on any psychological treatment of patients, which might have an effect on the psychological state and outcomes variables under investigation. Finally, the use of self-report instruments only, which may have introduced biases due to social desirability effects, casual responses, and potential lack of awareness of participants.

Future longitudinal studies with a larger sample of CRC patients are needed to increase knowledge of this specific population. In particular, longitudinal studies assessing the different variables of interest as early as the diagnosis of CRC are needed to further investigate the course and medium- to long-term predictive value of the various factors for positive and negative psychological outcomes.

3.8.2 Clinical implications

A cancer diagnosis may not only lead to negative outcomes such as psychological distress or psychopathological disorders but may also trigger positive psychological changes such as Post-Traumatic Growth. Overall, our data suggest that PTG and psychological distress have a different trajectory, linear and gradual in the former and fluctuating in the latter, with psychological distress increasing at diagnosis and after surgery. Several intrapsychic characteristics of the patients contributed to their adjustment to cancer and influenced the positive and/or negative psychological outcomes. In particular, psychological distress at follow-up was mainly influenced by emotion-related features, i.e., health anxiety and decreased positive affect experience, whereas the adoption of an active and positive coping style in the early phases of CRC treatment and an early onset of the psychological growth process led to a higher PTG outcome at follow-up. Although influenced by different psychological aspects, both positive and negative outcomes were closely related to patients' response to the different treatment phases, especially to the communication of the diagnosis and pre-operative treatment, suggesting that early adjustment may be crucial for medium- to long-term psychological outcomes.

From a clinical perspective, the data point to the need to implement psychological screening programmes that monitor the psychological adjustment of CRC patients in all phases of the disease, starting with the communication of the diagnosis, in order to identify early the aspects that could affect the psychological growth process and lead to a negative psychological outcome. Timely psychological assessments should be accompanied by tailored psychological support programmes aimed at supporting and improving the aspects (e.g., coping style, affectivity) that promote PTG and prevent psychological distress immediately and in the long term, from the earliest phases of CRC treatment.

Conclusions

The present dissertation aims to investigate the psychosomatic outcomes and components of CRC, attempting to understand the interrelation between medical and psychosocial factors in a biopsychosocial perspective. The former includes the impact of diagnosis, medical treatments and their consequences on QoL and mental health, while several personality and situational variables are included in the psychosocial factors.

Living with a cancer diagnosis can be considered an event of traumatic magnitude. CRC patients often emphasise the need to re-establish a sense of control over their own life and health, to reconsider the resources available to cope with therapeutic demands, and to re-evaluate the meaning of their existence in the context of a physically and mentally disabling condition (Sales et al., 2014). Active involvement in the care process can lead to greater satisfaction with the care itself, which is thus experienced with less anxiety and conflict, and a reflected effect on greater perceived well-being (Kunneman, et al., 2016).

Early screening of QoL levels, psychological distress and PTG is necessary given the effects on physical and mental health outcomes of a condition such as that experienced by CRC patients (Capaldi et al., 2023; Castelli et al., 2011; Mosher et al., 2016; Sales et al, 2014; Wang et al., 2023b).

Several psychosocial factors (e.g., alexithymia, psychological resilience, coping styles, perceived social support, trait and state affectivity) could concur in explaining individual variability in disease outcomes, such as symptoms experienced, adherence to health behaviours, positive and negative psychological conditions, and mortality rates (Cakmak et al., 2021; Casellas-Grau et al., 2016; Cordova, 2008; Cordova et al., 2017; De Vries et al., 2012; Gouzman et al., 2015; Knauer et al., 2022; Romeo et al., 2019; Schmidt et al., 2012; Sihvola et al., 2022; Tedeschi et al., 2018; Voogt et al., 2005; Wang Z. et al., 2023a; Ye et al., 2016). It is therefore crucial to better understand the impact of these factors in order to better tailor care pathways, considering that a large proportion of CRC patients report clinically relevant symptoms of psychological distress and that one in three patients do not receive psychological support at critical phases of the medical pathway, such as radiotherapy and surgery (Peng et al., 2019; Wagner et al., 2017).

Taking together the previous evidence that often only individually examined the different medical, psychological, and social aspects in CRC patients and considering the scarce literature present in relation to CRC patients and, indeed, the evidence in other oncological diseases, it was considered appropriate to develop an extensive exploratory research project, to investigate the trajectories and possible predictors of QoL, psychological distress and PTG, paying attention to the different treatment phases provided for this type of cancer. For the purposes of this dissertation, only a part of the many variables and data collected was considered and analysed, and two specific aspects were focused on (Objectives I and II). Therefore, some other sub-objectives of the broader study remain to be addressed, such as exploring the role of certain variables (e.g., type-D personality, attachment and emotion dysregulation) on positive and negative psychological outcomes or exploring the effects of certain psychosocial variables on QoL one year after surgery.

Objectives I of the study were: 1) to evaluate the changes in health-related QoL of CRC patients during active treatments phases, i.e. radiation oncologists' appointment, during which patients received indication for cancer treatments (T0 - diagnosis), after pre-operative (chemo)radiotherapy (T1), and after surgical resection (T2); 2) to explore which physical and psychosocial factors (i.e., disease-specific symptoms, psychological distress, trait and state affectivity, alexithymia, coping styles, and perceived social support) better predict health-related QoL at different early phases of CRC treatment, to also observe the impact of individual treatments.

The results show a general deterioration of QoL in CRC patients from the time of diagnosis until one month after surgical resection. Several medical and intrapsychic characteristics of the patients contributed to QoL at different treatment phases. In fact, at diagnosis tendency toward negative trait affectivity was the only predictive factor of QoL. Indeed, physical symptoms (i.e., pain at diagnosis and intestinal and urinary symptoms after pre-operative (chemo)radiotherapy) contributed to QoL levels after pre-operative treatment, while especially psychological factor played a role on QoL after surgery (i.e., psychological distress and mouth symptoms evaluated after surgery, and Fatalism coping style after pre-operative treatment).

Objectives II of the study were: 1) to evaluate the changes in psychological distress and PTG in CRC patients, following the successive treatment phases from diagnosis to follow-up (i.e. after radiation oncologists' appointment, during which patients received indication for cancer treatments – T0; after pre-operative (chemo)radiotherapy – T1; after surgical resection – T2; one year after surgery – T3); 2) to explore which physical and psychosocial factors (i.e., disease-specific symptoms, psychological distress and PTG at different timepoints, trait and state affectivity, alexithymia, coping styles, and resilience) better predict psychological distress and PTG at follow-up.

The results suggest that psychological distress has a fluctuating trend, with high levels at diagnosis, decreasing after radiotherapy, increasing again after surgery, and decreasing again at follow-up. Whereas, PTG had a linear and gradual trajectory, with increasing levels over time, although confirming low to moderate levels of psychological growth, as found in previous studies on CRC patients. Moreover, psychological distress at follow-up was mainly influenced by emotion-related features, such as health anxiety and decreased positive affect experience after the end of pre-operative treatment and increased negative affectivity at follow-up. The adoption of active and positive coping styles, i.e. Fighting Spirit at diagnosis and Fatalism after pre-operative treatment, and an early onset of the psychological growth process contribute to a higher PTG outcome at follow-up.

As mentioned above, the study has certain limitations that make it necessary to consider the results obtained with caution. Future studies will be needed to better understand the relationship between the different variables investigated, with a larger sample size and using more advanced analyses. For example, in a study with a more extended longitudinal design (i.e., following patients beyond the year after surgery, during the pre-survivoship period), it would be possible to analyse the growth curve of the outcomes considered by using growth models and to understand the interrelation between several variables by implementing mediation/moderation models or also, by evaluating the trend over time, longitudinal structural equation models (longitudinal SEM).

Taken together, the evidence of these studies points to the need for a biopsychosocial screening assessment of CRC patients since the diagnosis and in all subsequent phases of the treatment pathway, including physical and psychological variables, to monitor the psychological adjustment to the disease. Moreover, support services should be tailored to both the individual patient and the treatment phase, in particular through the implementation of multidisciplinary and multimodal preventive and pre-habilitation interventions immediately after diagnosis, in order to improve QoL and psychological health of patients in the medium and long term.

Interventions aimed at fostering positive psychological outcomes following cancer disease should take into account the medical and psychological specificities of patients, in order to: provide knowledge and normalising emotional reactions following the cancer diagnosis; facilitate the communication of emotions with support networks; guide the patient in the construction of a coherent narration of the event; re-assume one’s identity and life roles from before cancer; facilitate the evaluation of the costs of the disease, but also of the new resources that can emerge; provide the opportunity to talk about worries related to the future; provide tools to increase the sense of control over one's body and emotions, reducing levels of tension and anxiety; help the patient to focus and clarify one’s values, priorities and goals (Cordova, 2008). It is important to remember that the individual is not just his or her disease, but also carries a constellation of previous (the past) and current (the present) characteristics that in turn influence the response to the disease itself (the future).

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Supplementary Material

Translated informed consent forms.

The original version is in Italian and on headed paper. The informed consent contains the information of the investigator from the hospital responsible for the study, whom it was necessary to refer to in order to carry out the study.

PATIENT INFORMATION

Title of the study: Post-Traumatic Growth in patients with colon-rectal carcinoma: a longitudinal study. <<PTG-Onco>>

Promoter of the study: S.C. Radioterapia U. of the A.O.U. Città della Salute e della Scienza of Turin

Dear Sir/Madam,

We invite you to participate in a prospective, single-centre, clinical study, promoted by the S.C. Radioterapia U. of the A.O.U. Città della Salute e della Scienza of Turin, in which personal data, clinical-anamnestic and socio-demographic information will be collected from patients who, like you, are affected by colorectal cancer and undergo radiotherapy treatment at the above-mentioned facility.

The study will be conducted locally by Prof. Pierfrancesco Franco, as scientific leader.

The following information concerns this study and will help you decide whether or not to participate. Please read it carefully before making your decision. The doctor in charge of the study will discuss the following information with you, but it is important that you ask for any clarification of what is unclear to you. Take time to decide whether you want to take part in the study. If you decide not to participate, this decision will in no way affect your future medical care or the attention you will receive from your doctor.

WHAT IS THE PURPOSE OF THE STUDY?

The aim of this study is, considering it of primary importance to investigate which medical-clinical, socio-demographic and psychological elements favour the positive reworking of the knowledge of one's state of health and the post-traumatic growth process, to structure possible psychological interventions that may favour and enhance this growth process, thus improving the psychological impact and long-term quality of life.

Like you, a total of about 85 patients will come back to the centre.

WHAT HAPPENS DURING THE STUDY?

As per clinical practice, you will be informed about your treatment plan according to routine guidelines. During the course of treatment, at regular intervals below, you will be given questionnaires about your quality of life by the medical staff, which you will be asked to answer freely. The questionnaires will be submitted to you during the following visits: after enrolment and before the start of the neoadjuvant treatment; one month after the end of the neoadjuvant treatment, during the pre-surgical check-up for restage of the tumour; at approximately one month after surgery; follow-up evaluation carried out at six months after surgery or in the pre-intervention recanalization evaluation for those patients with temporary ostomy, and one last time at one year after surgery (at least three months in the case of recanalization surgery).

WHAT ARE THE POSSIBLE BENEFITS OF PARTICIPATING IN THE STUDY?

The benefits of participating in the study are first and foremost the possibility of collecting personal information, enabling medical personnel to gain a thorough understanding of your awareness of the disease, adapting treatment, supporting you and giving you the opportunity to benefit from targeted care at an early stage.

The support it will receive aims at better results in terms of preserving long-term quality of life.

WHAT ARE THE POSSIBLE RISKS OF PARTICIPATING IN THE STUDY?

There is no risk involved in your participation in the study, as you will only be asked to answer questionnaires.

The study was examined and approved by the Regulatory Authorities and the Intercompany Ethics Committee of the A.O.U. Città della Salute e della Scienza di Torino; it will be conducted in accordance with local and European laws for the protection of subjects involved in clinical research.

WHAT ARE THE COSTS TO BE INCURRED?

None and will receive no remuneration.

WHAT INFORMATION ON CONFIDENTIALITY?

In accordance with the rules of good clinical practice and with Legislative Decree 196/2003 (and subsequent amendments and/or additions), the confidentiality of your personal data will be guaranteed. The doctor who will follow you in the study will identify you with a code: the data concerning you collected during the study, with the exception of your name, will be recorded, processed and stored together with this code. Only the doctor and authorised persons will be able to link this code to your name.

All information (e.g. date of birth, gender, race, height, weight, health and socio-demographic data) obtained from you by healthcare personnel will be stored for at least 7 years, securely by the medical practitioner at the Hospital Centre and will remain confidential.

Your identity will not be revealed at any time during the clinical study. Furthermore, should your data be analysed and described in a report or should the results of this study be published, your anonymity will be guaranteed.

The A.O.U. Città della Salute e della Scienza di Torino is responsible for your personal data and agrees to comply with data protection laws by taking specific data protection measures.

The doctors involved in the study and their staff will be responsible for the management of the data, the results, and their reading in accordance with good clinical practice.

Qualified representatives of the Ethics Committee/Ministerial Authorities may check your data to verify the procedures and results of the clinical trial, without violating the confidentiality of the information contained, to the extent permitted by law.

Exercise of rights

You may exercise your rights under Art. 7 of the Personal Data Protection Code (e.g. access your personal data, supplement them, update them, rectify them, oppose their processing for legitimate reasons, etc.) by contacting the local testing centre directly, the person in charge Prof. Pierfrancesco Franco, tel. 011-6336626.

WHAT INFORMATION ON VOLUNTARY PARTICIPATION?

If you agree to participate in this clinical study, we ask you to sign the informed consent form, as a declaration that you understand the methods and aims of the study and that you wish to take part in it freely.

Your decision to participate in the clinical study is completely voluntary, so you may withdraw your consent at any time, upon simple request, without having to give any justification and without any modification of the treatment you will receive in the future or of your legal rights.

CONTACT PERSONS

You have the right to ask any questions you deem appropriate and to obtain further information about this protocol now or at any time during the study by referring to

Prof. Pierfrancesco Franco

Dr. Francesca Arcadipane

Tel: 011.6336626 - 011.6336606

S.C. Radiotherapy U.

A.O.U. Città della Salute e della Scienza di Torino Via Genova 3, 10126, Torino

INFORMED CONSENT

Study title: Post-Traumatic Growth in colorectal cancer patients: a longitudinal study. <<PTG-Onco>>

Study sponsor: S.C. Radiotherapy U., A.O.U. Città della Salute e della Scienza di Torino, Via Genova 3, 10126, Torino

Experimental Physician: ____

I, the undersigned____

born in ____on ___/___/___

Address____ Telephone_________________

I declare

- That he is suffering from colorectal neoplasia;
- To voluntarily participate in the study "Post-Traumatic Growth in colorectal cancer patients: a longitudinal study." with the aim of investigating what may be the medical-clinical, socio-demographic and psychological elements that favour the positive re-elaboration of the event and the PTG (Post-traumatic Growth) process, with a view to structuring possible psychological interventions aimed at favouring and enhancing this growth process, thus improving the psychological outcome and quality of life of cancer patients;
- That I have received from Dr._________________________ full explanations regarding the request to participate in the research, in particular regarding the aims and procedures;
- That I have had sufficient time to carefully read, understand and, if necessary, have explained to me what is contained in the attached information sheet, which I have signed for acknowledgement, and which confirms what was explained to me verbally, in particular that the trial will be conducted in accordance with international ethical codes;

- To have had the opportunity to ask questions and to have received satisfactory answers on the whole experiment;
- That I have been informed of any reasonably foreseeable risks or inconveniences;
- To consent/not to consent to the responsible doctor informing my GP;
- To consent to monitors, audits, national and foreign regulatory authorities having direct access to my clinical documentation for monitoring and verification purposes;
- To be aware that participation is voluntary, with the assurance that refusal to participate will not affect receiving the most suitable treatment;
- That I can withdraw from the trial I have already started at any time without any negative consequences;
- That the medical records will remain strictly confidential, and the data will be used for the purposes indicated in the study (in accordance with legislative decree 196/2003), that the data will only be accessible to expressly authorised personnel and will be rectified or deleted at my request;
- That I will be informed of any new data that may influence the risks or benefits, or of protocol changes that may influence them;
- That it is my right to have access to the documentation concerning me and to the evaluation expressed by the Ethics Committee to which I can turn if I deem it appropriate (___________)
- That a copy of the informed consent and of the documentation I have read will remain in my possession;
- That for any problems or further information I can contact the

Experimental Physician or Researcher

Dr. ____

Work address: Via Genova 3, 10126, Turin Telephone number: 011.633.6626

Therefore,
I confirm that I have had full answers to all my questions and, having taken note of the situation outlined,

I AGREE

FREELY, SPONTANEOUSLY AND IN FULL CONSCIENCE TO THE NON-PHARMACOLOGICAL EXPERIMENTAL STUDY PROPOSED TO ME.

I also declare that I am aware of the possibility of revoking this consent at any time before the start of the trial.

Date________________ Start interview time____________ End interview time___________

Patient signature____

Signature of parent/legal representative____________________________ (where applicable)

Any witnesses present (name, surname, signature): ___________________________________

Doctor's signature ____

OR

I DO NOT AGREE

FREELY, SPONTANEOUSLY AND IN FULL CONSCIENCE TO THE NON-PHARMACOLOGICAL EXPERIMENTAL STUDY PROPOSED TO ME.

I also declare that I am aware of the possibility of revoking this consent at any time before the start of the trial.

Date________________ Start interview time____________ End interview time____________

Patient signature____

Signature of parent/legal representative____________________________ (where applicable)

Any witnesses present (name, surname, signature): ___________________________________

Doctor's signature ____

Information for the attending physician

Post-Traumatic Growth in Colorectal Carcinoma Patients: A Longitudinal Study. <<PTG-Onco>>

Dear Colleague,
Your patient, Mr/Mrs.________________________________ to participate in an interventional, non-pharmacological, prospective, single-centre clinical trial promoted by our centre, the S. C. Radiotherapy U., afferent to the Department of Oncology of the A.O.U. Città della Salute e della Scienza of Turin.

Below you will find information about the firm; for further details, please contact the firm's managers directly.
As you know, colorectal cancer is the most frequent neoplasm of the gastrointestinal tract. According to Italian epidemiological data, excluding skin cancers (non-melanomas), colorectal cancer is the second most frequent neoplasm for both men (16% of all diagnosed cancers) and women (13%), and it is among the top five neoplasms in all three age groups considered (<50 years, 50-70 years, >70 years), with an increase in the percentage of cases after the age of 50. Data on oncological mortality in Italy for the five-year period 2008-2013 indicate that colorectal cancer ranks second as the cause of death as a proportion of total oncological deaths for both sexes, with survival rates at 5 and 10 years after diagnosis of 66% and 64% of patients with colon cancer and 62% and 58% of patients with rectal cancer, respectively. In most cases, surgery, which is the elective treatment modality for colorectal cancer, is preceded by a neoadjuvant radio/chemotherapy regimen aimed at downstaging, i.e. reducing the stage of the tumour, which improves local control of the disease and, in general, the outcome for these patients. Radio/chemotherapy and surgical treatments can lead to important physiological changes, some of which may persist even after healing, with important repercussions on the personal and social sphere of patients. One only has to think, for example, of the changes in habits and lifestyle that an ostomy patient has to cope with, or the repercussions on the affective life of the sexual dysfunctions that often result from such treatments. The ability to cope with the stress linked to the entire treatment course and to rework the traumatic experience, transforming it into a drive for psychological growth, therefore has an important impact on adaptation to the disease and consequently on the quality of life of patients with colorectal cancer.

The ultimate aim of the study is to investigate which medical-clinical, socio-demographic and psychological elements may favour the positive re-elaboration of the event and the PTG (Post-traumatic Growth) process, with a view to structuring possible psychological interventions aimed at favouring and enhancing this growth process, thus improving the psychological outcome and quality of life of cancer patients.
To this end, the protocol provides for the administration of quality-of-life questionnaires at predetermined times during the course of the study as part of the routine clinical practice for the treatment of the disease under study:

- T0: baseline assessment, performed following enrolment and prior to the start of neoadjuvant treatment;
- T1: performed one month after the end of adjuvant radiotherapy treatment, during the pre-surgical check-up for possible resection of the tumour;
- T2: performed approximately one month after surgery;
- T3a: follow-up evaluation carried out six months after surgery;
- T3b: Follow-up evaluation performed pre-intervention of recanalisation for patients with temporary ostomy;
- T4: follow-up evaluation carried out one year after surgery (and at least 3 months after recanalisation).

You will be promptly informed of any schedule changes that may be necessary and of the results of the study as soon as they become available.

This study is conducted in accordance with the principles of the Declaration of Helsinki (GCP-ICH) and following the approval of the Intercompany Ethics Committee A.O.U. Città della Salute e della Scienza di Torino - A.O. Ordine Mauriziano - A.S.L. Città di Torino and its Health Management.

Certain that the collaboration between the General Practitioner and the Specialist is necessary for the complete and integrated management of the patient, I send you my best regards.

The Principal Investigator
Prof. Pierfrancesco Franco
Via Genova 3, 10126 - Torino
Tel. 011-6336626 Fax 011-6336614

Appendix. My other research interest and publications

Psychological impact of the COVID-19 pandemic. Since March 2020, a research strand on the psychological impact (anxiety, depression and post-traumatic stress symptoms) of the COVID-19 pandemic on the general population and healthcare workers has been initiated.

Through systematic literature reviews and meta-analyses, collection of the available evidence on emotional regulation, and in particular alexithymia, and its possible implications in different populations with medical conditions (e.g., hypertension and HIV) and/or in different life situations (e.g., victims and perpetrators of intimate partner violence).

The role of psychological factors in fibromyalgia and other chronic pain syndromes. Clinical psychology and psychosomatic studies in patients with chronic pain (fibromyalgia), with particular emphasis on emotional dysregulation, alexithymia, psychological distress, and personality aspects.

Canadian Psychiatric Association
Association des psychiatres du Canada

Research Letter

The Canadian Journal of Psychiatry /
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The Spread of COVID-19 in the Italian Population: Anxiety, Depression, and Post-traumatic Stress Symptoms

Lorys Castelli, PhD[1], Marialaura Di Tella, PhD[1], Agata Benfante, MS[1], and Annunziata Romeo, PhD[1]

Keywords
post-traumatic stress symptoms, COVID-19, anxiety symptoms, depressive symptoms, logistic regression analysis, Italian population

The first case of COVID-19 in Italy emerged at the end of January 2020.[1] Following a series of increasingly severe restrictions, a new decree on March 9, 2020, imposed home lockdown on the entire nation.[2] The COVID-19 outbreak, similarly to previous epidemics, can trigger psychological disorders such as anxiety, depression, and post-traumatic stress disorder (PTSD) in exposed individuals in the short as well as in the long-term.[3]

This study aimed to investigate the prevalence of post-traumatic stress symptoms (PTSS) in the general Italian population and to explore the variables such as sociodemographic features, COVID-19-related aspects, quality of life, and health-related aspects that could predict the likelihood of PTSS occurrence. Moreover, anxiety and depressive symptoms, often observed in people exposed to highly stressful events, were evaluated.

Data were collected using an anonymous online survey from March 19, 2020, to April 5, 2020. A snowball sampling strategy was employed, wherein the participants were initially recruited via online advertisements and were encouraged to pass the survey link to others. Responses of 1,321 participants were included in the final data set. Participants were asked to provide sociodemographic information and complete (1) COVID-19-related questions, (2) quality of life and health-related visual analogue scales, (3) State-Trait Anxiety Inventory-Form Y1, (4) Beck Depression Inventory (BDI-II), and (5) PTSD Checklist for DSM-5 (PCL-5) in order to assess PTSS.

This study was approved by the University of Turin ethics committee and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

The total sample had a mean age of 35.1 (*SD* 14) years; 69% (922) of participants were females, and 71% (933) were from Northern Italy. Most of the participants had a degree or postgraduate qualification (53%, 140) and were employed (54%, 713).

Considering the COVID-19-related question responses, 12% (154) of the participants reported having contact(s) with COVID-19-positive individuals, whereas 16% (210) of the participants referred knowing of others who died due to COVID-19.

Twenty percent (265) of the participants presented evidence of significant PTSS, whereas 69% (914) and 31% (273) of the participants reported clinically relevant anxiety and depressive symptoms, respectively. Notably, these measures were found to be strongly associated with each other (BDI and PCL-5: $r = 0.673$, $p < 0.001$; STAI and PCL-5: $r = 0.682$, $p < 0.001$).

A hierarchical logistic regression analysis was conducted using the enter method to examine whether the sociodemographic variables (first step), COVID-19-related aspects (second step), and quality of life and health-related variables (third step) predict the likelihood of PTSS occurrence. Adjusted odds ratios and 95% confidence intervals were calculated as predictors of logistic regression.

The final model was statistically significant, with χ^2 (10) $= 181.926$, $p < 0.001$. It explained 20% (Nagelkerke R^2) of the variance and accurately classified 81.4% of the cases. Among the predictors, gender, education level, contact with individual(s) positive for COVID-19, life satisfaction, health evaluation, and health concern were statistically significant.

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BRIEF REPORTS

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Mental health of healthcare workers during the COVID-19 pandemic in Italy

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Abstract

Background: The COVID-19 pandemic represents one of the most stressful events of recent times. Among the population, healthcare professionals who treat COVID-19 patients are most likely to develop psychological distress and posttraumatic stress symptoms (PTSS). The present study thus aimed to investigate the psychological impact of the COVID-19 outbreak on Italian healthcare workers.

Methods: The responses of 145 healthcare workers (72 medical doctors and 73 nurses) were included in the final dataset. Participants were asked to provide sociodemographic and clinical information, and to complete: (a) quality of life and health-related Visual Analogue Scales, (b) State-Trait Anxiety Inventory-Form Y1, (c) Beck Depression Inventory, and (d) PTSD Checklist for DSM-5.

Results: A comparison between healthcare professionals working in COVID-19 wards and other units revealed that the former reported higher levels of both depressive symptoms and PTSS. Moreover, the results of regression analyses showed that in healthcare professionals working with COVID-19 patients, gender and marital status, and gender and age significantly predicted depressive symptoms and PTSS, respectively. Particularly, being female and not in a relationship were found to be associated with higher levels of depressive symptoms, whereas being female and older were found to be related to higher levels of PTSS.

Conclusions: The current findings suggest that specific predisposing factors could identify healthcare workers who are at high risk of developing mental health symptoms when faced with COVID-19 patients.

KEYWORDS
COVID-19 pandemic, depressive symptoms, healthcare workers, mental health, posttraumatic stress symptoms

1 | INTRODUCTION

The COVID-19 pandemic represents one of the most stressful events in recent times worldwide. This pandemic poses a major challenge to social, economic, and, above all, the psychological resources of the population. Undoubtedly, healthcare workers are the most exposed category. Their psychological burden is likely due to the staff reorganization, the working intensity, and the anxiety of being exposed to the virus at hospital and, in turn, of bringing the infection home.[1] The healthcare workers directly involved in the care of patients with COVID-19 are at high risk of developing psychological distress and other mental health symptoms such as posttraumatic stress symptoms (PTSS).[2,3]

The main aim of the present study was to investigate the psychological impact of the COVID-19 outbreak on Italian healthcare

frontiers in Psychology

MINI REVIEW
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Traumatic Stress in Healthcare Workers During COVID-19 Pandemic: A Review of the Immediate Impact

Agata Benfante, Marialaura Di Tella, Annunziata Romeo and Lorys Castelli*

Department of Psychology, University of Turin, Turin, Italy

The disease caused by respiratory syndrome coronavirus 2 (SARS-CoV-2) called COVID-19 resulted in a pandemic that has demanded extraordinary physical and mental effort from healthcare workers. This review provides an overview of studies that have explored traumatic stress in healthcare workers and associated factors between January and May 2020. The focus is on the most relevant literature investigating the prevalence of trauma- and stressor-related symptoms. Articles were selected from PubMed and PsycINFO databases using the search terms, "healthcare workers," "COVID-19," and "posttraumatic stress" in different combinations and with various synonyms. Among the seven studies that fulfilled our criteria, five assessed traumatic stress response, one assessed acute stress symptoms, and one focused on vicarious traumatization. Overall, the available findings highlight the presence of trauma-related stress, with a prevalence ranging from 7.4 to 35%, particularly among women, nurses, frontline workers, and in workers who experienced physical symptoms. Future studies should clarify the long-term effects of the COVID-19 pandemic on the mental health of healthcare workers, with particular focus on posttraumatic stress disorder.

Keywords: trauma, acute stress, vicarious traumatization, COVID-19, healthcare workers

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INTRODUCTION

The World Health Organization (WHO) declared COVID-19 as a pandemic on March 11, 2020, when infections and deaths began to increase exponentially worldwide. The first cases were reported during December 2019 in Wuhan, China (WHO, 2020).

This virus belongs to the coronavirus family, which can cause respiratory infections in humans that resemble the common cold, as well as lethal illness similar to that associated with Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS; Carver and Phillips, 2020). The symptoms of the new respiratory syndrome coronavirus 2 (SARS-CoV-2) can be fever, cough, tiredness, pains, nasal congestion, headache, and conjunctivitis, but they can also include pneumonia, acute respiratory syndrome, kidney failure, and death. Transmission is believed to occur *via* droplets (Carver and Phillips, 2020; Lechien et al., 2020; WHO, 2020). By May 22, 2020 the number of global confirmed infections and deaths had reached ~4,893,000 and ~323,000, respectively (WHO, 2020). Such an extraordinary event will have long-term effects on mental health according to previous studies of epidemics and quarantine (Maunder et al., 2006; Brooks S. K. et al., 2020; Kisely et al., 2020). The COVID-19

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Correspondence

The psychological impact of COVID-19 on general practitioners in Piedmont, Italy

ARTICLE INFO

Keywords
COVID-19
Anxiety symptoms
Depressive symptoms
Post-traumatic stress symptoms
General practitioners

Dear Editor,

The spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has produced unprecedented pressure on healthcare systems.

In Italy, the first western nation to be affected by the pandemic, to date, 226.699 people have been found COVID-19 positive, and 32.169 have died due to this condition. Among the latter, 164 were medical doctors and 57 were general practitioners (GPs) (FNOMCeO, 2020).

While hospitals are involved in the treatment of patients with moderate/severe symptoms of COVID-19, GPs exert incredible effort as gatekeepers of the healthcare system by detecting patients with suspected infection. Furthermore, this effort is made without clear guidelines on COVID-19 management or protection, risking infection and spread to the community (De Sutter et al., 2020; Shanafelt et al., 2020).

On these bases, the present study aimed to investigate the psychological impact of the COVID-19 pandemic on GPs. Specifically, we aimed to investigate anxiety, depression, and post-traumatic stress symptoms (PTSS) on a convenience sample of GPs practicing in Piedmont, one of the most affected Italian regions. In addition, we explored whether any sociodemographic or work-related variables could be associated with these psychological symptoms.

In order to reach these goals, a convenience sample of 2049 GPs (out of a total of 3100 GPs in Piedmont) affiliated with the regional FIMMG, Italy's most popular general practitioner union, were contacted via email and asked to participate in an anonymous online survey about the spread of SARS-CoV-2. Data were collected from April 28, 2020 to May 10, 2020.

A total of 246 GPs (12% of the contacted GPs) completed the survey. For the purpose of this study, we analysed sociodemographic information, work-related variables, and the results of three self-report scales investigating symptoms of anxiety, depression, and post-traumatic stress: the State-Trait Anxiety Inventory-Form Y1 (STAI Y1), the Beck Depression Inventory (BDI-II), and the PTSD Checklist for DSM-5 (PCL-5), respectively.

The study was approved by the University of Turin Ethics Committee and conducted in accordance with the Declaration of Helsinki. All the participants gave their written informed consent to participate in the study.

With regard to sociodemographic and clinical characteristics of the total sample, participants had a mean age of 51.1 (SD = 13.1) years and 56% (138) of them were female. The majority of the GPs had at least one child (64%, 157) and had no previous medical condition (69%, 170).

Results of the psychological assessment showed that 32% (79) of the GPs presented significant PTSS, whereas 75% (185) and 37% (91) of the GPs reported clinically relevant anxiety and depressive symptoms, respectively. Furthermore, concerning the work-related questions, 41% (100) of GPs reported not having Personal Protective Equipment (PPE) at their disposal, 48% (119) reported not receiving adequate information to protect their families, and 61% (149) did not receive clear diagnostic/therapeutic guidelines on COVID-19 to do their jobs.

Comparisons between GPs based on psychopathology scale results are reported in Table 1.

GPs with clinically relevant anxiety and depressive symptoms were younger, more likely to be female, and had been practicing for fewer years, than GPs without anxiety/depression symptoms.

Moreover, GPs that showed clinically relevant PTSS in addition to anxiety and depression, are the ones that have reported in significantly higher percentage that they have not received adequate information to protect their families and clear diagnostic/therapeutic guidelines on COVID-19 to do their jobs.

The results of the present study highlight that an extremely high percentage of GPs experienced clinically relevant anxiety and depressive symptoms, as well as significant PTSS, because of the SARS-CoV-2 pandemic.

GPs who were female, younger, and less experienced showed significantly higher levels of anxiety and depressive symptoms compared to male, older, and more experienced GPs. This evidence confirmed the data in the general health care population (Kisely et al., 2020). Conversely, no significant differences on the levels of psychopathological symptoms were found between GPs who had or not a medical condition and between GPs who had or not children. As regards to the medical condition, we think that this is due to the extreme variability of the medical conditions reported by the participants. Further studies with larger sample should investigate this issue. As regards to the children variable, we can hypothesize that our negative evidence can be

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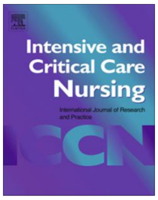

Correspondence

Anxiety, depression, and posttraumatic stress in nurses during the COVID-19 outbreak

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Dear Editor,

During the COVID-19 pandemic, nurses and physicians faced exhausting work conditions, making ethically and morally difficult decisions, and taking health risks for themselves and their loved ones (Maben and Bridges, 2020). This situation also affected their mental health, with high levels of posttraumatic stress symptoms (PTSS) that have been reported by nurses and physicians since the early months of pandemic (Benfante et al., 2020).

The present study mainly aimed to assess the psychological impact of the COVID-19 outbreak on nurses and physicians working in Italy.

The responses of 73 nurses and 72 physicians were collected through an anonymised online survey. The current data were acquired as part of a larger project investigating the psychological impact of COVID-19 in Italian population. Participants were asked to indicate sociodemographic, clinical and work-related information, and to complete three self-report questionnaires to assess

Table 1
Sociodemographic, clinical, and work-related characteristics of nurse and physician groups. Mean (SD), percentage, *t*-test, chi-square test, and Cohen's *d* are listed.

	Nurses (N = 73)	Physicians (N = 72)	Test (df)	*p*	Effect size
Age (years)	44.3 (10.6)	41.5 (11.7)	t(143) = –1.51	0.134	*d* = 0.25
Sex			$\chi^2(1) = 0.63$	0.427	
Male	18 (24.7%)	22 (30.6%)			
Female	55 (75.3%)	50 (69.4%)			
Marital status			$\chi^2(1) = 0.61$	0.433	
Not in a relationship	31 (42.5%)	26 (36.1%)			
In a relationship	42 (57.5%)	46 (63.9%)			
Type of ward			$\chi^2(1) = 0.01$	0.925	
COVID-19 unit	32 (43.8%)	31 (43.1%)			
Other unit	41 (56.2%)	41 (56.9%)			
Medical condition			$\chi^2(1) = 2.14$	0.144	
Yes	23 (31.5%)	15 (20.8%)			
No	50 (68.5%)	57 (79.2%)			
Psychological aspects					
Health evaluation (VAS)[*]	7.11 (2.0)	8.4 (1.4)	t(126.64) = 4.62	**<0.001**	*d* = 0.77
Health concern (VAS)[#]	7.04 (2.5)	6.0 (2.6)	t(143) = -2.42	**0.017**	*d* = 0.40
STAI Y1	53.8 (14.5)	48.8 (12.9)	t(143) = -2.21	**0.029**	*d* = 0.37
Scored above the STAI Y1 cut-off point (≥41)	55 (75.3%)	48 (66.7%)	$\chi^2(1) = 1.33$	0.250	
BDI-II	12.3 (10.5)	10.7 (8.4)	t(143) = -0.96	0.340	*d* = 0.20
Scored above the BDI-II cut-off point (>13)	21 (28.8%)	24 (33.3%)	$\chi^2(1) = 0.35$	0.552	
PCL-5	29.1 (18.6)	20.3 (14.2)	t(134.52) = -3.19	**0.002**	*d* = 0.53
Scored above the PCL-5 cut-off point (≥33)	24 (32.9%)	14 (19.4%)	$\chi^2(1) = 3.38$	0.066	

SD = Standard Deviation; VAS = Visual Analogue Scale; BDI-II = Beck Depression Inventory; STAI Y1 = State-Trait Anxiety Inventory Form Y1; PCL-5 = PTSD Checklist for DSM-5.

P-values in bold indicate statistically significant differences between nurses and physicians ($p < .05$).

[*] Health evaluation question = 'How do you currently rate your health?'.

[#] Health concern question = 'How concerned are you about contracting COVID-19?'.

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Brief Report

Psychological Distress among Italian University Students Compared to General Workers during the COVID-19 Pandemic

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Abstract: The COVID-19 pandemic induced numerous changes in the daily life of every individual, with important social, economic, and psychological consequences. Particularly, the psychological impact encountered among students might be affected by social isolation, concern for personal health and for the health of family members and friends, and uncertainty about academic progress. The present study aimed to investigate the psychological impact of the COVID-19 outbreak on Italian university students compared to general workers. The responses of 956 participants (478 university students and 478 workers) were included in the final dataset. Participants were asked to provide sociodemographic and occupation-related information, and to complete: (1) COVID-19-related questions; (2) health-related visual analogue scales; (3) State-Trait Anxiety Inventory-Form Y1 (STAI Y1); and (4) the Beck Depression Inventory (BDI-II). Results of comparisons between university students and general workers revealed that the former reported higher levels of anxiety and depressive symptoms. Furthermore, regression analyses showed that in university students, gender, health evaluation, and health concern and gender, educational level, and health evaluation significantly predicted anxiety and depressive symptoms, respectively. Taken together these findings suggest that specific factors could predispose University students to a high risk of developing mental health symptoms as a consequence of the COVID-19 pandemic.

Keywords: COVID-19 pandemic; mental health; anxiety symptoms; depressive symptoms; university students; workers

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1. Introduction

The COVID-19 pandemic induced numerous changes in daily life of every individual as a result of the measures to contain the infection, with important social, economic, and psychological consequences.

In Italy, as in the rest of the world, high levels of psychological distress have been found in both the general population and specific categories of workers, such as healthcare workers [1–3]. Several studies have also focused on the prevalence of psychological distress in young people who have experienced drastic change in their daily habits, as a result of the closure of schools and universities and the transition to online teaching [4–10]. Previous studies have found that university students are at high risk of developing mental health problems, such as anxiety and depression [11–13]. Therefore, this category might be even more at risk of experiencing high levels of psychological distress as a result of the COVID-19 outbreak. The reduction of social interactions due to the measures introduced to contain the spread of contagion, the concern for personal health and for the health of family members and friends, the uncertainty about the future and academic progress, but also the financial and work-related worries might affect the psychological well-being and the mental health of university students [5,6,14,15].

The main aim of the present study was to investigate the psychological impact of the COVID-19 outbreak on Italian university students. Firstly, we compared the levels of anxiety and depression symptoms between university students and general workers. Secondly,

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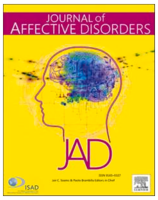

Love in the time of COVID-19: The negative effects of the pandemic on psychological well-being and dyadic adjustment

ARTICLE INFO

Keywords
Dyadic adjustment
Romantic relationship
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The COVID-19 outbreak represented a particularly stressful event that put a strain on social and interpersonal relationships (Xiong et al., 2020). Both the first lockdown and the restraining measures during the second wave have forced people to self-isolate and to work at home, prolonging cohabitation with the partner and children. For couples, particularly, confinement and isolation may have had an impact on both psychological well-being and dyadic adjustment (Coop Gordon and Mitchell, 2020; Donato et al., 2021). More generally, previous studies showed a high prevalence of mental health symptoms in the general population as a consequence of the COVID-19 outbreak (Castelli et al., 2020; Wang et al., 2021a, 2021b).

The main aim of this study was to explore the impact that the COVID-19 outbreak could have had on the participants' relationship. Specifically, we aimed to investigate mental health (anxiety/depressive symptoms and posttraumatic symptoms – PTSS) and dyadic adjustment in people who were in a stable romantic relationship.

The data were collected using an online survey from December 4, 2020, to January 10, 2021. A snowball sampling strategy was employed, wherein the participants were initially recruited via online advertisements and were encouraged to pass the survey link to others. The responses of 410 participants who were in a steady romantic relationship at the time of the evaluation were included in the final dataset.

Participants were asked to provide sociodemographic and COVID-19-related information (age, gender, educational level, profession, romantic relationship duration, having/not having children, current job status). They expressed the impact of the COVID-19 pandemic on their romantic relationship with the following item: "Do you think that the restraining measures introduced to stem the COVID-19 emergency and the new daily life that resulted from it have had an impact on your romantic relationship?", choosing from three response options: "positive, negative or no impact". Moreover, participants were asked to complete: (1) State-Trait Anxiety Inventory-Form Y1 (STAI Y1) to evaluate anxiety symptoms; (2) Beck Depression Inventory (BDI-II) to assess depressive symptoms; (3) PTSD Checklist for DSM-5 (PCL-5) to investigate PTSS; (4) and Dyadic Adjustment Scale (DAS) to evaluate dyadic adjustment.

The study was approved by the University of Turin Ethics Committee (protocol n. 488,755) and conducted according to the Declaration of Helsinki. All the participants gave their written informed consent to participate in the study.

In order to explore the impact (i.e., positive, negative, or none) that the COVID-19 outbreak could have had on the participants' relationship, descriptive analyses were first run (see **Appendix A** for results).

As a next step, Pearson's chi-squared test (χ^2) for categorical variables and one-way analyses of variance (ANOVAs) for continuous variables were performed to evaluate the presence of possible statistically significant differences between subgroups of participants (based on the impact – positive, negative, or none – that the COVID-19 outbreak had on their relationship) on sociodemographic and psychological variables.

Results of chi-squared tests showed the presence of statistically significant differences between the three subgroups of participants on children ($p = .001$) and current job status ($p = .030$) variables, whereas univariate ANOVAs revealed a significant difference on both age and relationship duration, as well as on all the psychological variables we assessed (**Table 1**). Particularly, Games-Howell post hoc tests showed statistically significant differences between the negative impact group and both the positive and no impact groups on age (negative vs. positive: −5.764, 95% CI (−10.07 to −1.46), $p = .005$; negative vs. none: −7.187, 95% CI (−10.49 to −3.88), $p < .001$), relationship duration (negative vs. positive: −55.300, 95% CI (−103.76 to −6.84), $p = .021$; negative vs. none: −79.450, 95% CI (−114.64 to −44.26), $p < .001$), and PCL-5 (negative vs. positive: 7.353, 95% CI (2.06 to 12.65), $p = .004$; negative vs. none: 7.310, 95% CI (2.89 to 11.73), $p < .001$). Similarly, Tukey HSD post-hoc analyses showed statistically significant differences between the negative impact group and both positive and no impact groups on STAI Y1 (negative vs. positive:6.168, 95% CI (1.80 to 10.53), $p = .003$; negative vs. none: 4.868, 95% CI (1.48 to 8.26), $p < .001$), BDI-II (negative vs. positive: −55.300, 95% CI (−104.98 to −5.82), $p = .025$; negative vs. none: −79.450, 95% CI (−118.10 to −40.80), $p < .001$), and DAS (negative vs. positive: −7.899, 95% CI (−12.58 to −3.21), $p < .001$; negative vs. none: −6.971, 95% CI (−10.61 to −3.33), $p < .001$).

The present results revealed that people who declared a negative impact of the COVID-19 outbreak on their romantic relationship were younger and reported higher levels of anxiety/depressive symptoms and

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behavioral sciences

Article

Personality, Defense Mechanisms and Psychological Distress in Women with Fibromyalgia

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Abstract: Background: Previous studies have shown that many personality traits are associated with fibromyalgia (FM), worsening both the quality of life and psychological distress of patients. Despite the high comorbidity of psychopathological disorders in this syndrome and their association with immature defense styles, few studies have examined the defense mechanisms used by FM patients. The main aim of our study was to investigate personality traits and defense mechanisms in FM patients compared to in a healthy control group (HC). Moreover, we investigated the effect of personality traits and defense mechanisms on psychological distress in both FM and HC groups. Methods: A total of 54 women with FM and 54 healthy women completed the (1) Temperament and Character Inventory—Revised; (2) the Toronto Alexithymia Scale; (3) the Defense Style Questionnaire; and (4) the Hospital Anxiety and Depression Scale. Results: The results indicated that FM patients display higher alexithymia, higher harm avoidance, lower self-directedness, lower persistence, and the higher use of a maladaptive defense style compared to HC. We found that alexithymia, harm avoidance, and maladaptive defense style are significant predictors of patients' psychological distress. Moreover, harm avoidance and adaptive defense style significantly predicted psychological distress in the HC group. Conclusion: The present study is the first to explore the contribution of both defense mechanisms and personality characteristics on the psychological distress of FM patients. Our findings have important clinical implications and may help diagnose and treat FM patients more in depth.

Keywords: personality traits; alexithymia; defense mechanisms; psychological distress; fibromyalgia

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1. Introduction

Fibromyalgia (FM) is a chronic syndrome that is characterized by widespread musculoskeletal pain [1] and has a high incidence among women [2,3]. FM is the third most prevalent musculoskeletal condition, and its etiopathogenesis is still debated due to its complexity and multi-factoriality. A series of other physical, psychological, and cognitive symptoms are often associated with FM [3]. This condition negatively affects patient quality of life and can have significant psychological and relational consequences. The literature suggests that FM patients experience excessive levels of psychological distress: 20–80% experience anxiety and 13–64% experience depression [4]. Furthermore, some studies have highlighted frequent psychosomatic disorders, insecure attachment styles, traumatic experiences, and dissociative symptoms in FM patients [5–8].

Environmental factors such as stressful events, emotional and physical traumas, lack of social support, and certain individual characteristics may be associated with the onset of FM and a worsening of perceived pain and psychological distress [4]. Other individual aspects such as personality traits may influence both adaptation to chronic pain conditions and psychological distress, which are often associated with FM [4,9].

Indeed, several theoretical models have suggested that some personality characteristics lead to a worse response to stressors and adjustment to diseases in people with chronic

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Brief Report

From the First to the Second Wave of COVID-19: Anxiety, De-Pressive, and Post-Traumatic Stress Symptoms in the Italian Population

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Abstract: In the early stages of the COVID-19 outbreak, high rates of clinically relevant anxiety, depression, and post-traumatic stress symptoms (PTSS) have been reported in the Italian population. The persistence of the pandemic and related restrictive measures highlight the need for a reassessment of psychopathological symptoms. The present longitudinal study consisted of two evaluations conducted during the two waves of infection. Participants were asked to complete the State-Trait Anxiety Inventory-Form Y1 (STAI Y1), the Beck Depression Inventory (BDI-II), and the PTSD Checklist for DSM-5 (PCL-5). There were no significant differences in depressive symptoms and PTSS scores reported by participants between T0 and T1, with single-case analysis revealing that in 71% and 69% of the participants, depressive symptoms and PTSS symptoms, respectively, remained stable during this period. On the contrary, mean scores comparison showed a significant decrease in anxiety levels, with 19% of participants in whom anxiety symptoms improved at single-case analysis. Taken together, these results suggest that depressive symptoms and PTSS not only occurred in a high percentage of participants but also tended to remain stable over time, thus warranting the importance of large-scale psychological screening and interventions to prevent the chronicization of these symptoms and their evolution to psychopathological disorders.

Keywords: COVID-19; anxiety symptoms; depressive symptoms; post-traumatic stress symptoms; longitudinal design; Italian population

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Citation: Benfante, A.; Tesio, V.; Di Tella, M.; Romeo, A.; Castelli, L. From the First to the Second Wave of COVID-19: Anxiety, De-Pressive, and Post-Traumatic Stress Symptoms in the Italian Population. *Int. J. Environ. Res. Public Health* **2022**, *19*, 1239. https://doi.org/10.3390/ijerph19031239

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1. Introduction

In December 2019, the first SARS-CoV-2 infections were reported in China. The world was plagued by the COVID-19 outbreak in a matter of months [1]. The population had to adapt to drastic changes in routine life and live with constant fear of contagion. It was immediately evident that an event of this magnitude would have a negative impact on the mental health of the general population [2,3] and certain sub-populations, such as healthcare workers, who were directly affected by the consequences of the disease [4,5].

Since 9 March 2020, several restrictive measures have been introduced in Italy to contain the infections, defining different scenarios based on infection data trends [6]. In particular, two so-called "waves of infection" emerged, with an increasing number of cases. Specific to Italy, the first wave began in March 2020, followed by a decline in cases in early summer, and the second wave began in November 2020.

A few weeks following the onset of the March 2020 lockdown, a study investigated the psychological impact of COVID-19 on the Italian population. The results showed that at the early stage of the pandemic, 69%, 31%, and 20% of the 1321 participants in the study, respectively, reported scores higher than the cut-off for measures of anxiety, depression, and post-traumatic stress symptoms (PTSS), suggesting the presence of clinically relevant symptoms [7]. Similarly, other studies have found high levels of psychological distress in this population [8,9].

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SUBSTANTIVE REVIEW

Alexithymia Among People Living with HIV: A Scoping Review

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Abstract

The present scoping review aimed to identify studies that investigated alexithymia, defined as a difficulty in identifying and describing one's own emotions, in people living with HIV (PLWH). A literature search, in line with the guidelines of PRISMA-ScR, was conducted in the following bibliographic databases: PubMed, PsycINFO, and Web of Science. The databases were queried using the following strings (using Boolean operators): ("alexithymia" OR "alexithymic") AND ("HIV" OR "Human Immunodeficiency Virus"). In line with the eligibility criteria, fourteen articles were found. Ten studies showed the involvement of alexithymia in disease severity (e.g., viral load levels), and adherence to antiretroviral therapy. Three studies revealed an association between alexithymia and cardiovascular disease, and three studies highlighted the implication of alexithymia in cognitive impairment. This review revealed the complex role of alexithymia in HIV disease. A careful clinical assessment of the emotional regulation process of PLWH can provide useful prognostic information.

Resumen

La presente revisión panorámica está orientada a identificar estudios que han investigado la alexitimia, definida como la dificultad de identificar y describir las propias emociones, en personas que conviven con el VIH. Siguiendo las directrices de PRISMA-ScR, se realizó una búsqueda bibliográfica en las siguientes bases de datos: PubMed, PsycINFO y Web of Science. Las bases de datos se consultaron utilizando las siguientes cadenas (utilizando el operador Boolean): ("alexithymia" OR "alexithymic") AND ("HIV" OR "Human Immunodeficiency Virus"). De acuerdo con los criterios de elegibilidad, se encontraron catorce artículos. Específicamente, diez estudios mostraron la implicación de la alexitimia en la gravedad de la enfermedad (por ejemplo, niveles de carga viral) y la adherencia a la terapia antirretroviral, tres estudios revelaron la asociación entre la alexitimia y la enfermedad cardiovascular, y tres estudios resaltaron la implicación de la alexitimia en el deterioro cognitivo. Esta revisión reveló el complejo rol de la alexitimia en la enfermedad del VIH. Una evaluación clínica detallada del proceso de regulación emocional de las personas que viven con el VIH puede proporcionar información útil para el pronóstico.

Keywords alexithymia · HIV infection · emotional regulation, scoping review

Introduction

In recent years, the construct of alexithymia has become relevant in several medical settings for its implication in patients' health [1].

Alexithymia is considered a personality trait rather than a disorder, and it is definable as a psychological construct with implications for affective processes. Patients suffering from psychosomatic diseases presented difficulties in the subjective awareness and processing of affects, their connection with specific situations, and their memories [2–6]. "Alexithymia construct reflects a deficit in the cognitive processing of emotions" [7], these limited capacities should not be thought of as an all-or-nothing phenomenon, but as a dimensional construct [1, 5, 8].

The characteristic aspects of alexithymia are: (1) difficulty identifying one's own emotions and distinguishing

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PSYCHOLOGICAL ASPECTS OF CARDIOVASCULAR DISEASES (IM KRONISH, SECTION EDITOR)

Alexithymia and Hypertension: Does Personality Matter? A Systematic Review and Meta-analysis

Marialaura Di Tella[1] · **Agata Benfante**[1] · **Lorenzo Airale**[2] · **Lorys Castelli**[1] · **Alberto Milan**[2]

Accepted: 8 May 2023 / Published online: 22 May 2023

Abstract

Purpose of review Personality characteristics, such as alexithymia, may lead to alterations in the autonomic nervous system functionality, predisposing individuals to an increased risk of hypertension (HTN). The present meta-analysis aimed to quantify the presence of alexithymia in people with HTN and to assess for potential sources of heterogeneity between studies. PubMed, PsycINFO and Scopus databases were systematically searched, using the following strings: ("alexithymia" OR "alexithymic") AND ("hypertension" OR "hypertensive"). Data were meta-analyzed with random-effects models.

Recent findings A total of 13 studies met the inclusion criteria. The prevalence of alexithymia in people with and without HTN were obtained from 5 studies (26.3% vs 15.0%; pooling of odd ratios, 3.15 [95% CI, 1.14;8.74]), whereas the mean level of alexithymia between people with and without HTN was obtained from 7 studies Hedges g, 1.39 [95% CI, -0.39;3.16]). There was a significant association between alexithymia prevalence and year of article publication ($\hat{g}$ = -0.04; 95% CI, -0.07;-0.01), whereas no significant relationship was detected between the former and both sex and age.

Summary Findings revealed a greater prevalence of alexithymia in people with HTN than in participants without HTN. These findings suggest that alexithymia may contribute to both the onset and persistence of HTN symptomatology. However, future research is needed to clarify this association.

Keywords Alexithymia · Hypertension · Psychological factors · Systematic review · Meta-analysis

Introduction

Hypertension (HTN) is a global public health concern, with 1.13 billion people currently diagnosed with stable high (or raised) blood pressure worldwide [1]. It represents a major cause of premature death and is a known factor for increased risk of heart, brain, kidney, and other diseases, especially for those cases in which adequate control of blood pressure is not implemented [e.g., 2–4].

HTN has a multifactorial etiology, with a number of genetic and behavioral factors that have been associated with increased blood pressure, such as obesity, insulin resistance, high alcohol intake, high salt intake, aging, sedentary lifestyle, and low potassium/calcium intake [e.g., 5]. Growing evidence is showing that psychological factors may also play an important role in the onset and maintenance of HTN. In particular, anger, anxiety/depressive symptoms, acute stress, and specific personality characteristics (e.g., type D and type A personality) have been frequently reported in people with HTN [6–9]. Among those psychological dimensions, personality traits deserve special attention for two main reasons. On the one hand, personality patterns can enhance behavioral risk factors for HTN, such as smoking, alcohol intake, obesity, and negative lifestyle. On the other hand, the presence of certain personality characteristics, together with other psychological symptoms, may lead to alterations in the autonomic

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Marialaura Di Tella and Agata Benfante are equally contributed to this work

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Review

Inflammatory Bowel Disease and Irritable Bowel Syndrome: What Differences in Mentalization Abilities? A Scoping Review

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Abstract: Mentalization is a psychological process that enables individuals to understand the self and others in terms of intentional mental states. The aim of this scoping review was to provide an overview of the findings on mentalization in patients with inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). A literature search, in line with the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols extension for Scoping Review guidelines, was conducted in the following bibliographic databases: PubMed, PsycINFO, and Scopus. Databases were queried using the following strings (with Boolean operators): ("mentaliz*" OR "metacogniti*" OR "theory of mind" OR "ToM" OR "reflective function*") AND ("irritable bowel syndrome" OR "IBS" OR "inflammatory bowel disease" OR "IBD"). In line with the eligibility criteria, seven articles were included. Results showed that no significant differences in metacognitive ability were found between patients in the IBD and IBS groups. This review revealed the mentalizing difficulties for patients with IBD and IBS. These results should be interpreted with caution since they are based on a few studies that used different instruments to assess mentalizing processes. Future studies are needed to clarify the role of mentalization in patients with these gastrointestinal conditions.

Keywords: inflammatory bowel disease; irritable bowel syndrome; mentalization; metacognition; quality of life

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1. Introduction

Mentalization is a psychological process that enables an individual to understand, implicitly and explicitly, the self and others in terms of intentional mental states (e.g., feelings, desires, beliefs, attitudes, goals, and needs) [1,2]. Implicit mentalization refers to unconscious and automatic operations of the capacity to imagine mental states, whereas explicit mentalization implies a conscious use of such operations, which occurs, for example, during psychotherapeutic work [3].

This capacity, which develops from early childhood in a secure attachment relationship with the caregiver [1,4,5], allows the individuals an affective and interpersonal understanding of their own and others' mental states, with consequences for the social dimension of life [6]. Furthermore, an effective ability to mentalize provides support for individuals coping with adversity [7].

The concept of mentalization is connected to and partially overlaps with other constructs derived from different study fields [2,3]. Among these, particular attention should be paid to the concepts of the Theory of Mind (ToM), metacognition, and reflective func-

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Intimate Partner Violence and Alexithymia: Do Emotions Matter? A Systematic Review and Meta-Analysis

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Abstract

Intimate partner violence (IPV) encompasses physical, sexual, or psychological abuse. Recent evidence suggests that victims and perpetrators might share some common psychological characteristics. Particularly, high levels of alexithymia, a difficulty in identifying and expressing emotions, and an externally oriented thinking style were found in both victims and perpetrators when compared to the general population. This systematic review and meta-analysis aimed to quantify the levels of alexithymia in victims and perpetrators of IPV and compare these levels to controls. We systematically searched PubMed, PsycINFO, Web of Science, and Scopus databases, using the following strings: ("intimate partner violence" OR "IPV" OR "partner abuse") AND ("alexithymia" OR "alexithymic"). The inclusion criteria were: adult perpetrators or victims of IPV; with or without a rehabilitation program; having or not a comparison group from the general population; alexithymia as outcome; all types of study design. Seventeen studies met the inclusion criteria. Data were meta-analyzed with random-effects models. Results showed comparable levels of alexithymia in victims and perpetrators of IPV (mean = 55.92 vs. 55.15, respectively). Furthermore, we found increased alexithymia in victims (Hedges' g, 0.87 [95% CI 0.43, 1.31]) and perpetrators (Hedges' g, 0.94 [95% CI 0.77, 1.12]) compared to controls. These results highlight that both perpetrators and victims exhibited high levels of alexithymia. A deeper understanding of this psychological dimension can help professionals to plan better-tailored interventions, in which all relevant factors associated with IPV are considered.

Keywords

intimate partner violence, victims, perpetrators, alexithymia, systematic review, meta-analysis

Introduction

Intimate partner violence (IPV) has been defined as a type of violence that includes "behaviour by an intimate partner or ex-partner that causes physical, sexual or psychological harm, including physical aggression, sexual coercion, psychological abuse and controlling behaviours" (World Health Organization [WHO], 2013). It is a worldwide phenomenon, with high social, economic, and human costs (Pagliaro et al., 2022; Vilariño & Arce, 2018).

Based on global estimates (Sardinha et al., 2022), approximately 27% of ever-partnered women, aged 15 to 49, are reported to have experienced physical or sexual IPV, or both, in their lifetime, with younger women living in social isolation and economic disadvantage being particularly at risk (Capaldi et al., 2012).

Although victims of IPV are predominantly women, recent evidence has shown that this phenomenon can also affect men (Zara et al., 2022). While women are more likely to be victims of physical and sexual violence, men are more likely to report being psychologically and verbally abused (Coker et al., 2002; Muftić et al., 2007).

Regardless of being women or men, victims and perpetrators of IPV seem to share common psychological characteristics. Particularly, previous studies have found reduced empathy and poorer emotion regulation abilities in IPV perpetrators compared to non-violent controls (Clements et al., 2007; Romero-Martínez et al., 2021; Shorey et al., 2015). Similarly, difficulties in emotion regulation have been associated with greater psychopathology and higher risk of re-victimization, with several episodes of IPV by different partners reported among victims of IPV (Muñoz-Rivas et al., 2021; Zamir & Lavee, 2016).

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Brief Report

The role of adult attachment and alexithymia in dyadic adjustment

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ABSTRACT

Background: The present study aimed to investigate if romantic attachment dimensions and alexithymia could significantly predict the dyadic adjustment of individuals in a romantic relationship.

Methods: To achieve these goals, 410 participants, who were in a romantic relationship, were asked to complete an anonymous online survey, which included the following measures: Toronto Alexithymia Scale, Experience in Close Relationship Scale and Dyadic Adjustment Scale.

Results: The hierarchical regression analysis revealed that only avoidant attachment dimansion was a significant predictor of dyadic adjustment in the final model. However, alexithymia was found to be negatively and indirectly associated with dyadic adjustment through the effect of avoidant attachment. Indeed, avoidant attachment significantly mediated the association between alexithymia and dyadic adjustment.

Limitations: We used self-report measures, and we adopted a cross-sectional design. The sample comprised a higher number of women and well-educated participants.

Conclusions: The current findings highlight the importance, from a clinical perspective, of paying attention to the planning of tailored psychological treatments directed at individuals who are in a relationship to reduce the levels of insecure attachment and alexithymia.

1. Introduction

Research on romantic relationships has often been focused on dyadic adjustment, a multidimensional construct that includes the subjective perception of tensions in the couple and degree of happiness, agreement, affective expression, and cohesion between the partner (Spanier, 1976). Several personal, relational, and psychological characteristics of an individual can play a role in dyadic adjustment (Constant et al., 2021; Romeo et al., 2022).

Among those factors, attachment determines the way of being in a relationship with the other, in terms of defining the image of self and the image of the other (Constant et al., 2021; Li and Chan, 2012). Particularly, the anxious attachment dimension characterises individuals who worry about being abandoned by their partners, while the avoidant dimension is typical of individuals who fear closeness and dependence on others (Li and Chan, 2012). Both those insecure attachment dimensions have been negatively associated with the quality of romantic relationships (Siegel et al., 2019). Those dimensions are also associated with difficulties in emotion recognition and regulation processes (Besharat et al., 2014; Lyvers et al., 2021; Mikulincer and Shaver, 2007; Montebarocci et al., 2004; Taylor et al., 2014).

Alexithymia is characterised by difficulties in identifying and describing one's own emotions and an externally oriented thinking (Taylor et al., 2003). Since it has often been associated with difficulties in sentimental communication with partners and lower relationship satisfaction (Hesse and Gibbons, 2019; Lyvers et al., 2021), alexithymia can play a role in dyadic adjustment, together with attachment dimensions (Besharat et al., 2014; El Frenn et al. 2022; Karukivi et al., 2014; Taylor et al., 2014).

Although some evidence of the relationship between attachment dimensions, alexithymia, and romantic relationship is present in the literature, it is not extensive and previous studies often investigated the quality of intimate relationship using different constructs that only partly overlap with that of dyadic adjustment (Besharat et al., 2014; El Frenn et al. 2022; Karukivi et al., 2014; Taylor et al., 2014). Interestingly, in addition to the negative association between insecure attachment dimensions and relationship quality (Siegel et al., 2019), and between alexithymia and relationship satisfaction (Hesse and Gibbons, 2019; Lyvers et al., 2021), studies that have examined both alexithymia and attachment dimensions have shown that the association between those constructs and relationship satisfaction may not be direct (Besharat et al., 2014; El Frenn et al., 2022; Karukivi et al., 2014; Taylor

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