Peer Review File

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<mark>Reviewer A</mark>

Dear Authors,

Thank you for writing an article about therapeutic intervention in the oncology setting. Caring for the patients and not letting them fall into depression is always a priority.

Unfortunately, the manuscript requires a new translation to English before anything. The grammar mistakes and misused words lack precision and make this article challenging to read, and also partially tricky to understand (e. g. terms like "oral therapy" and "psychical disease").

Reply: Thanks for the tip, the study has been extensively reviewed regarding English grammar.

The study itself lacks a control group that might show which changes in the therapy group are caused by psychotherapy and which are related to the natural process of adaptation to cancer.

Reply: Thanks for the remark. Using a control group would have helped make the work better by reducing confounding factors. However, it would have made the study design much more complex to organize and, above all, it would have been unethical towards patients who would not have received any support. In fact, the professional figure of the psychologist is required by the regulation of our hospital to support our patients.

There is too little on psychotherapy details including modality, frequency, and the setting of the psychotherapy (group? or individual?).

Reply: Thank you for your suggestion. An explanation of how psychotherapy is carried out is already present. However, we have added more details on the frequency, modality and type of psychotherapy administered (lines 123-127).

Mixed groups of different patients, with all stages of the disease, and treatments, also not including data on whether pts were undergoing radiotherapy or not, or on taking opioids or steroids. These are confounding factors in psycho-oncology, due to the heavy side effects of radiotherapy, opioid and steroid intake, more than the patients' education you have analysed. It all makes the results difficult to interpret.

Reply: Radiotherapy data has not been included because we do not believe it affects the population of this study. In fact, most of the patients had types of cancer (such as breast or colon cancer) in which radiotherapy is a treatment that is not used in the early stages of the disease. Our population is represented by people in the initial post-diagnosis phase and who therefore did not receive radiotherapy during the study period. A similar discourse concerns the use of opioid or steroid drugs, which are usually used in the advanced stages of the disease.

Additionally, one single short screening measurement tool seems to be not enough to measure psychotherapy effects.

Reply: Thanks for the remark. We agree that we cannot measure the effects of psychotherapy with a single short test, but we believe that even adding some other parameters it is difficult to arrive at an objective result. Indeed, the effectiveness of a psychotherapy represents a parameter that is difficult to objectively evaluate. Instead, the possibility of having a simple test available that can be done in any center represents an advantage for those who do not have specific skills at the time of the first visit of an oncological patient.

<mark>Reviewer B</mark>

The article highlights the importance of psychological care for cancer patients, emphasizing the usefulness of

the K10 questionnaire as a tool to assess psychological distress levels and the efficacy of psychotherapy in improving their well-being. It discusses the common occurrence of psychological distress in cancer patients, its impact on their quality of life and tolerance of cancer treatments, and provides scientific evidence for the inclusion of psychotherapy in the treatment of cancer patients. The study's relevance in the broader context of cancer care is clear, and the information presented is organized and understandable. However, there are several improvements that should be addressed for publication, and I have several suggestions that may enhance the clarity and value of this manuscript.

Reply: Thank you for considering our study. We are happy to welcome your requests and suggestions to increase the work of the manuscript.

Introduction:

It would be beneficial to provide more information regarding previous literature on the role of psychological distress in cancer patients and the use of K10 in this population. In this way, readers can better appreciate the context of this study.

Reply: Thanks for the remark. We believe that providing context for psychological distress in cancer patients and its consequences is important. This therefore has already been done extensively in the introduction (lines 75-84 and 204-216 of "track change" version).

Methods:

The manuscript could benefit from a detailed explanation of the psychotherapy applied to the patients and how the severity of distress influenced the selection of therapy type or frequency.

The study design and the use of K10 as an assessment tool are justified. However, you could provide more context as to why this particular scale was chosen over other available mental health screening tools. Are there any specific attributes of the K10 that make it more suited for this study population?

Reply: Thanks for the remark. We have specified further how the psychotherapy was administered (lines 120-124). The K10 test is a test widely used in the literature by psychologists to assess psychological distress. Its advantages consist in being a very quick screening test (2-3 minutes) and easily understandable even by people with a low level of education. These characteristics were suited to our population which included a fair percentage of poorly educated patients.

Consider adding a subheading from line 122 to 135 for "data analyses".

Reply: We have added this subheading (line 123)

Results:

The authors should take care to associate the reported p-values with specific statistical tests, thereby enhancing the clarity and transparency of the results. Additionally, including more detailed statistical analysis would contribute to the production of more robust and reliable findings. The authors correctly interpret the data, making assertions about psychotherapy's efficacy across different stages of the disease, patient ages, and cancer types. However, they should consider specifying the statistical significance or effect size for their findings to lend greater weight to their conclusions.

Reply: Thanks for the suggestion We modified the text and added the p-value when it was statistically significant.

Figures:

Table 2 seems to be missing in the text.

Figure 2 would benefit from including the percentages in the graphs. The legend and the table have an unreadable size. Title should include "of K10 test scores".

The rest of the figures lack consistency in the use of "K10". Consider including significance levels and error bars.

Consider using a color blinded friendly palette.

Reply: Thank for your suggestion. Table 2 and Figure 2 have been modified according to your indications. Error bars cannot be added because these are defined values (count of patients with a certain K10 score). For the same reason, it seemed right to include significance values only in the text.

Discussion:

Importance of early psychological care: Although the study demonstrated a reduction in psychological distress following therapy, it did not address the significance of providing psychological care from the moment of diagnosis. Early detection and psychological intervention can have significant benefits on patients' quality of life and their ability to cope with cancer treatment. It would be relevant to discuss the importance of early psychological care and the need to implement it as an integral part of oncological care.

Reply: We agree with your point of view. We integrated the introduction by inserting these concepts and deepening them with some works in the literature (lines 91-94).

Although analyzed subgroups are mentioned, such as cancer type, treatment (intravenous or oral), age, level of education, and employment status, the implications of these findings are not thoroughly discussed. It would be interesting to explore and discuss the possible reasons for the observed differences in subgroups, as well as their clinical relevance. For instance, it is mentioned that the reduction in K10 scores was statistically significant among patients with different educational levels, but the implications of this difference are not explored, nor is there a discussion on how to effectively address psychological distress in patients with lower levels of education.

Furthermore, the article suggests that patients with greater work responsibilities may experience higher levels of stress and anxiety, which can influence the effectiveness of psychological therapy. However, a thorough discussion regarding this relationship and how it could impact the care and management of psychological distress in cancer patients is not provided.

Reply: Thank you for your suggestion. We have edited the text and added an extensive discussion (lines 225-238) of the differences between the various subgroups and possible reasons.

Limitations:

A limitation of the study is the absence of a control group that did not receive psychotherapy. This makes it challenging to assess the specific effectiveness of psychological therapy compared to other interventions or the absence of intervention. I believe this should be specified.

Another limitation that could be included is related to selection bias: The study relies on voluntary participation of patients, which could introduce selection bias. It is possible that the patients who chose to participate in psychological therapy and the study had different characteristics or levels of distress compared to those who chose not to participate. This could influence the results and limit the generalizability of the findings.

Reply: Thanks for the suggestion, the limitations of the work had already been expressed in the conclusions, but they have been further explored according to your indications.

Future lines of research:

The study primarily focused on changes in levels of psychological distress before and after therapy. However, there are other important variables that could impact psychological distress, such as social support, socioeconomic status, cancer stage, and the presence of comorbidities. These variables could influence the effectiveness of psychological therapy and should be taken into account in future studies.

Reply: We agree with your observation. We have added this consideration also in the last lines of the manuscript.

Language:

There are several grammatical errors and awkward sentence structures that should be corrected for clarity.

Line 34: The word "before" is unnecessary.

Line 72: "The diagnosis of cancer has a great impact in the lives" should be "The diagnosis of cancer has a great impact on the lives".

Line 75: "develop a psychical disorder" should probably be "develop a psychological disorder".

Line 85: Consider replacing "overall with his familiar" with "especially for their families".

Line 86: The phrase "or don't want to work more" might be better as "or who are unable to continue working".

Line 91: Consider replacing "people don't receive adequate support" with "many patients do not receive adequate psychological support".

Line 92: Consider replacing "the patient that we can consider like "fragile people" with "patients, who could be considered as "vulnerable" or "fragile" due to these circumstances".

Line 107: "new diagnosis of cancer" would be better as "newly diagnosed cancer".

Line 115: Instead of saying "different cancer type", consider using "different types of cancer".

Line 116: Replace "different setting: adjuvant and metastatic." with "different treatment settings: adjuvant and metastatic."

Line 129: Consider rephrasing the sentence for clarity: "K10 scores were coded as dichotomous variables, where a score decrease after treatment was coded as '1', while equal or higher scores were coded as '0'."

Line 130: Clarify the meaning of "event" in this context, as it can be ambiguous.

Line 134: To maintain academic tone, replace "All the frequency tables, crosstabulations and relative graphs" with "Frequency tables, crosstabulations, and relevant graphs".

Line 139: Use "There were" instead of "There was".

Line 141: The term "urothelial" might be more clearly expressed as "urothelial cancer".

Line 142: Replace "was treated" with "were treated".

Line 143: A space should be added between "30-50" and "(Figure 1 and 2)".

Line 147: "We then analysed in various subgroup the variation of K10 score." might be better stated as "We then analyzed the variation of K10 scores across various subgroups."

Line 152: Add "the" before "metastatic setting".

Line 156: "k 10" should be "K10" for consistency.

Line 157: Consider replacing "In the K10" with "Of the K10 scores".

Line 158: Replace "who take" with "who took" to match the tense in the rest of the paragraph. Also, consider rephrasing "neurological/psychiatric drug" to "neurological or psychiatric medication".

Line 160: Replace "there is a reduction" with "there was a reduction" to maintain past tense.

Line 166: The sentence "This could be explained by the difference in the number of the patients of the two group." could be better phrased as "This difference could be due to the varying sizes of the two patient groups."

Line 168: Replace "that have experienced cancer disease" with "who have had cancer".

Line 171: Replace "we did it is between" with "We performed another sub-group analysis".

Line 177: It would be better to specify "the first one" and "the second" as "the worker group" and "the non-worker group" for clarity.

Line 180: Replace "not workers" with "non-workers".

Line 181: You might consider adding a period or further elaboration after "workers with high responsibility" as it currently appears as an incomplete sentence.

Line 183-184: The phrase "The diagnosis of a cancer disease, frequently or in any case a life-threatening disease, determined in patients a series of painful circumstances" is somewhat unclear and could be rephrased. A potential suggestion: "The diagnosis of cancer, which is frequently a life-threatening disease, places patients in a series of challenging circumstances."

Line 187-188: This sentence is repeated from lines 185-186. Please consider removing the repetitive sentence.

Line 189: The term "negatively impact" should be "negatively impacts".

Line 192: The phrase "the clinician that are overworked" is grammatically incorrect. It should be "clinicians who are overworked".

Line 194: The term "it is possible adopt" is missing a word. It should be "it is possible to adopt".

Line 199: The phrase "the therapy is efficacy" is grammatically incorrect. It should be "the therapy is effective".

Line 201: Again, the phrase "The psychotherapy is also efficacy" is incorrect. It should be "The

psychotherapy is also effective".

Line 202: The phrase "it is efficacy" is incorrect. It should be "it is effective".

Line 202: The sentence "We only see a statistically significant difference in the efficacy in patient with a different education level" is slightly awkward. Consider revising to "We observed a statistically significant difference in therapy efficacy among patients with different education levels".

Line 205: The phrase "patient who have more responsibilities" is grammatically incorrect. It should be "patients who have more responsibilities".

Line 206: The phrase "the psychotherapy is really efficacy" is incorrect. It should be "the psychotherapy is really effective".

Line 213: The term "includes" should be "included". It is repeated.

Line 214: The term "the rapid intervention of psychologist" should be "the rapid intervention of a psychologist" or "rapid interventions from psychologists".

Cites:

I have noticed that the quotes in the text have been placed after the point, when they should go within the same sentence. E.g., "...worsening of the quality of life. (3) About..." should be "...worsening of the quality of life (3). About..."

Reply: Thanks for the precise suggestions. We have extensively modified the grammar and syntax according to your indications.

<mark>Reviewer C</mark>

The abstract sounded very unspecific and the methodology questionable (what kind and dosage of psychotherapy? what psych. diagnoses did the patients have?). It is also not a "new" topic since effectiveness has already been proven.

Reply: Thank you for paying attention to our manuscript and for your suggestions. The manuscript has been extensively modified in grammar, syntax and content (see "track changes" document). However, we know that our work has limitations that cannot be overcome. In particular, regarding the heterogeneity of the population (which generates confounding factors), the number of studies, the assessment of psychological distress using a single test. These limits have also been stated in the discussion section. However, our aim was only to evaluate the usefulness of a simple test available to all (K10 test) and understand how psychological distress was modified in a real-life population after psychological support. This objective was achieved and the data we obtained gave us the opportunity to investigate, in future studies, how we can decrease the psychological distress in patients whose K10 score has remained unchanged.