Dear Editors and Reviewers,

Thank you for handling our manuscript, entitled " Bibliometric Analysis of the global research status and Trends of Mechanotransduction in Cancer ". We appreciated the reviewers' constructive and insightful comments, which were all addressed by us. We hope the revised manuscript has now met the publication standard of the *World Journal of Clinical Oncology*.

Again, thank you very much for your consideration.

Best wishes

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Reviewer #1:

Major Revision:

Comment 1: Please explain your methods in the abstract

Response: Thank you for this suggestion. As you suggested, we have explained the method of bibliometric analysis in the abstract as follows:

Bibliometric analysis is a statistical method that involves investigating different aspects (including authors' names and affiliations, article keywords, journals, and citations) of large volumes of literature. This provides an objective evaluation of the dynamics and emerging trends of a specific research area.

Comment 2: There are typos and weird choices of words in the text that need to be taken care of.

Response: We thank the reviewer very much for pointing out the language problems. A native English-speaking academic editor proofread the revised

manuscript and provided us with the English Language Certificate as attached to the F6Publishing system.

Comment 3: Some important sentences in the introduction section lack supportive references. Please add.

Response: We have checked the manuscript carefully and added more references to the introduction part.

Comment 4: Why did not the authors remove the review articles from the pool? Review papers must have been disregarded! This is a scientific shortcoming of paramount importance! Please explain! How did you divide the articles into categories?

Response: We strongly agree with you, that review articles should be included as an integral part of bibliometric analyses. We rechecked the methodology and contents in our manuscript and made sure that we did not exclude any review articles. Once the retrieved articles were determined using the strategy illustrated in Fig.1, the research categories were automatically divided by the Web of Science (www.webofknowledge.com) by clicking the research area button in its side tool panel.

Comment 5: In reference to the countries, is it England or UK?

Response: We have checked the original articles and it should be UK. We've replaced 'England' with 'UK' throughout the manuscript.

Comment 6: In Figure 4, institution names must be written in full. Please revise. Also, in Figure 5, the first and last name of each author must have their first letter in capital.

Response: Thanks for your suggestions. We had revised the Figure 4 and Figure 5 as suggested.

Comment 7: In section "keyword analysis" in Results, materials and methods are detailed. Please move these parts to M&M.

Response: Many thanks for your comments. We have detailed the methodology of 'keyword analysis', and moved this part to M&M as follows:

Keyword Analysis

The keywords were extracted from the keyword section of articles. To avoid potential deviations, similar or same keywords with different expressions were manually standardized to correct and/or group similarities as previously suggested[1-3], before VOSviewer or CiteSpace analysis. The burst keywords were assessed using CiteSpace (V6.2R4 SE) with the following parameters: time slicing (from Jan.,1994 to Dec., 2022), years per slice (1), node type (keyword), the minimum burst duration (1 year), γ (0.39) and others (default). The keyword co-occurrence analysis was conducted by VOSviewer (version 1.6.18) with the following parameters: type of analysis (co-occurrence), unit of analysis (keywords), counting method (full counting), minimum number of occurrences of a keyword (3).

Reviewer #3:

Comment 1: Clarify the methodology for selecting and analyzing keywords from the 597 papers to ensure transparency and replicability.

Response: Many thanks for your suggestion. The keywords were extracted from the keyword section of articles. Since different expressions of similar or same keywords may lead to potential deviations in the results, therefore, keywords were manually standardized to correct and/or group similarities as previously suggested[1-3], before VOSviewer or CiteSpace analysis. This methodology was detailed in M&M.

Comment 2: Consider including non-English studies through translation services or collaborating with researchers familiar with non-English publications to reduce language bias.

Response: Thank you for your suggestions. We agreed that too many non-enrolled non-English publications would result in result deviations, and therefore, we conducted the literature screening again without language limitations; Interestingly, we found that only two reviewer papers (one written in Chinese and the other written in Russia) were neglected[4, 5]. Since the review topics (autophagy, extracellular matrix, and mechanotransduction) in these two papers were already concluded in the 597 papers, and the number of non-English publications in this field is very small; Therefore, it would have a very limited impact on our results. In addition, when performing bibliometric analysis, it is also common to retrieve English-language articles for deep analysis, which is accepted by many high-quality journals such as JAMA Netw Open[6], and J Transl Med[7]. Taken together, to maintain the whole body of the manuscript, we did not enroll these two non-English publications, and we also deleted the language shortage in the limitation section as the influence is very minimal.

Comment 3: Provide more context on the criteria for determining research themes and the rationale for dividing keywords into clusters for a deeper understanding of the results.

Response: Thank you for the suggestions. We apologize for the inadequate explanations for our methodology. VOSviewer software can classify keywords with high co-occurrence frequencies into several clusters and simultaneously color them over time to identify research hotspots and trends. The keyword classification, using a weighted and parameterized variant of modularity-based clustering, is a default function of VOSviewer[8]. After keyword clustering, we manually summarized the keyword information in each cluster to clarify the research theme as previously described[3, 9, 10].

Comment 4: Discuss potential implications of the identified research themes and hot topics on cancer diagnosis, treatment, and patient outcomes to highlight the practical significance of the findings.

Response: Thanks for your excellent suggestions. It was well-accepted that tumorigenesis is not an independent process but requires close interactions with tumor microenvironments. Compared to the versatile function of biochemical stimuli (such as small molecules, growth factors, and cytokines) in cancer progression, it was becoming clear that mechanical stimulation is on par with those chemical factors during cancer development; however, the underlying mechanisms are still relatively underexplored. Through bibliometric analysis, we found that "plasma membrane", "autophagy", "piezo1/2", "heterogeneity", "cancer diagnosis", and "post-transcriptional modification" are the hot topics in this field, and our findings suggested that further investigations should focus on how the plasma membrane and its localized mechanosensors transduce mechanical forces through post-transcriptional modifications. We expect that elucidating the key molecules involved in mechanotransduction would benefit the diagnosis, treatment, and prognosis of cancers. For example, the increase in stiffness is a well-recognized feature of cancer mechanics that has been used previously for cancer diagnosis and prognosis [11]. The continued development and validation of mechanobiological biomarkers that reflect the mechanical properties of tissue microenvironments are likely to facilitate the clinical application of mechano-oncology. Moreover, the mechanosensitivity of cancer cells is suggested to promote malignant cell behaviors [12, 13], and mechanical abnormalities are the main culprit that drives cancer chemoresistance *via* the activation of cellular drug efflux or DNA repair systems [14]. Therefore, deciphering the detailed signaling pathways such as autophagy and post-transcriptional modifications involved in mechanotransduction might allow the development of new drugs that can be used in combination with current cancer therapies. This would

increase the likelihood of therapeutic success and minimize the chance of developing drug resistance, which is advantageous for the prognosis of cancer patients.

Comment 5: Explore potential factors influencing the lower average citation time for Chinese publications to better understand and address the quality improvement needs.

Response: Thank you for your suggestions. This might be due to the relatively low quality of the publications so far, even though the quantity is high. In addition, the low number of publications in the past from China and the more recent fast growth rate might inherently overly inflate the contribution of highly cited papers to the average citation time. To address this phenomenon, the Chinese government should provide more financial and political support for this research field and encourage original research. For Chinese scholars, discovering new research frontiers as early as possible and carrying out in-depth research is indispensable for improving their international influence and academic standing.

Comment 6: Discuss the role of interdisciplinary collaborations in the field and how collaborations between institutions and countries could be promoted to further advance research.

Response: We sincerely appreciate the valuable comments. In addition to collaboration between research groups, interdisciplinary collaborations are also essential for a research field to flourish. Mechanotransduction-related cancer research involves various different disciplines, including biology, physics, and medicine, and so interdisciplinary exchanges are beneficial for the diversity of research and to create new perspectives and questions. For example, in vivo mechanosensing is based on force-dependent protein deformation and reorganisation [15]. However, due to a lack of molecular resolution in cellular imaging techniques, the intracellular mechanisms are unknown. Recently, with

the development of super-resolution microscopy (SRM) and molecular force sensors, it is now possible to gain molecular insights into mechanosensing in living cells[16]. Moreover, the development of novel imaging techniques has helped to advance our knowledge of the molecular mechanisms involved in mechanotransduction[17].

We also give some reasonable suggestions on how to promote cooperation between institutions and countries as follows:

The study of mechanotransduction in cancer not only requires an in-depth exploration of molecular mechanisms but also necessitates a large number of clinical samples or populations for clinical validation or translation. At this point, inter-country or inter-institutional collaboration should be advocated, either by sharing clinical databases or by dividing the project into concrete tasks based on the respective expertise. With this approach, significant breakthroughs in this field might be achieved at the earliest time.

Reviewer #3:

Comments: This is like a general survey of current trends in cancer research. This reviewer cannot aware of what clinical implications (especially in clinical oncology) can be derived from this study. Unfortunately, it is considered correct to submit this manuscript to a journal in the field of medical statistics.

Response: Thank you for your suggestions. We have improved our manuscript to fit the journal criteria and added more discussion on how the future direction of this field would influence the clinical implications (especially in clinical oncology).

Reference

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JOURNAL EDITOR-IN-CHIEF'S REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 87296

Title: Bibliometric analysis of the global research status and trends of mechanotransduction in cancer

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Country/Territory: Germany

Editorial Director: Jin-Lei Wang

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SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[Y] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Rejection
[Y] Grade D: Fair		[ ] Minor revision
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Major revision

JOURNAL EDITOR-IN-CHIEF (ASSOCIATE EDITOR) COMMENTS TO AUTHORS

It was a pleasure to read this manuscript. There are a few minor suggestions that might be considered prior to publication.(i) Page 6, last paragraph. Authors have mentioned "To this end, here we present the first bibliometric analysis of researchconducted on mechanotransduction in cancer and reveal the current researchbeing conducted in this field." I would suggest considering rephrasing the word "first" with "an updated". While searching google, I can find similar papers, even though not as updated and intensive as this work. (ii) grammar and language must be checked carefully prior to publication

Answer: Thanks for your comments, I had revised manuscript according to your comments.