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OPEN PEER REVIEW

Prognostic Value of Computed Tomography Texture Features in Patients with Hepatocellular Carcinoma Following Stereotactic Ablative Radiotherapy

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

4 comments · 4 Sep 2021 – 2 Oct 2021

Referee 1 Reviewer

MINOR REVISION 4 Sep 2021

We thank the authors for selecting our journal for their manuscript.
Overall, the manuscript has an important and interesting title, an appropriate scientific writing structure, and a relatively adequate sample size, but it needs some revisions as follows:
1. The study design is a case-control study, which should be stated in the abstract and the methods section of the full text.
2. The basis for dividing the samples into two groups, those with a poor prognosis (cases) and those with a good prognosis (controls), should be fully explained in the method section.
3. The sentences related to the results given in the method section should be moved to the next section: "There were 45 males and 12 females aged 36-80 years old and (61.12±6.31) years old on average in good prognosis group. Poor prognosis group consisted of 36 males and 7 females aged 35-81 years old, with an average age of (55.36±6.47) years old."
4. The code of the ethics committee should be written in parentheses.
5. Complete specifications of the statistical software must be provided.
6. In the statistical analysis section, the terms numerical and measurement data should be replaced by qualitative and quantitative data, respectively.
7. In the statistical analysis section, multivariate logistic regression analysis should be explained before ROC analysis. Finally, the significance level used in univariate and multivariate analyses should be stated.
8. In Tables 1 and 2, it is better to report the odds ratio for qualitative variables.
9. In Table 3, is the crude or adjusted odds ratio reported? The adjusted OR should be reported, and the controlled variables should be listed below the table.

Referee 2 Reviewer

MAJOR REVISION 22 Sep 2021

Thank you for submitting your valuable manuscript to the Iranian Journal of Radiology.
The main goal of this study was to assess the value of CT imaging features in patients with hepatocellular carcinoma (HCC) to predict prognosis after stereotactic ablation radiotherapy (SABR). This study was conducted on 100 patients with HCC who underwent SABR. A predictive model based on imaging and clinical features was established using multivariate logistic regression analysis. According to the suggested model, age ≤40 years, serum alpha-fetoprotein (AFP) >9 ng/mL, gamma-glutamyl transpeptidase (GGT) >60 U/L, aspartate aminotransferase (AST) >40 U/L, lesion size >5 cm, unsmooth tumor margin, no or incomplete capsule, multiplicity, percentage of portal phase CT value of cancer >135% and relative washout ratio in the portal phase of cancer >-24% were reported as risk factors for poor prognosis.
Major advantages of this article include:
1. The aim and design of this study are relatively novel.
2. The results could help physicians to select the optimal candidates for SABR in HCC.

Major disadvantages of this article include:
1. The advantages and applications of SABR in HCC treatment plans are not discussed.
2. It is not clear what criteria are used to select patients as candidates for SABR instead of alternative treatment strategies.
3. Some patients may undergo chemotherapy regimens concurrently, affecting tumor response to SABR,

which should be considered in the study.
4. HCC pathologic grading, which could predict tumoral prognosis, is not discussed in this article.
5. The authors did not mention the definition of the therapeutic response in multifocal HCC or whether all HCC lesions underwent SABR or just the largest ones.
6. A valid reference for the definition of tumor response to SABR is not provided in the manuscript. (The routinely used RECIST guideline is entirely different.)
Overall, this manuscript has significant methodological issues.

Associate Editor MAJOR REVISION 30 Sep 2021

The manuscript was studied by two expert reviewers and by me. I agree with the reviewers' comments and think it could be reconsidered again following the suggested revisions. Please add two figures representing CT samples from the good- and bad-prognosis groups.

Editor-in-Chief MAJOR REVISION 2 Oct 2021

Dear authors,
Your article needs Major Revision.
Regards

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 118338
Title: Prognostic value of texture features of computed tomography images for patients with hepatocellular carcinoma after stereotactic ablation radiotherapy

Reviewer 1:
Thank you for submission of your valuable manuscript to the Iranian journal of radiology.
The main goal of this study was to assess the value of CT imaging features in patients with hepatocellular carcinoma (HCC) to predict prognosis after stereotactic ablation radiotherapy (SABR). This study was conducted on 100 patients with HCC who underwent SABR. After using multivariate logistic regression analysis, a predictive model based on imaging and clinical features was established. According to the suggested model, Age ≤40 years old, serum alpha-fetoprotein (AFP) >9 ng/mL, gamma-glutamyl transpeptidase (GGT) >60 U/L, aspartate aminotransferase (AST) >40 U/L, lesion size >5 cm, unsmooth tumor margin, no or incomplete capsule, multiplicity, percentage of portal phase CT value of cancer >135% and relative washout ratio in the portal phase of cancer >-24% were reported as risk factors for poor prognosis.
Major advantages of this article include:
1. The aim and design of this study are relatively novel.
2. The results could help physicians to select the optimal candidates for SABR in HCC.
Response: Thank you very much for your positive comments.

Major disadvantages of this article include:
1. The advantages and applications of SABR in HCC treatment plans are not discussed.
Response: We have added the required discussion and corresponding references.

2. It is not clear that based on what criteria, patients are selected as candidates for SABR instead of alternative treatment strategies.
Response: In this retrospective case-control study, only HCC patients treated with SABR were included.

3. Some patients may undergo chemotherapy regimens concurrently, affecting tumor response to SABR, which should be considered in the study.
Response: We have mentioned the information as a limitation of this study at the end of the revised manuscript.

4. HCC pathologic grading is not discussed in this article which could predict tumoral prognosis.
Response: We have added the grading method in the Patients and Methods section.

5. The authors did not mention the definition of the therapeutic response in multifocal HCC and whether all HCC have undergone SABR or just the largest ones.
Response: Only HCC patients treated with SABR were included in this study.

6. The valid reference for the definition of tumor response to SABR is not stated in the manuscript. (The routinely used RECIST guideline is entirely different.)
Overall, this manuscript has significant methodological issues.
Response: We have added the definition according to your requirement.

Reviewer 2:

Thanks from author for selecting our journal for their manuscript.
Totally, it can be said that it has important and interesting title, appropriate scientific wring structure, and relative enough sample size; but in needs some revisions as follows:
1. The study design is a case-control that should be written in the abstract and full text method.
Response: We have added the required information.

2. The basis for dividing the samples into two groups, with bad prognosis (cases) and good prognosis (controls) should be fully explained in the method section.
Response: We have added the detailed grouping method in the Patients and Methods section.

3. The sentences related to the results given in the method section should be moved to the next section: "There were 45 males and 12 females aged 36-80 years old and (61.12±6.31) years old on average in good prognosis group. Poor prognosis group consisted of 36 males and 7 females aged 35-81 years old, with an average age of (55.36±6.47) years old."
Response: We have made the required revision.

4. The code of the ethics committee should be written in parentheses.
Response: We have added the required ethics committee code.

5. Complete specifications of statistical software must be written.
Response: We have completed the specifications according to your requirement.

6. In the statistical analysis section, the terms of numerical and measurement data should be replaced by qualitative and quantitative data, respectively.
Response: We have replaced the terms according to your valuable comment.

7. In the statistical analysis section, multivariate logistic regression analysis should be explained before ROC analysis. Finally, the significant level used in univariate and multivariate analysis should be stated.
Response: We have added the required descriptions.

8. In Tables 1 and 2, it is better to report the odds ratio for qualitative variables.
Response: We have added the data according to your requirement.

9. In Table 3, crud or adjusted odds ratio reported? Adjusted OR should be reported and the controlled variables should be listed below the table.
Response: The data are adjusted OR.

Associate Editor 1:
The manuscript was studied by two expert reviewers and by me. I agree with the reviewers' comments and think it could be reconsidered again following suggested revisions. Please add two figures representing CT samples from two groups of good and bad prognosis.
Response: We have added the representative CT images according to your requirement.

EIC Decision:
Dear authors,
Your article needs Major Revision.

Response: We have revised the manuscript thoroughly according to all valuable comments.

2 Revision 1

4 comments · 13 Nov 2021 – 21 Dec 2021

Referee 1 Reviewer

ACCEPT 13 Nov 2021

Thanks to the authors for their revisions.
Currently, this manuscript is acceptable in terms of methodology.

Referee 2 Reviewer

MINOR REVISION 1 Dec 2021

Thank you for revising your manuscript according to the comments.
The exact definition of the therapeutic response in multifocal HCC is not stated, and I think you must mention it as a limitation of the study.
Also, pathologic grading is not discussed as another limitation.

Associate Editor

MINOR REVISION 21 Dec 2021

The suggested corrections and modifications have been made by the authors. Two minor concerns have been raised by reviewer 1, which need to be addressed. Meanwhile, the added figure seems to be related to one case (A and B), probably showing precontrast and post-contrast images of one patient. Please show two patients with pre- and post-treatment images and mention the clinical scenario of each case, as is routinely done in figures presented in radiology-based journals (clinical history plus image descriptions).

Editor-in-Chief

MINOR REVISION 21 Dec 2021

Dear authors,
Your article needs Minor Revision.
Regards

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 118338
Manuscript Title: Prognostic value of texture features of computed tomography images for patients with hepatocellular carcinoma after stereotactic ablation radiotherapy
Revision: [1]

Reviewer 1:
Thanks from authors for their editions.
Currently, this manuscript is acceptable according to methodology.
Response: Thank you very much for your positive comment.

Reviewer 2:
Thank you for the edition of your manuscript, according to the comments.
The exact definition of the therapeutic response in multifocal HCC is not stated, and I think you must mention it as a limitation of the study.
Also, pathologic grading is not discussed as another limitation.
Response: Thank you very much for your valuable comment. We have mentioned these as the study limitations.

Associate Editor 1:
The suggested corrections and modifications have been made by the authors. Two minor concerns have been raised from reviewer 1 which need to be addressed. Meanwhile, the added figure seems to be related to one case (A and B) as probably precontrast and post-contrast images of one patient. Please show two patients with pre and post-treatment images and mention the clinical scenario of each case similar to the figures routinely presented in the radiology-based journals (clinical history plus image descriptions).
Response: Thank you very much for your valuable comment. We have added the required figures.

EIC Decision:
Dear authors,
Your article needs Minor Revision.
Response: We have revised the manuscript according to all valuable comments.

3 Revision 2

0 comments

No public comments in this round.

4

Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 118338
Manuscript Title: Prognostic value of texture features of computed tomography images for patients with hepatocellular carcinoma after stereotactic ablation radiotherapy
Revision: [1]

Reviewer 1:
Thanks from authors for their editions.
Currently, this manuscript is acceptable according to methodology.
Response: Thank you very much for your positive comment.

Reviewer 2:
Thank you for the edition of your manuscript, according to the comments.
The exact definition of the therapeutic response in multifocal HCC is not stated, and I think you must mention it as a limitation of the study.
Also, pathologic grading is not discussed as another limitation.
Response: Thank you very much for your valuable comment. We have mentioned these as the study limitations.

Associate Editor 1:
The suggested corrections and modifications have been made by the authors. Two minor concerns have been raised from reviewer 1 which need to be addressed. Meanwhile, the added figure seems to be related to one case (A and B) as probably precontrast and post-contrast images of one patient. Please show two patients with pre and post-treatment images and mention the clinical scenario of each case similar to the figures routinely presented in the radiology-based journals (clinical history plus image descriptions).
Response: Thank you very much for your valuable comment. We have added the required figures.

EIC Decision:
Dear authors,
Before starting the review processing of your article, it is necessary to clarify the following items:
Please mention ethical code with the link address.
Response: We have mentioned the ethical code in both the submission system and main text for your information. We are really sorry that but the ethical approval file was not put online at the time of approval (the year 2018).

Please clarify the financial resource and mention the number grant.
Response: This study was not financially supported.

Regarding the importance of "conflict of interest" clarification, corresponding author should fill the "ICMJ form" form and upload in the submission process. (The form exists in "conflict of interest" section of the site: https://brief.land/iranjradiol/knowledgebase/category/tree.html#conflicts_of_interest.html).
Response: We have completed and uploaded the required form.

4 Revision 3

0 comments

No public comments in this round.

5

Revision 4

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 118338
Manuscript Title: Prognostic value of texture features of computed tomography images for patients with hepatocellular carcinoma after stereotactic ablation radiotherapy
Revision: [1]

Reviewer 1:
Thanks from authors for their editions.
Currently, this manuscript is acceptable according to methodology.
Response: Thank you very much for your positive comment.

Reviewer 2:
Thank you for the edition of your manuscript, according to the comments.
The exact definition of the therapeutic response in multifocal HCC is not stated, and I think you must mention it as a limitation of the study.
Also, pathologic grading is not discussed as another limitation.
Response: Thank you very much for your valuable comment. We have mentioned these as the study limitations.

Associate Editor 1:
The suggested corrections and modifications have been made by the authors. Two minor concerns have been raised from reviewer 1 which need to be addressed. Meanwhile, the added figure seems to be related to one case (A and B) as probably precontrast and post-contrast images of one patient. Please show two patients with pre and post-treatment images and mention the clinical scenario of each case similar to the figures routinely presented in the radiology-based journals (clinical history plus image descriptions).
Response: Thank you very much for your valuable comment. We have added the required figures.

EIC Decision:
Dear authors,
Before starting the review processing of your article, it is necessary to clarify the following items:
Please mention ethical code with the link address.
Response: We have mentioned the ethical code in both the submission system and main text for your information. We are really sorry that but the ethical approval file was not put online at the time of approval (the year 2018).

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Response: We have completed and uploaded the required form.

5 Revision 4

1 comment · 16 Mar 2022

Editor-in-Chief

MINOR REVISION 16 Mar 2022

Dear authors,
Your article needs Minor Revision.
Regards

6

Revision 5

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Manuscript ID: 118338
Manuscript Title: Prognostic value of texture features of computed tomography images for patients with hepatocellular carcinoma after stereotactic ablation radiotherapy
Revision: [4]

Reviewer 1:
Due to the fact that in this article only CT scan modality used in order to evaluation.
In the legend of Figure 1, you mentioned all 4 images (A,B,C,D) related to CT scan , but seems that about A,C and D images, they are related to MRI (T1 post contrast). Please remove the MRI images and replace them with CT images that match the text and legend.
Response: We are really sorry for the mistake, and have replaced this figure.

Associate Editor 1:
The suggested corrections and modifications have been done completely.
Response: Thank you very much for your positive comment.

Associate Editor 2:
1-the authors mentioned: "the HCC cases account for 80% of the total cases in the world" please clarify in this sentence what is the meaning of total cases? Total HCC cases?
Response: We have clarified this description according to your requirement.

2-based on title and objective, it seems the texture features has been done on CT images that are performed after the SABR while based on conclusion of abstract, the CT imaging have been performed before SABR. I recommend the authors clarify this point in title and objectives.
Response: Actually, CT was performed before and after SABR treatment (Figure 1).

3- please add full data of CT manufacturer [Philips Brilliance].
Response: We have supplemented the information according to your requirement.

4-the authors mentioned: "Specifically, complete remission, partial remission, stable disease and progressive disease were defined as the decrease of lesions" it is unclear what is the meaning of "decrease of lesions" here. Do you mean decrease of lesion size? Please clarify.
Response: We have clarified the description according to your valuable comment.

5-in table 2, the part related to lesion size does not elucidate the lesions size equal to 5 cm. this value should be mentioned in one of the groups.
Response: We are really sorry for the mistake, and have revised the description in Table 2.

6-please mention at the footnote of table 2 that the data have been mentioned as No. (%) or mean±SD.
Response: We have clarified the information in Table 2 according to your requirement.

7-please introduce abbreviations at the footnote of tables such as OR, GGT, SABR, …..
Response: We have spelt out the abbreviations according to your requirement.

8-legends of tables are not appropriate. We can complete them as follows:
Table 1-Comparison of baseline demographic, clinical and laboratory data between poor and good prognosis groups

Table 2- Comparison of Texture features of CT images between poor and good prognosis groups
Response: We have made corresponding revisions according to your valuable comment.

9-please correct the figure 1 legend as: Representative CT images of good prognosis group (A and B) and poor prognosis group (C and D). …..
Response: We have revised the figure legend according to your requirement.

10-one of the images is ROC curve. It is better the authors mention ROC curve in the legend of this image.
Response: We have mentioned ROC curve in the figure legend according to your requirement.

11-Due to the fact that in this article only CT scan modality used in order to evaluation. In the legend of Figure 1, you mentioned all 4 images (A,B,C,D) related to CT scan , but seems that about A,C and D images, they are related to MRI (T1 post contrast). Please remove the MRI images and replace them with CT images that match the text and legend.
Response: We are really sorry for the mistake, and have replaced this figure.

EIC Decision:
Dear authors,
Your article needs Minor Revision.
Response: We have revised the manuscript again according to all valuable comments.

6 Revision 5

1 comment · 29 Mar 2022

Editor-in-Chief

ACCEPT 29 Mar 2022

Dear authors,
Your article is acceptable for publication in IJR.
Regards