Iranian Journal of Radiology
Volume 19 · Issue 3 · e121392

OPEN PEER REVIEW

Diagnostic Accuracy of Opportunistic Breast Cancer Screening Based on Mammography in Iran

Azin Ebrahimi, Nasrin Ahmadi Nejad, Aryan Arvin, Ali Akbari Sari

SUBMITTED	REVISED	ACCEPTED	DOI
24 Nov 2021	28 Aug 2022	3 Sep 2022	10.5812/iranjradiol-121392

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.

More about open peer review: brieflands.com/knowledgebase/opr

Contents

1 **Original submission** Referee 1, Editor-in-Chief 2
2 **Revision 1** Editor-in-Chief 4
Authors' reply to reviewers 5
Reviewer and editor comments 10
3 **Revision 2** Editor-in-Chief 11
Authors' reply to reviewers 12
Reviewer and editor comments 17
4 **Revision 3** Editor-in-Chief 18
Authors' reply to reviewers 19
Reviewer and editor comments 24
5 **Revision 4** Referee 1, Editor-in-Chief 25
Authors' reply to reviewers 26
Reviewer and editor comments 29
6 **Revision 5** Referee 1, Editor-in-Chief 30
Authors' reply to reviewers 31
Reviewer and editor comments 34
7 **Revision 6** Editor-in-Chief 35
Authors' reply to reviewers 36
Reviewer and editor comments 39

1 Original submission

2 comments · 1 Dec 2021 – 9 Feb 2022

Referee 1 Reviewer

MAJOR REVISION 1 Dec 2021

First of all, I would like to thank the respected authors for choosing our journal for their submission. Regarding this manuscript, it should be said that it needs fundamental amendments in various aspects, which are mentioned below:

1. The scientific writing structure: The structure of the manuscript needs to be fundamentally revised according to the general principles of scientific writing. In addition, it should be written in accordance with the journal guidelines. The discussion section should be removed from the last paragraph of the abstract, and a conclusion should be added instead.

2. The methods section is written very theoretically, whereas the process for each step of the study should be explained clearly and completely so that others can repeat the study and achieve similar results.

3. If the study is longitudinal, the frequency of measurements, the interval between measurements, and loss to follow-up should be explained. In the results section, no follow-up data were provided, and the results are similar to those of a cross-sectional study.

4. The inclusion and exclusion criteria of the study are ambiguous.

5. The imaging and image analysis process should be described in the methods section.

6. The statistical analysis section should start with descriptive indicators, then describe the analytical tests for each variable separately, followed by an explanation of the ROC analysis. Finally, the significance level, statistical software, and software versions must be mentioned.

7. In the Results section, all important demographic and clinical characteristics of the patients must first be presented in Table 1 and briefly described in the first paragraph.

8. The correlation coefficient was presented in the results section but was not mentioned in the statistical analysis section. Is it not necessary to use a correlation coefficient?

9. In Table 1:

9.1. Positive predictive values should be 42% and negative predictive values 98%.

9.2. What is meant by population-level accuracy, and how was it calculated? It should be explained in the statistical analysis section.

9.3. Tables 1 and 4 must be merged.

10. In Table 2:

10.1. Show the number of samples in each class of variables.

10.2. Delete the sig. column for the post hoc test.

10.3. Sensitivity and specificity should be provided with 95% confidence intervals.

10.4. The Significant column should be renamed p-value, and 0.05 should be deleted from parentheses.

11. The order of the figures is not correct. In addition, you should make the following changes:

11.1. Figures 2 and 3 should be omitted, and their data should be presented in Table 1 for clinical and demographic results.

11.2. Figure 5 should be deleted.

12. Figure and table titles should be self-explanatory. The title of a table should be written above it, and the title of a figure should be written below it.

Editor-in-Chief MAJOR REVISION 9 Feb 2022

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.

:In response to EIC

,Thank you for your helpful tips and comments

Figure of study matrix is inserted into the text as a table drawn by Microsoft .Word

.Tables are drawn by word

.All changes including English edits are highlighted

.Comments are deleted

References are in Vancouver style. (Mentioned as the briefland style file cannot be downloaded)

:In response to first reviewer

,First we must thank the reviewer for kind and helpful comments

The response to each comment is written under it and highlighted in article :body

Yellow: rewritten or English edit

Green: specific comments

.1 The scientific writing structure: General principles of scientific written structure needs to be fundamentally edited. In addition, it should be written in accordance with the journal guideline, the discussion section should be removed from the last .paragraph of the abstract and conclusion should be added instead

The subtitle of last paragraph of abstract is corrected and general edits in different .parts are done

.2 The method part is written very theoretically, while the process of doing each of the study steps should be explained clearly and completely; so that, it is possible to .repeat the study and achieve to similar results by others

.The method part is revised

.3 If the study is longitudinal, the frequency of measurements, the interval between measurements, and loss to follow-up should be explained. In the results section, no .follow-up data were provided and the results are similar to a cross-sectional study

It is an observational study. For the aim of screening and for determination of real disease status we assessed reports in intervals of one year until the final disease status is determined (by stability overtime or pathology result). The inclusion criteria indicate that a person must have the proper follow up for determination of final status and the study aim is to determine accuracy considering current attendance to screening. For the number of 491 cases, we assessed 1190 screening reports for .availability of proper follow up

.4 The inclusion and exclusion criteria of the study are ambiguous

.The inclusion and exclusion criteria are revised

The imaging and image analysis process should be described in the method section .5

.In the study we assessed reports. The device is explained

The statistical analysis section should start with descriptive indicators, then write .6 about analytical tests according to each variable separately, afterwards explain about the Roc analysis, and finally must be mentioned about the level of significance, .statistical software (s), and their version

.They are rewritten

In Results section, firstly must be presented all important demographic and clinical .7 characteristics of patients in a table 1 and briefly stated about them in the first .paragraph

.It is rewritten

The correlation coefficient was presented in the results section, but was not .8 expressed in the statistical analysis section. Is it not necessary to use a correlation ?coefficient

.It is mentioned in statistics

:In Table 1 .9

Positive predictive values should be 42% and negative predictive values 98% .9.1

.NPV and PPV are calculated using the matrix and current prevalence

What is meant by population-level accuracy and how was it calculated? It should .9.2 be explained in the statistical analysis section

:It means the same test assuming the prevalence of community

Taking the sensitivity and specificity derived from our study and by assuming the real prevalence of breast cancer in Iran, we calculated accuracy at population level

.

.Tables 1 and 4 must be merged .9.3

.The manuscript had two tables

:In Table 2 .10

Show the number of samples in each class of variables .10.1

.It is shown

Delete the sig. column of the post hack .10.2

.It is deleted

Sensitivity and specificity should be provided with 95% confidence interval .10.3

.The 95 % confidence intervals of indices are written

Significant column changed to p-value and 0.05 deleted from parenthesis .10.4

.It is done

:The order of the shapes is not correct, in addition you should .11
Figures 2 and 3 are omitted, and their data presented in table 1 for clinical and .11.1
.demographic results

.Figure 2 is omitted. The number of each subgroup samples is added to table one

.Figure 5 should be deleted .11.2

.Figure 5 is deleted

Figures and tables title should be self-explanatory. The title of the table is written .12
.above of it, and the title of the figure is written below of it

.Changes are made to these parts

.

:In response to second reviewer

:First we must thank the reviewer for kind and helpful comments

Each comment is answered here and mentioned in article body:

Yellow: rewritten or English edit

Green: specific comments

:Reviewer 2
I've read the manuscript thoroughly and I must admit that it effectively addresses the issue mentioned in the title. Although the subject of this study is novel, the study was well designed and the number of included specimens were higher than previous studies and I have found no studies on Iranian population. The manuscript is not properly written and many grammatical errors are present. I recommend a thorough revision by a native or fluent English speaker. A few comments have been suggested .to further be corrected by the authors

Abstract
The background needs to be properly rewritten :#1

.Background is rewritten

.
"Discussion" should be changed to "Conclusion" :#2

.The subtitle of last paragraph of abstract is changed to conclusion

.
Introduction

The introduction is not written properly. The first paragraph is only one sentence :#3
and does not elaborate on the epidemiology and cost of breast cancer in Iranian
population. Perhaps the first paragraph can start with the global prevalence and
attributed mortality of breast cancer and then continue with a thorough comparison
.of these results with the prevalence and mortality of breast cancer in Iran

.The background part is revised

The second paragraph should be rewritten. Different diagnostic modalities should :#4
be introduced first and the efficacy and accuracy of these modalities should be
compared. It should then be explained that why opportunistic mammography is
.preferred over those other diagnostic tools

.The second paragraph is rewritten

The last paragraph of the introduction is vague and the aim of the study is not :#5
comprehensible, therefore, it needs to be properly rewritten

.The last paragraph is rewritten

Methods
.Duration of study should be added :#6

.The duration of the study is mentioned 2019-2020

How many observers did evaluate the mammographies? If more than one, inter- :#7
.observer agreement should be calculated

For the purpose of this study we used patients' records. For the study all reports –for
.first screening and the follow up study- are evaluated by one observer

Results
The results should be revised regarding grammatical mistakes. And avoid using :#8
too many subtitles

.The results part is edited

Discussion
Again, I should mention that the whole manuscript needs to be revised and it can :#9
.be rewritten more eloquently

.The whole manuscript is revised

Recent studies should also be added and discussed. A recent study with the :#10
.same subject is published in BMC on the Swiss population

.New studies are added

In response to 3rd reviewer:

First we must thank the reviewer for kind and helpful comments:

Each comment is answered here and also mentioned in article body :

Yellow: rewritten or English edit

Green: specific comments

Dear author

1$:References 1 and 5 should be deleted.

References 1 and 5 are deleted and we mentioned IARC in the text.

2$: Please refer to up to date references.

New references are added.

3$:Please clarify the financial resource and mention the number grant.

We did not receive any grant rather than usual thesis fund from TUMS.

2 Revision 1

1 comment · 11 Apr 2022

Editor-in-Chief

MINOR REVISION 11 Apr 2022

Dear authors,
Before the review process for your article begins, it is necessary to clarify the following items:

Given the importance of “conflict of interest” clarification, the corresponding author should fill out the “ICMJE form” and upload it during the submission process. (The form is available in the “conflict of interest” section of the site:
https://brief.land/iranjradiol/knowledgebase/category/tree.html#conflicts_of_interest.html.)

As some authors are faculty members of Tehran University of Medical Sciences, this should be mentioned as a conflict of interest. (Ali Akbari Sari is a faculty member of Tehran University of Medical Sciences.)
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.

:In response to EIC

,Thank you for your helpful tips and comments

Figure of study matrix is inserted into the text as a table drawn by Microsoft .Word

.Tables are drawn by word

.All changes including English edits are highlighted

.Comments are deleted

References are in Vancouver style. (Mentioned as the briefland style file cannot be downloaded)

:In response to first reviewer

,First we must thank the reviewer for kind and helpful comments

The response to each comment is written under it and highlighted in article :body

Yellow: rewritten or English edit

Green: specific comments

The scientific writing structure: General principles of scientific written structure .1 needs to be fundamentally edited. In addition, it should be written in accordance with the journal guideline, the discussion section should be removed from the last .paragraph of the abstract and conclusion should be added instead

The subtitle of last paragraph of abstract is corrected and general edits in different .parts are done

The method part is written very theoretically, while the process of doing each of .2 the study steps should be explained clearly and completely; so that, it is possible to .repeat the study and achieve to similar results by others

.The method part is revised

If the study is longitudinal, the frequency of measurements, the interval between .3 measurements, and loss to follow-up should be explained. In the results section, no .follow-up data were provided and the results are similar to a cross-sectional study

It is an observational study. For the aim of screening and for determination of real disease status we assessed reports in intervals of one year until the final disease status is determined (by stability overtime or pathology result). The inclusion criteria indicate that a person must have the proper follow up for determination of final status and the study aim is to determine accuracy considering current attendance to screening. For the number of 491 cases, we assessed 1190 screening reports for .availability of proper follow up

The inclusion and exclusion criteria of the study are ambiguous .4

.The inclusion and exclusion criteria are revised

The imaging and image analysis process should be described in the method section .5

.In the study we assessed reports. The device is explained

The statistical analysis section should start with descriptive indicators, then write .6 about analytical tests according to each variable separately, afterwards explain about the Roc analysis, and finally must be mentioned about the level of significance, .statistical software (s), and their version

.They are rewritten

In Results section, firstly must be presented all important demographic and clinical .7 characteristics of patients in a table 1 and briefly stated about them in the first .paragraph

.It is rewritten

The correlation coefficient was presented in the results section, but was not .8 expressed in the statistical analysis section. Is it not necessary to use a correlation ?coefficient

.It is mentioned in statistics

:In Table 1 .9

Positive predictive values should be 42% and negative predictive values 98% .9.1

.NPV and PPV are calculated using the matrix and current prevalence

What is meant by population-level accuracy and how was it calculated? It should .9.2 be explained in the statistical analysis section

:It means the same test assuming the prevalence of community

Taking the sensitivity and specificity derived from our study and by assuming the real prevalence of breast cancer in Iran, we calculated accuracy at population level

.

.Tables 1 and 4 must be merged .9.3

.The manuscript had two tables

:In Table 2 .10

Show the number of samples in each class of variables .10.1

.It is shown

Delete the sig. column of the post hack .10.2

.It is deleted

Sensitivity and specificity should be provided with 95% confidence interval .10.3

.The 95 % confidence intervals of indices are written

Significant column changed to p-value and 0.05 deleted from parenthesis .10.4

.It is done

:The order of the shapes is not correct, in addition you should .11
Figures 2 and 3 are omitted, and their data presented in table 1 for clinical and .11.1
.demographic results

.Figure 2 is omitted. The number of each subgroup samples is added to table one

.Figure 5 should be deleted .11.2

.Figure 5 is deleted

Figures and tables title should be self-explanatory. The title of the table is written .12
.above of it, and the title of the figure is written below of it

.Changes are made to these parts

.

:In response to second reviewer

:First we must thank the reviewer for kind and helpful comments

Each comment is answered here and mentioned in article body:

Yellow: rewritten or English edit

Green: specific comments

:Reviewer 2
I've read the manuscript thoroughly and I must admit that it effectively addresses the issue mentioned in the title. Although the subject of this study is novel, the study was well designed and the number of included specimens were higher than previous studies and I have found no studies on Iranian population. The manuscript is not properly written and many grammatical errors are present. I recommend a thorough revision by a native or fluent English speaker. A few comments have been suggested .to further be corrected by the authors

Abstract
The background needs to be properly rewritten :#1

.Background is rewritten

.
"Discussion" should be changed to "Conclusion" :#2

.The subtitle of last paragraph of abstract is changed to conclusion

.
Introduction

The introduction is not written properly. The first paragraph is only one sentence :#3
and does not elaborate on the epidemiology and cost of breast cancer in Iranian
population. Perhaps the first paragraph can start with the global prevalence and
attributed mortality of breast cancer and then continue with a thorough comparison
.of these results with the prevalence and mortality of breast cancer in Iran

.The background part is revised

The second paragraph should be rewritten. Different diagnostic modalities should :#4
be introduced first and the efficacy and accuracy of these modalities should be
compared. It should then be explained that why opportunistic mammography is
.preferred over those other diagnostic tools

.The second paragraph is rewritten

The last paragraph of the introduction is vague and the aim of the study is not :#5
comprehensible, therefore, it needs to be properly rewritten

.The last paragraph is rewritten

Methods
.Duration of study should be added :#6

.The duration of the study is mentioned 2019-2020

How many observers did evaluate the mammographies? If more than one, inter- :#7
.observer agreement should be calculated

For the purpose of this study we used patients' records. For the study all reports –for
.first screening and the follow up study- are evaluated by one observer

Results
The results should be revised regarding grammatical mistakes. And avoid using :#8
too many subtitles

.The results part is edited

Discussion
Again, I should mention that the whole manuscript needs to be revised and it can :#9
.be rewritten more eloquently

.The whole manuscript is revised

Recent studies should also be added and discussed. A recent study with the :#10
.same subject is published in BMC on the Swiss population

.New studies are added

In response to 3rd reviewer:

First we must thank the reviewer for kind and helpful comments:

Each comment is answered here and also mentioned in article body :

Yellow: rewritten or English edit

Green: specific comments

Dear author

1$:References 1 and 5 should be deleted.

References 1 and 5 are deleted and we mentioned IARC in the text.

2$: Please refer to up to date references.

New references are added.

3$:Please clarify the financial resource and mention the number grant.

We did not receive any grant rather than usual thesis fund from TUMS.

3 Revision 2

1 comment · 9 May 2022

Editor-in-Chief

MINOR REVISION 9 May 2022

Dear authors,
Your article needs Minor Revision.
Regards

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.

First we must thank the reviewers for their comments:

There is another version of table 4 in this text which the authors believe it may be more consistent with comments and replies but as it does not include the CIs, it is not changed in the article body.

In reply to reviewer 1:

1. An important point to note in the conclusion of the study is the low positive predictive value of the test, which indicates its ineffectiveness for screening. Because, only positive cases of screening test are subject to subsequent diagnostic procedures. In addition, the sensitivity of the screening test is 73%, which is not appropriate. As a result, screening test is not a appropriate for screening in this group of women.

The lower sensitivity is mentioned in the text. The PPV is lower than some studies in the same way. (both mentioned) The possible causes are also discussed. It is suggested that even with the lower sensitivity in an opportunistic setting it is an acceptable screening test.

2. Full-text method: The inclusion and exclusion criteria of the study are ambiguous. The incidence of breast cancer is higher (26/491*100,000=5,295) than total population.

The incidence in this study includes some prevalence cases as it is an opportunistic setting.

Inclusion and exclusion criteria are revised.

3. In the results section, no follow-up data were provided and the results are similar to a cross-sectional study

We evaluated screening based on patients' status at subsequent screenings. We followed them over time for at least another screening and at least one year after the first screening. It was considered a longitudinal study as we used follow-up screenings but we cannot provide uniform follow-up data for all patients. The follow up period is different based on initial BIRADS as we had to follow BIRADS 3 for at least 2 years to confirm that they are cancer free.

The term longitudinal is changed in the text.

4. In Table3: Positive predictive values should be 42% (19/45*100) and negative predictive values 98% (439/446*100)

PPV and NPV are calculated using current prevalence of breast cancer in Iran. (It is mentioned in the text too).

5. How is it possible that in Table 4, the value of sensitivity in the age group of 70 and above is negative (-8)? It is better to reduce the age classes, so that, the sample size of the classes is more appropriate.

They are two age classifications in the study one is two age groups above and under 50.

It is not -8. It is the number referring to a footnote.

6. In table 4, all sensitivity and specificity values must be reported by %95 confidence intervals.

All CIs are written as required in previous revision. We used nonparametric tests so maybe CI is not proper in this setting as it is about the mean.

7. In table 4, it is better that the number column be divided into two columns positive and negative*.*

The idea will make the table more informative if we write positive and negative for both test results and disease status.

The contingencies are written.

8. Small sample size must be added as limitation of the study. Because in table 4, the confidence intervals are very wide. In addition, despite the large differences in the values of some classes such as age variable, their differences are not significant.

It is added in the text. We calculated the sample size for a diagnostic test accuracy and then we compared subgroups. If the sample size was larger there may be more significant relationships.

9. In Table 4, for the prior intervention variable, the significance level should not be less than 0.05, while the confidence intervals of the positive and negative groups overlap*.*

We used nonparametric test but the idea of t CI is based on T test.

The authors believe they have to omit the Cis from the table as all distributions needed nonparametric tests.

If we used T test for this distribution the p value might be greater than 0.05.

The new version without Cis is in replies but we did not omit the Cis in the text.

Reviewer 2:
I would like to thank the authors for submitting the manuscript in IJR. Although the article has undergone major revision there are still some mistakes that should be corrected before publication.
In general, you should revise the article grammatically and use well-placed punctuation especially comma. For instance, you should omit 'comma' before 'and' or 'but' such as in the line 17,18, 80, 86, 94 and ….

There is a comma before "and" and "but" only when but is connecting two independent clauses *(as English revision made changes).*

There are several problems which should be taken into account and corrected as following:

1. Background and Objectives

1# line 38 : (omit comma) especially to screen women with an increase in the risk of breast cancer

done

2# Through the screening program, mammograms are to be offered to women aged 40-44. However, annual screening and mammograms conducted once every two years are recommended to women aged 45-54 and those over 55 years of age respectively.

done

2. Methods
2.1. Patients and setting

3# line 66 and 67: this sentence is vague . Please change it into a comprehensible content.

done

2.2. Tools and follow-up

4# line 73 : Codes one (negative findings)

done

5# line 77 and 78: these sentences are vague. Please change it into a comprehensible content.

done

4 Discussion

6# line 153 and 154: these sentences are vague. Please change it into a comprehensible content.

done

7# line 162: Strategies for increasing the sensitivity of screening are divided into three categories.

done

8# line 165: The second solution is to use computer aid

done

9# line 179: it could be due to

done

10 # line 188: Studies have shown that

Done

11# line 212: could improve their cancer detection

done

12# line 216: we did not have access to the other patients' risk factors such as BMI

done

13# line 217: the specificity of the test results decreases. However, sensitivity does not show significant changes.

done

Reviewer 3:

This paper is suitable for publication in IJR.

The other version of table 4 (without Cis)

Subgroup		Number of samples in contingency		Sensitivity	p-value	Specificity	p-value
		S[1] + D[2]+	S + D -				
		S - D+	S - D -				
Age: Ten year groups	Under 30	1	0	100 %[3]	0.932	-	0.483
		0	0				
	30-39	3	4	60.0 %		90.9 %	
		2	40				
	40-49	4	7	66.7 %		96.0 %	
		2	170				
	50-59	8	12	80.0 %		93.0 %	
		2	159				
	60-69	4	2	80.0 %		96.8 %	
		1	60				
	70 and over	0	1	-[4]		90.0 %	
		0	9				
Age: Two group	Under 50	7	11	63.6 %	0.407	95.0 %	0.687
		4	211				
	50 and over	12	15	80.0 %		93.8 %	
		3	228				

[1] S=screening result
[2] D= disease status in follow up
[3] Only one case
[4] No disease positive case on follow up

Breast density	A	1	2	50.0 %	0.826	97.7 %	0.267
		1	72				
	B	5	13	71.4 %		92.6 %	
		2	163				
	C	12	11	80.0 %		94.1 %	
		3	175				
	D	1	0	50.0%		100.0 %	
		1	29				
Family history	Positive	2	4	66.7 %	0.794	95.0 %	0.800
		1	76				
	Negative	17	22	73.9 %		94.3 %	
		6	363				
Prior intervention	Positive	3	8	42.9 %	0.039	96.5 %	0.061
		4	218				
	negative	19	26	84.2 %		92.5 %	
		7	439				

4 Revision 3

1 comment · 18 Jun 2022

Editor-in-Chief

MINOR REVISION 18 Jun 2022

Dear authors,
Your article needs Minor Revision.
Regards

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.

First we must thank the reviewers,

Reviewer 1:

At the moment, it can be said that the required editions have been made to some extent, but they have not been implemented completely; which include:

1. The calculations in Table 3 should be based on your study data (i.e., Table 2) and not on other data.

   All parameters except PPV NPV and accuracy at population level are measured by the study data. We needed prevalence for calculation of these indices.

   These 3 indices are calculated by using prevalence from WHO.

   Accuracy is both calculated for the study population and prevalence in Iran.

2. Due to the small number of samples, it is better to present in Table 4, only the age group below and above 50 years.

   The numbers are mentioned. The authors request the editor-in-chief of the journal to remove this section at his discretion as it was in previous revisions and we are not sure for the deletion.

   Please inform the authors for any change for this purpose. We will change the table as soon as the EIC requires us.

   The suggested table:

Subgroup		Number of samples in contingency		Sensitivity	p-value	Specificity	p-value
		S[1] + D[2]+	S + D -				
		S - D+	S - D -				
Age: Two group	Under 50	7	11	63.6 % (30.8- 89.1)	0.407	95.0% (91.3-97.5)	0.687
		4	211				
	50 and over	12	15	80.0 % (51.9- 95.7)		93.8% (90.0-96.5)	
		3	228				
Breast density	A	1	2	50.0 % (1.3- 98.8)	0.826	97.3% (90.6-99.7)	0.267
		1	72				
	B	5	13	71.4 % (29.04-96.33)		92.6% (87.7-96.0)	
		2	163				
	C	12	11	80.0 % (51.9- 95.7)		94.1% (89.7-97.0)	
		3	175				
	D	1	0	50.0% (1.3- 98.7)		100.0% (88.1-100.0)	
		1	29				
Family history	Positive	2	4	66.7 % (9.4- 99.2)	0.794	95.0% (87.7-98.6)	0.800
		1	76				
	Negative	17	22	73.9 % (51.6- 89.8)		94.3% (91.5-96.4)	
		6	363				
Prior intervention	Positive	3	8	42.9 % (9.9 - 81.6)	0.120	96.5% (93.1-98.5)	0.061
		4	218				
	negative	16	18	84.2 % (60.4-96.6)		92.5% (88.4-95.5)	
		3	221				

[1] S=screening result
[2] D= disease status in follow up

3. The authors' argument regarding the inconsistency of significance level and confidence intervals for the prior intervention variable is incorrect. If the appropriate statistical tests are used, these two parameters must be aligned. Moreover, methodologically, the confidence interval is preferred over the significant level, because of giving more information (direction and magnitude).
   Thank you for your comment. We calculated CI with nonparametric assumptions. We also changed it as the CI still overlap and instead sig. of an exact test is calculated.

Reviewer 2:

This article is well-prepared for publication in IJR.

5 Revision 4

2 comments · 28 Jun 2022 – 10 Aug 2022

Referee 1 Reviewer

MINOR REVISION 28 Jun 2022

Although the authors made two of the three required corrections, the method of calculating the positive and negative predictive values of the test is still not based on their own study data and needs to be corrected. Unfortunately, despite the fact that this issue has been explained twice so far, there is still an insistence on the wrong procedure. As in the second review, the calculations for positive and negative predictive values should be as follows: The positive predictive value should be 42% (19/45*100) and the negative predictive value 98% (439/446*100).

Editor-in-Chief

MINOR REVISION 10 Aug 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.

Reviewer 1:
Although the authors made two of the three required corrections; but, the method of calculating the positive and negative predictive value of test is still not based on their own study data and it needs to be corrected. Unfortunately, despite the fact that this issue has been explained twice so far, there is still an insistence on the wrong procedure. As in the second review, the calculations for positive and negative predictive value should be as follows: Positive predictive values should be 42% (19/45*100) and negative predictive values 98% (439/446*100).

First we must thank the reviewer for their comments:

The NPV and PPV are rewritten considering sample prevalence.

In previous reply the authors provided two version of table 4 considering the comment:

Comment: Due to the small number of samples, it is better to present in Table 4, only the age group below and above 50 years.

Reply: The suggested change is made. The authors request the editor-in-chief of the journal to choose this section at his discretion as it was in previous revisions and we are not sure for the deletion. Please inform the authors for any change for this purpose. We will change the table as soon as the EIC requires us.

Regards

The suggested table is included in the text

Also the previous version is brought here:

Subgroup		Number of samples in contingency		Sensitivity	p-value	Specificity	p-value
		S[1] + D[2]+	S + D -				
		S - D+	S - D -				
Age: Ten year groups	Under 30	0	0	-	0.932	100.0 % [3] (2.5-100.0)	0.483
		0	1				
	30-39	3	4	60.0 % (14.7-94.7)		90.9% (78.3-97.5)	
		2	40				
	40-49	4	7	66.7 % (22.28-95.67)		96.0% (92.0-98.4)	
		2	170				
	50-59	8	12	80.0 % (44.4-97.5)		93.0% (88.1-96.3)	
		2	159				
	60-69	4	2	80.0 % (28.4- 99.5)		96.8% (88,8-99.6)	
		1	60				
	70 and over	0	1	- [4]		90.0% (55.5-99.8)	
		0	9				
Age: Two group	Under 50	7	11	63.6 % (30.8- 89.1)	0.407	95.0% (91.3-97.5)	0.687
		4	211				
	50 and over	12	15	80.0 % (51.9- 95.7)		93.8% (90.0-96.5)	
		3	228				
Breast density	A	1	2	50.0 % (1.3- 98.8)	0.826	97.3% (90.6-99.7)	0.267
		1	72				
	B	5	13	71.4 % (29.04-96.33)		92.6% (87.7-96.0)	
		2	163				

[1] S=screening result
[2] D= disease status in follow up
[3] Only one case
[4] No disease positive case on follow up

	C	12	11	80.0 % (51.9- 95.7)		94.1% (89.7-97.0)	
		3	175				
	D	1	0	50.0% (1.3- 98.7)		100.0% (88.1-100.0)	
		1	29				
Family history	Positive	2	4	66.7 % (9.4- 99.2)	0.794	95.0% (87.7-98.6)	0.800
		1	76				
	Negative	17	22	73.9 % (51.6- 89.8)		94.3% (91.5-96.4)	
		6	363				
Prior intervention	Positive	3	8	42.9 % (9.9 - 81.6)	0.120	96.5% (93.1-98.5)	0.061
		4	218				
	negative	16	18	84.2 % (60.4-96.6)		92.5% (88.4-95.5)	
		3	221				

6 Revision 5

2 comments · 15 Aug 2022 – 23 Aug 2022

Referee 1 Reviewer

ACCEPT 15 Aug 2022

At present, this manuscript is appropriate in terms of methodology.

Editor-in-Chief

MINOR REVISION 23 Aug 2022

Dear authors,
Your article needs Minor Revision.
Regards

7

Revision 6

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.

Associate Editor 1:
Dear authors,
The manuscript could be accepted for final processing.
Associate Editor 2:
121392

First we must thank the editors,

The mentioned comments are applied and answered:

1-please add full term of abbreviations in the first time usage [separately in abstract and paper] for example; CI, …. In addition, please add fuii term of abbreviations in text not un footnote.

Full terms are used.

2-please add objective part to the paper based on journal format.

It is added.

3-please change methods section to patients and methods.

It is changed.

4-it is better the authors change title 2.3 to Statistical Analysis

It is changed.

5-in line 95, it is better the authors replace prevalence with frequency

It is changed.

6-please add SPSS and MEDCALC manufacturer data [SPSS based on IBM website guideline]

It is added.

7-in line 108; please correct: "with the mean±standard deviation(SD) of 50.56±8.52 years"

It is changed.

8-I think the word "matrix" in table 2 and in text could be replaced by cross table

It is changed.

9-table 2 and 3 legends are better as: table 2-Cross Tabulation of disease situation based on gold

standard versus screening mammography
Table 3-Diagnostic indices results of screening mammography

They are changed.

10-please introduce abbreviations in table footnote [for example NPV, ….]

It is applied.

11-please arrange table 1 horizontally.

It is rearranged.

12-i can not see the usage of Mann Whitney and Kruskal-Wallis tests in results?

They are used for comparing subgroups in terms of specificity and sensitivity. The results are shown in table 4.We added to line 90:

" Patients were divided into groups based on age, family history, history of prior intervention and breast density. Sensitivity and specificity were also compared between these groups."

13-please correct p-value = 0.000 as p-value<0.001.

They are changed

14-the authors can delete this part: "There was a significant difference in comparison with 0.500"

The part is deleted and we kept (p-value<0.001)

15-in part 3.3, please replace sig. with P-Value.

It is changed.

16-what is the meaning of it in line 141? [it can give a better estimate]. Do you mean current study? in this case, why did you add references 8-10 at the end of sentence?

We meant current study. we referred to previous studies which we compared with this study.

17-this part is unclear: "had to diagnose prevalent and incident cases"

It means when screening program is established for the first time, it has to diagnose both prevalent cases (women who already have cancer but do not know about it) and incident cases (women who go from negative to positive cancer in current screening interval e.g. this year new cases)

It is added to the text.

18-what is the meaning of comes in line 152 and 153? [brings???]

It means if we have a bigger coverage of population, the screening program will diagnose more of disease cases compared to a smaller coverage which we will lose some true disease cases and it is like the power of a test with a larger sample the test will have a higher power for detecting possible relations.

Regards

7 Revision 6

1 comment · 3 Sep 2022

Editor-in-Chief

ACCEPT 3 Sep 2022

Dear authors,
Your article is acceptable for publication.
Regards