OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Asian Journal of Sports Medicine
Article DOI: 10.5812/asjsm.83927
Published in: Asian Journal of Sports Medicine: 10(4); e83927

Peer Review Report for "The Effectiveness of Exercise Therapy and Dry Needling on Wrist Range of Motion, Pinch and Grip Force in Carpal Tunnel Syndrome: A Randomized Clinical Trial"

Author(s): Shahin Salehi, Omid Hesami, Mehrshad Poursaeed Esfehani, Shahrzad Khosravi, Amir Rashed, Mahsa Haghighatzadeh , Mohammad Hassabi, Amir Hosein Abedi Yekta

Review Timeline:

Submit Date: 4 Sep 2018
Revised Date: 31 Aug 2019
Accepted Date: 9 Sep 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0)

17 Sep 2018

Dear AE,
This is a respectable manuscript, it is written straightforward and concisely, but I believe it can be improved with some changes. some general comments first:
1. justification for doing the study is my main concern here. I was looking for the justification in its introduction, but it has failed to demonstrate the need for conducting a new study, their reference for controversy about using acupuncture for CTS dates back to 2009, there has been a number of reviews about the Effects of acupuncture therapy on the carpal tunnel syndrome. are the authors familiar with this systematic review of 2011: https://www.ncbi.nlm.nih.gov/pubmed/21093382
2. There is no Sham acupuncture group which compromises the quality of the study. it would be acceptable if there hasn't been a vast number of studies with sham acupuncture arms for studying acupuncture for CTS.
3. there is a dissociation between the results, discussion, and abstract. according to the results, there is no significant difference between treatment groups, but the authors have

suggested in the discussion that Acupuncture has shown better results in pinching force and the exercise has had a better effect on the gripping force, they have also suggested adding exercise and acupuncture to the splinting based on these findings:
results: Results of the ANOVA test showed no statistical difference in gripping force (P=0.398), pinching force (P=0.233), bending (P=0.089), and opening the wrist (P=0.250) before treatment among three groups of the brace, brace + exercise therapy, and brace+acupuncture,
discussion: But exercises had the most effect on gripping and acupuncture had the most effect on pinching.
Abstract: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in [THE] management of these patients.
I have also some specific comments:
4. The manuscript needs some English improvement: (just a number from Abstract)
The efficacy of acupuncture and exercise therapy in [THE] treatment of carpal tunnel syndrome (CTS) has been
The aim of this study was to comparison [compare] the short-term efficacy of acupuncture (2 times a day for 6 weeks [s])
except for [THE] flexion of the wrist in [THE] control group
Also [,] the efficacy of splint
be adopted in [THE] management of these patients
5. The introduction is not focused on the main question of study and it has mentioned other methods of treatment like massage therapy which is unrelated to the scope of this study. it can be rewritten in a standard form of introduction (3-4 paragraphs in the order of known>unknown>the question)
6. Methods: "the study was completely blinded", the blindness should be described.
7. results: "which these results show [s is redundent] the complete randomization of samples and the absence of bias in sample selection" this assumption is beyond my understanding, would the authors elaborate on that?
8. Discussion: the first sentence of the discussion usually describes the main finding of the study, and the discussion should also show how the proposed treatment can affect the results (physiologically), it should be more than just referencing previous studies.
Thanks.

REFEREE: Reviewer | **Revision** (0) 23 Sep 2018

Dear AE,
The writing of the paper needs to be checked by a native. Sentences are too long and difficult to follow. The following points are comments for the authors:
- The introduction is written so generally and has not focused on the topic accurately. In your introduction, you are talking about CTS and there is not enough explanation about acupuncture and exercise therapy for it. Your references are also mostly about CTS. The novelty of the paper is not clear to me.
Method:
- If it is an RCT, you have to add your IRCT number clearly and also explain about ethic

approval and ethic number. Your method section is not following a standard format and it is not acceptable in its current form (follow CONSORT checklist).
- Allocation and randomization are not explained accurately.
- It is not clear how you recognized 237 patients??
- How you recognized symptoms of atrophy or muscle weakness?
- There are some general sentences and need to be explained clearly. For example “At first, all patients were under full clinical examination”.
- Figure 2. You are not allowed to use other pictures. You have to use your own pictures.
- Duration of therapy for different groups seems different. Is it correct?? In my view, it is not acceptable. Your study design does not seem correct.
- How you defined the locations of acupuncture?
- In the evaluation section, you mentioned that evaluations were done at baseline and after treatment but this time is different for different groups.
- ROM evaluation is not explained correctly. The techniques should be explained accurately. Details of the goniometer are necessary to be written. It is not clear if it was active or passive?
- There is no detail about blinding. It is not clear if the assessor was blind. Again I repeat that this RCT is not following a standard format.
- Table 1: why here do you have 15 participants???????
- Your results should be written based on within-group and between-group comparison and talk about the effect size.
- Discussion in current form is very general and not acceptable.
- The theory behind your findings should be mentioned clearly and then compare with opposite and similar studies.
- Your conclusion is a repetition of your results.
- Please use real pictures.
- Please replace the patient with the participant in the whole paper.
- Please replace sex with gender in the whole paper.
Thanks.

REFEREE: Reviewer | **Revision** (0) 29 Sep 2018

Dear AE,
This manuscript needs major revision.
Title: The effectiveness of exercise therapy and acupuncture on wrist range of motion, pinch, and grip force in carpal tunnel syndrome: a randomized clinical trial
Relevant topic nevertheless, some points should be improved.
Abstract
- Question 1. In the abstract of result part please explain; At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of wrist in control group ($p=0.098$);??
- Please make your point clear.
- Question 2. In the abstract of result part please explain; our findings indicate that acupuncture affected the pinch force more than exercise therapy;
There were no between-group analyses, how did you make that judgment?
- Question 3. In the abstract of result part please explain; But the efficacy of exercise

therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension).
There were no between-group analyses, how did you make that judgment?
- Question 4. In the abstract of result part please explain; Also the efficacy of splint alone was less than intervention groups in all parameters;
There was no between groups analyses, how did you make that judgment?
Methods
- Question 5.Please define mild, moderate, and severe CTS with details.
- Question 6. Please mention the ethical code
- Question 7. Please give complete information about the exact anatomic location of two points of acupuncture including PC-6 (Daling) and PC-7 (Neiguan).
- Question 8. Please explain why you selected PC-6 (Daling) and PC-7 (Neiguan) points among other points.
Discussion
- Question 9. please explain ;But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients;
According to your analyses which did not include between groups difference, you can not make that judgment.
Conclusion
- Question 10. please explain; when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also a range of motion in the wrist was more than using splint alone. Also the effectiveness of exercise therapy in most cases was better than electroacupuncture.
Either omit this information or do a complementary analysis between groups.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 4 Oct 2018

Dear EIC,
Thanks for submitting this manuscript to ASJSM for consideration of publication. The first round of peer review of the manuscript is complete. There are comments and suggestions from three peer reviewers embedded in this letter (see below). Overall, the subject of this paper is interesting and relevant to the readership of this journal. However, there are a variety of issues that will require the authors' attention and revision prior to offering a final editorial decision. At this time, the manuscript is not yet accepted for publication and needs major revision.
Please carefully address all of the comments and provide a separate Word document outlining each change made (point by point) as raised in the reviewer comments.
To submit your revision, please go to http://asjsm.com
Sincerely,

REFEREE: EIC | **Revision** (0) 13 Oct 2018

Dear Author,
Thank you for submitting your manuscript to Asian J Sports Med. I now have the reports of the Referees, which suggest that your manuscript might be suitable for publication following

a number of revisions. I attach some reviewer comments and invite you to submit a revised version of your manuscript addressing the points made.

Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

October 30, 2018

Dr. Vahid Ziaee
Editor-in-chief
Journal of Injury and Violence Research

Re: Manuscript ID: 83927

Dear Dr. Ziaee,
Please find a revised version of the manuscript “The effectiveness of exercise therapy and dry needling on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial", which we would like to resubmit for publication as an original article in the “Asian Journal of Sports Medicine”

Your comments and those of the reviewers were highly insightful and enabled us to revise it, thus greatly improved the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers. Revisions in the text are shown using yellow highlight for additions.

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in “Asian Journal of Sports Medicine”.

We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

Yours sincerely,

Corresponding author
Shahin Salehi
Sports Medicine Specialist
Department of Sport Medicine
School of Medicine
Shahid Beheshti University of Medical Sciences
Phone: 0098-912-1406684 Email: salehi2955@yahoo.com

Reviewer 1:

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1.justification of doing the study is my main concern here. I was looking for the justification in its introduction, but it has failed to demonstrate the need for conducting a new study , their reference for controversy about using acupuncture for CTS dates back to 2009, there has been a number of reviews about Effects of acupuncture therapy on the carpal tunnel syndrome. are the authors familiar with this systematic review of 2011:
https://www.ncbi.nlm.nih.gov/pubmed/21093382

Response:
We appreciate this concern and in accordance with reviewer's suggestion, the following explanation have now edited in the last part of introduction section now with red colour.

There is limited evidence regarding the efficacy of acupuncture (even according to reviewer's systematic review on 2011) and exercise therapy. Moreover, According to newest a systematic and meta-analysis on 2018 most of studies (10 trails) compare the surgical treatment versus conservative treatment (manual therapy, injection, and splint) and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones. The specific questions which drive the research is which to comparison and determining the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

https://www.ncbi.nlm.nih.gov/pubmed/20490348

https://www.ncbi.nlm.nih.gov/pubmed/27117725

https://www.ncbi.nlm.nih.gov/pubmed/30015499

https://www.ncbi.nlm.nih.gov/pubmed/27749538

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2. There is no Sham acupuncture group which compromises the quality of the study. it would be acceptable if there hasn't been a vast number of studies with sham acupuncture arm for studying acupuncture for CTS.

Response:
We appreciate this concern. As the reviewer said there hasn't been a vast number of studies with sham for CTS even in the reviewers systematic reviews of 2011 suggestion there were only 2 studies with sham.

---

3. there is a dissociation between the results, discussion and abstract. according to the results, there is no significant difference between treatment groups, but the authors have suggested in the discussion that Acupuncture has shown better results in pinching force and the exercise has had a better effect on the gripping force, they have also suggested adding exercise and acupuncture to the splinting based on these findings:

results: Results of ANOVA test showed no statistical difference in gripping force (P=0.398), pinching force (P=0.233), bending (P=0.089) and opening the wrist (P=0.250) before treatment among three groups of brace, brace + exercise therapy and brace+acupuncture,

discussion: But exercises had the most effect on gripping and acupuncture had the most effect on pinching.

Abstract: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in [THE] management of these patients.

Response:
We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It's about the P-value of before treatment among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

I have also some specific comments:

4. The manuscript needs some English improvement: (just a number from Abstract)

The efficacy of acupuncture and exercise therapy in [THE] treatment of carpal tunnel syndrome (CTS) has been

The aim of this study was to comparison [compare] the short-term efficacy of acupuncture

(2 times a day for 6 week [s])

except [THE] flexion of wrist in [THE] control group

Also [,] the efficacy of splint

be adopted in [THE] management of these patients

Response:

Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with yellow highlight.

---

5. The introduction is not focused on the main question of study and it has mentioned other methods of treatment like massage therapy which is unrelated to the scope of this study. it can be rewritten in a standard form of introduction (3-4 paragraphs in the order of known>unknown>the question)

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

---

6. Methods: "the study was completely blinded", the blindness should be described.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

---

7. results: "which these results shows[s is redundent] the complete randomization of samples and the absence of bias in sample selection" this assumption is beyond my understanding, would the authors elaborate on that?

Response:
We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It's about the P-value of before treatment among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

---

8. Discussion: the first sentence of discussion usually describe the main finding of the study, and the discussion should also show how proposed treatment can affect the results (physiologically), it should be more than just referencing previous studies.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

Reviewer 2:

Dear author/s,
The writing of paper needs to be checked by a native. Sentences are too long and difficult to follow.

Introduction *is written so general and has not focused on topic accurately. In your introduction, you are talking about CTS and there is not enough explanation about acupuncture and exercise therapy for it. Your references are also mostly about CTS. Novelty of paper is not clear for me.*

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Method:
If it is a RCT, you have to add your IRCT number clearly and also explain about ethic approval and ethic number.
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color. The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Your method section is not following a standard format and it is not acceptable in current form (follow CONSORT checklist).
Allocation and randomization are not explained accurately.
It is not clear how you recognized 237 patients??

There are some general sentences and need to be explained clearly. For example "At first, all patients were under full clinical examination".
How you defined the locations of acupuncture?

In evaluation section you mentioned that evaluations were done in baseline and after treatment but this time is different for different groups.

ROM evaluation is not explained correctly. The techniques should be explained accurately. Details of goniometer are necessary to be written. It is not clear if it was active or passive?

Response:

Done. We appreciate this concern. We have now rewritten the method section and write all reviewer's suggestion in above with red color.

How you recognized symptoms of atrophy or muscle weakness?
Response:
We appreciate this concern. It recognized by neurologist based on clinical criteria and comparisons with the opposite hand

Figure 2. You are not allowed to use other pictures. You have to use your own pictures. Duration of therapy for different groups seems different. Is it correct?? In my view, it is not acceptable. Your study design does not seem correct

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now replaced the pictures by the own pictures.

There is no detail about blinding. It is not clear if the assessor was blind
Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Table 1: why here you have 15 participants???????

Response:
We appreciate this concern. Pardon us, it was a miswritten and have now changed the word "15" to "20" have now edited with red color.

Your results should be written based on within group and between group comparison and talk about the effect size.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data, and we added the results in the section with red color.

Discussion *in current form is very general and not acceptable.*
The theory behind your findings should be mentioned clearly and then compare with opposite and similar studies.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

---

*Your **conclusion** is a repetition of your results.*

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

Please use from real pictures.
Please replace patient with participant in whole paper.
Please replace sex with gender in whole paper.

Response:
Done. We appreciate this concern and have now changed the word "sex" to "gender" and the word "participant" to "patient" have now edited with red color.

Reviewer 3:

HI
This manuscript needs major revision.
Title: The effectiveness of exercise therapy and acupuncture on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Relevant topic nevertheless, some points should be improved.

Abstract
Question 1. In the abstract of result part please explain; At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of wrist in control group ($p=0.098$);??
Please make your point clear.

Response:
We appreciate this concern. Pardon us, it was a miswritten there is no exception, all parameters had significant improvements. the authors eliminate the sentence.

Question 2. In the abstract of result part please explain; our findings indicate that acupuncture affected the pinch force more than exercise therapy;
There was no between groups analyses, how did you make that judgment?

Question 3. In the abstract of result part please explain; But the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension).

There was no between groups analyses, how did you make that judgment?

Question 4. In the abstract of result part please explain; Also the efficacy of splint alone was less than intervention groups in all parameters;
There was no between groups analyses, how did you make that judgment?

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data and we added the results in the section with red color

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Methods
Question 5.Please define mild, moderate and severe CTS with details

Response:
Done. We appreciate this concern. We have now rewritten that method section with red colour.

Question 6. Please mention the ethical code

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red colour.

Ethics approval

The trial was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Question 7. Please give complete information about the exact anatomic location of two points of acupuncture including PC-6 (Daling) and PC-7 (Neiguan).

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Question 8. Please explain why you selected PC-6 (Daling) and PC-7 (Neiguan) points among other points.

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Discussion
Question 9. please explain ;But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients;
According to your analyses which did not include between groups difference, you can not make that judgment.

Conclusion
Question 10. please explain ; when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also range of motion in wrist was more than using splint alone. Also the effectiveness of exercise therapy in most cases was better than electroacupuncture.
Either omit this information or do a complementary analysis between groups.

Response:
Done. We appreciate this concern. and in accordance with reviewer's suggestion We have now rewritten the section with red colour.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision (1)** 16 Nov 2018

Dear Authors,
According to our journal policy, we can not accept new author(s) after first submission.
Please remove all new names.
Thanks.

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

October 30, 2018

Dr. Vahid Ziaee
Editor-in-chief
Journal of Injury and Violence Research

Re: Manuscript ID: 83927

Dear Dr. Ziaee,
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Your comments and those of the reviewers were highly insightful and enabled us to revise it, thus greatly improved the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers. Revisions in the text are shown using yellow highlight for additions.

We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in “Asian Journal of Sports Medicine”.

We would like also to thank you for allowing us to resubmit a revised copy of the manuscript.

Yours sincerely,

Corresponding author
Shahin Salehi
Sports Medicine Specialist
Department of Sport Medicine
School of Medicine
Shahid Beheshti University of Medical Sciences
Phone: 0098-912-1406684 Email: salehi2955@yahoo.com

We deleted new name from authors

Reviewer 1:

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1.justification of doing the study is my main concern here. I was looking for the justification in its introduction, but it has failed to demonstrate the need for conducting a new study , their reference for controversy about using acupuncture for CTS dates back to 2009, there has been a number of reviews about Effects of acupuncture therapy on the carpal tunnel syndrome. are the authors familiar with this systematic review of 2011:
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2. There is no Sham acupuncture group which compromises the quality of the study. it would be acceptable if there hasn't been a vast number of studies with sham acupuncture arm for studying acupuncture for CTS.

Response:
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Abstract: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in [THE] management of these patients.

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We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It's about the P-value of before treatment among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

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Response:
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5. The introduction is not focused on the main question of study and it has mentioned other methods of treatment like massage therapy which is unrelated to the scope of this study. it can be rewritten in a standard form of introduction (3-4 paragraphs in the order of known>unknown>the question)

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

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6. Methods: "the study was completely blinded", the blindness should be described.

Response:
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7. results: "which these results shows[s is redundent] the complete randomization of samples and the absence of bias in sample selection" this assumption is beyond my understanding, would the authors elaborate on that?

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Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

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The writing of paper needs to be checked by a native. Sentences are too long and difficult to follow.

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Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Method:
If it is a RCT, you have to add your IRCT number clearly and also explain about ethic approval and ethic number.
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color. The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Your method section is not following a standard format and it is not acceptable in current form (follow CONSORT checklist).
Allocation and randomization are not explained accurately.
It is not clear how you recognized 237 patients??

There are some general sentences and need to be explained clearly. For example "At first, all patients were under full clinical examination".
How you defined the locations of acupuncture?

In evaluation section you mentioned that evaluations were done in baseline and after treatment but this time is different for different groups.

ROM evaluation is not explained correctly. The techniques should be explained accurately. Details of goniometer are necessary to be written. It is not clear if it was active or passive?

Response:

Done. We appreciate this concern. We have now rewritten the method section and write all reviewer's suggestion in above with red color.

How you recognized symptoms of atrophy or muscle weakness?
Response:
We appreciate this concern. It recognized by neurologist based on clinical criteria and comparisons with the opposite hand

Figure 2. You are not allowed to use other pictures. You have to use your own pictures. Duration of therapy for different groups seems different. Is it correct?? In my view, it is not acceptable. Your study design does not seem correct

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now replaced the pictures by the own pictures.

There is no detail about blinding. It is not clear if the assessor was blind
Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Table 1: why here you have 15 participants???????

Response:
We appreciate this concern. Pardon us, it was a miswritten and have now changed the word "15" to "20" have now edited with red color.

Your results should be written based on within group and between group comparison and talk about the effect size.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data, and we added the results in the section with red color.

Discussion *in current form is very general and not acceptable.*
The theory behind your findings should be mentioned clearly and then compare with opposite and similar studies.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

---

*Your **conclusion** is a repetition of your results.*

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

Please use from real pictures.
Please replace patient with participant in whole paper.
Please replace sex with gender in whole paper.

Response:
Done. We appreciate this concern and have now changed the word "sex" to "gender" and the word "participant" to "patient" have now edited with red color.

Reviewer 3:

HI
This manuscript needs major revision.
Title: The effectiveness of exercise therapy and acupuncture on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Relevant topic nevertheless, some points should be improved.

Abstract
Question 1. In the abstract of result part please explain; At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of wrist in control group ($p=0.098$);??
Please make your point clear.

Response:
We appreciate this concern. Pardon us, it was a miswritten there is no exception, all parameters had significant improvements. the authors eliminate the sentence.

Question 2. In the abstract of result part please explain; our findings indicate that acupuncture affected the pinch force more than exercise therapy;
There was no between groups analyses, how did you make that judgment?

Question 3. In the abstract of result part please explain; But the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension).

There was no between groups analyses, how did you make that judgment?

Question 4. In the abstract of result part please explain; Also the efficacy of splint alone was less than intervention groups in all parameters;
There was no between groups analyses, how did you make that judgment?

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data and we added the results in the section with red color

---

Methods
Question 5.Please define mild, moderate and severe CTS with details

Response:
Done. We appreciate this concern. We have now rewritten that method section with red colour.

Question 6. Please mention the ethical code

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red colour.

Ethics approval

The trial was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Question 7. Please give complete information about the exact anatomic location of two points of acupuncture including PC-6 (Daling) and PC-7 (Neiguan).

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Question 8. Please explain why you selected PC-6 (Daling) and PC-7 (Neiguan) points among other points.

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Discussion
Question 9. please explain ;But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients;
According to your analyses which did not include between groups difference, you can not make that judgment.

Conclusion
Question 10. please explain ; when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also range of motion in wrist was more than using splint alone. Also the effectiveness of exercise therapy in most cases was better than electroacupuncture.
Either omit this information or do a complementary analysis between groups.

Response:
Done. We appreciate this concern. and in accordance with reviewer's suggestion We have now rewritten the section with red colour.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (2) 26 Nov 2018

Dear AE,
Thanks for the responses, but I couldn't find any red parts which the authors indicated were edited. I would like to see a track changed file.
Thanks.

REFEREE: Reviewer | **Revision** (2) 2 Dec 2018

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Reviewer | **Revision** (2) 3 Dec 2018

Dear AE,
The authors have not highlighted the corrections (and also the changes related to proofreading) on the manuscript.
They should send me the highlighted version.
Regards

REFEREE: Associate Editor | **Revision** (2) 3 Dec 2018

Dear EIC,
Thanks for submitting the manuscript to AsJSM for consideration of publication. The second round of peer review of the manuscript is complete. There are comments and suggestions from three peer reviewers embedded in this letter (see below). Overall, the subject of this paper is interesting and relevant to the readership of this journal. However, there are a variety of issues that will require the authors' attention and revision prior to offering a final editorial decision. At this time, the manuscript is not yet accepted for publication and needs major revision.
Sincerely,

REFEREE: EIC | **Revision** (2) 7 Dec 2018

Dear Author,

The third round of peer review of your manuscript is completed. I now have the reports of the Referees, which suggest that your manuscript needs more correction.

Thanks.

OPEN PEER REVIEW

Revision (3)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

The effectiveness of exercise therapy and dry needling on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Dr. Omid Hessami [1], Dr. Shahin Salehi*[2], Mehrshad PourSaeed Esfehani[2] Dr. Amirhossein Abedi Yakta[2], Dr., Dr. Mohammad Hasabi[2], MSc. Hamid Mahdavi Mohtasham[3], Dr. Amir Rashed [4], Dr. Shahrzad Khosravi[2], Dr. Mahsa Haghighatzadeh[5],

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3- Researcher, Department of Sports Medicine, School of Medicine, Shahid Beheshti University of Medical S5ciences, Tehran, Iran
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**** Reviewer 1:

This is a respectable manuscript, it is written straightforward and concise, but I believe it can be improved with some changes. some general comments first:

1.justification of doing the study is my main concern here. I was looking for the justification in its introduction, but it has failed to demonstrate the need for conducting a new study , their reference for controversy about using acupuncture for CTS dates back to 2009, there has been a number of reviews about Effects of acupuncture therapy on the carpal tunnel syndrome. are the authors familiar with this systematic review of 2011:
https://www.ncbi.nlm.nih.gov/pubmed/21093382

Response:
We appreciate this concern and in accordance with reviewer's suggestion, the following explanation have now edited in the last part of introduction section now with red colour.

There is limited evidence regarding the efficacy of acupuncture (even according to reviewer's systematic review on 2011) and exercise therapy. Moreover, According to newest a systematic and meta-analysis on 2018 most of studies (10 trails) compare the surgical treatment versus conservative treatment (manual therapy, injection, and splint) and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones. The specific questions which drive the

research is which to comparison and determining the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

https://www.ncbi.nlm.nih.gov/pubmed/20490348

https://www.ncbi.nlm.nih.gov/pubmed/27117725

https://www.ncbi.nlm.nih.gov/pubmed/30015499

https://www.ncbi.nlm.nih.gov/pubmed/27749538

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2. There is no Sham acupuncture group which compromises the quality of the study. it would be acceptable if there hasn't been a vast number of studies with sham acupuncture arm for studying acupuncture for CTS.

Response:
We appreciate this concern. As the reviewer said there hasn’t been a vast number of studies with sham for CTS even in the reviewers systematic reviews of 2011 suggestion there were only 2 studies with sham.

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3. there is a dissociation between the results, discussion and abstract. according to the results, there is no significant difference between treatment groups, but the authors have suggested in the discussion that Acupuncture has shown better results in pinching force and the exercise has had a better effect on the gripping force, they have also suggested adding exercise and acupuncture to the splinting based on these findings:

results: Results of ANOVA test showed no statistical difference in gripping force (P=0.398), pinching force (P=0.233), bending (P=0.089) and opening the wrist (P=0.250) before treatment among three groups of brace, brace + exercise therapy and brace+acupuncture,

discussion: But exercises had the most effect on gripping and acupuncture had the most effect on pinching.

Abstract: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in [THE] management of these patients.

Response:
We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It’s about the P-value of before treatment

among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

I have also some specific comments:

4. The manuscript needs some English improvement: (just a number from Abstract)

The efficacy of acupuncture and exercise therapy in [THE] treatment of carpal tunnel syndrome (CTS) has been

The aim of this study was to comparison [compare] the short-term efficacy of acupuncture

(2 times a day for 6 week [s])

except [THE] flexion of wrist in [THE] control group

Also [,] the efficacy of splint

be adopted in [THE] management of these patients

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with yellow highlight.

---

5. The introduction is not focused on the main question of study and it has mentioned other methods of treatment like massage therapy which is unrelated to the scope of this study. it can be rewritten in a standard form of introduction (3-4 paragraphs in the order of known>unknown>the question)

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

---

6. Methods: "the study was completely blinded", the blindness should be described.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

---

7. results: "which these results shows[s is redundent] the complete randomization of samples and the absence of bias in sample selection" this assumption is beyond my understanding, would the authors elaborate on that?

Response:
We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It's about the P-value of before treatment among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

---

8. Discussion: the first sentence of discussion usually describe the main finding of the study, and the discussion should also show how proposed treatment can affect the results (physiologically), it should be more than just referencing previous studies.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

Abstract

Background and aim: Carpal tunnel syndrome (CTS) is the most prevalent form of peripheral neuropathy. The efficacy of acupuncture and exercise therapy in the treatment of carpal tunnel syndrome (CTS) has been investigated in limited studies with controversial results. The aim of this study was to compare the short-term efficacy of acupuncture and exercise therapy in patients with mild to moderate CTS.
Materials and Methods: This is a randomized controlled clinical trial study conducted on 60 patients with mild to moderate CTS referring to Imam Hossein Hospital in Tehran in 2017. The patients were randomly divided in to 3 equal groups (20 patients in each group) In the first group only night splint was used for 6 weeks (control), in the second group splint and tendon and nerve gliding exercises (2 times a day for 6 weeks) were applied, and the third group splint and electroacupuncture was performed for 12 sessions of 40- minute duration (2 sessions/week). The parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment.
Results: In this study, 55 women and 5 men with the average age of 49.23±8.96 were enrolled. At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of the wrist in the control group ($p=0.098$). Our findings indicate that acupuncture affected the pinch force more than exercise therapy. But the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension). Also, the efficacy of splint alone was less than intervention groups in all parameters.

Conclusion: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in the management of these patients.

Keywords: Carpal Tunnel syndrome, Splint, Exercise, Acupuncture.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). The entrapment of the median nerve within the carpal tunnel which is limited by carpal bones and the transverse carpal ligament is the main cause of CTS (3). Physiologic evidence shows the increased pressure in the carpal tunnel and therefore decrease of middle nerve function in that surface (2, 4). CTS found in 3.8% of the general population and can occur in all ages (4), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (4, 5). CTS risk factors include job conditions such as repeating movements of the hand when using the computer, medical conditions, and other factors (1). Repeated striking due to intense flexion and extension of the wrist such as working with machines creating vibration or long flexion is also known as factors worsening carpal tunnel syndrome (6, 7). Considering the above risk factors and fast use of the computer in the society, we face to increasing prevalence of CTS and this disease reduces the quality of an individual's life. Moreover, the late treatment of CTS sometimes causes permanent damage to the median nerve (some or all nerve fibers are damaged) and therefore permanent sensory or motor damage occurs in affected patients (8).

Different treatments methods for CTS which are divided into two group: conservative treatment and surgery (9). Conservative treatment is usually selected for CTS patients with mild to moderate symptoms (10), which include: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint. (9). Although the effectiveness of using splints and steroids as primary treatments to improve the patient’s symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (11). Also,

each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (12, 13). In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (4, 14, 15). Also although National Institute of Health (NIH) has approved the use of acupuncture for management of mild to moderate CTS there is controversy about its effectiveness (16).

The studies over a couple decade have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (17-20). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that "acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression." (21) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (17, 22). Vincent et al (2016)'s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (23). On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization. They concluded that adding nerve mobilization to standard care does not cause improvement in outcome of CTS patients. They also determined several reasons for the lack of acceptable result in nerve gliding group including more than 50% rate of exclusion of patients which is common in hospitals and weak conformity of symptom severity in both groups (24). So it is recommended that more controlled studies on using mobilization techniques in CTS treatment be done.

Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improve wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (23). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (25).

Akalin et al study on 28 CTS patients indicate that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (26). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (27).

Carpal tunnel syndrome is the most common neuropathy of upper limbs. In many guidelines, including National Institute for Health and Care Excellence (NIHCE) (28), American Academy of Orthopedic Surgeons (AMOS) (29) and American College of Occupational and Environmental Medicine (ACOEM), wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (30). Also among different management options for this disease using acupuncture and exercise therapy is increasing. But there is no specific recommendation about the use of acupuncture and effectiveness of exercise therapy (23, 31, 32). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

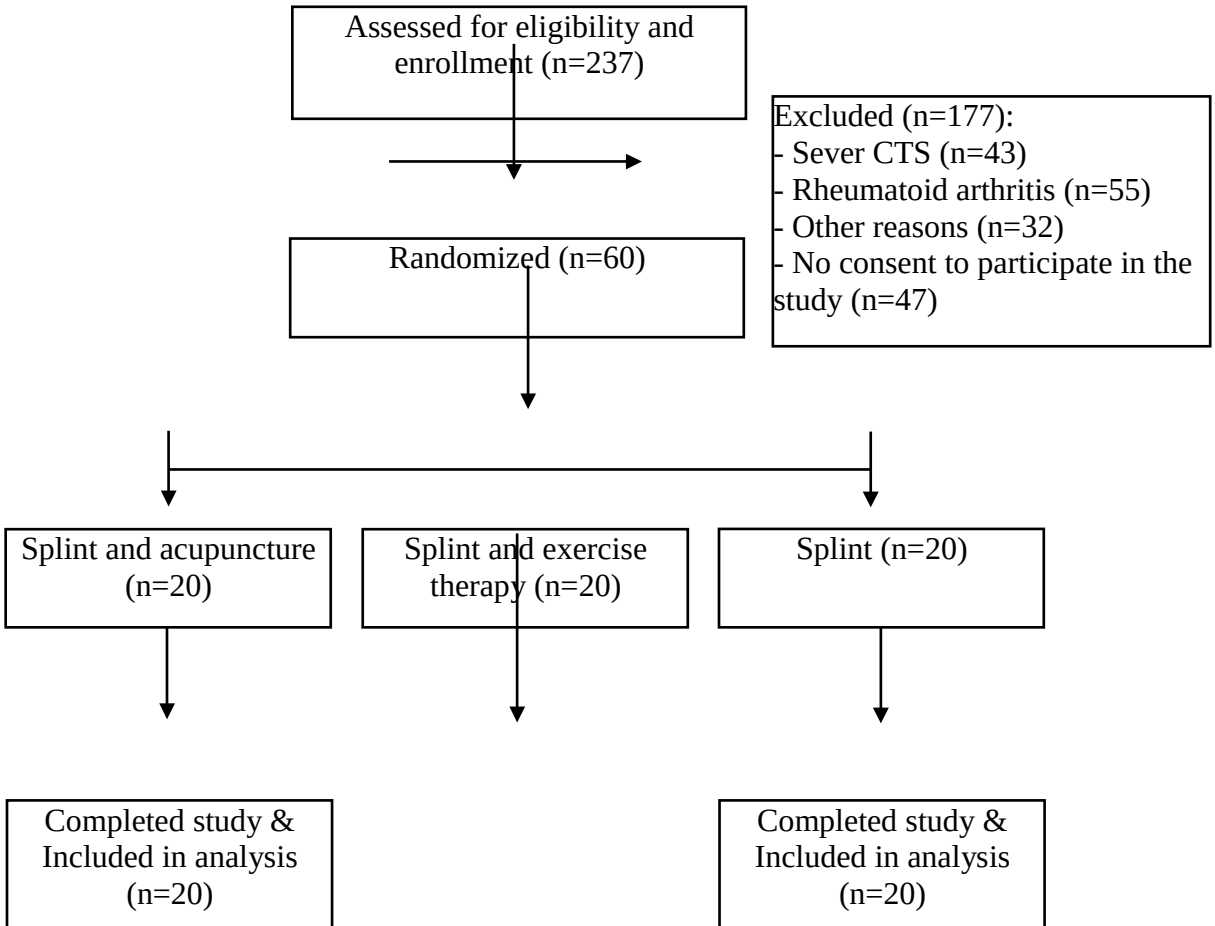
Methods

The present study is a randomized, controlled clinical trial which is performed on 60 CTS patients referring to the Sports Medicine Clinic of Imam Hossein Hospital in Tehran in 2017. The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV. Patients enrolled in the study after receiving explanations by researchers regarding the purpose of the study and by obtaining informed consent.

The inclusion criteria for the study including: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of atrophy or muscle weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment regarding CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, non-performing of the exercises requested, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as bleeding tendency, local infection, or a history of needling shock.

At first, all patients were under full clinical examination. The demographic and history profiles were also completed for all patients. This form includes demographic characteristics (age, sex, place of living, marital status), medical history and clinical information including smoking and alcohol consumption, underlying diseases, weight, height, drugs used and characteristics of CTS including pain severity, affected hand, and duration of CTS. The diagram of the study process is presented in Figure 1.



Completed study & Included in analysis (n=20)

Figure 1. The study flowchart.

Intervention

Patients were randomly divided into three equal groups (20 patients in each group) with an adjusted age of 10 years. In the first group, the patients received only night splint for a period of 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes electroacupuncture was performed (2 times a week) in two points of PC-6 (Daling) and PC-7 (Neiguan) using the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz up to patient's pain threshold (Figure 3). The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

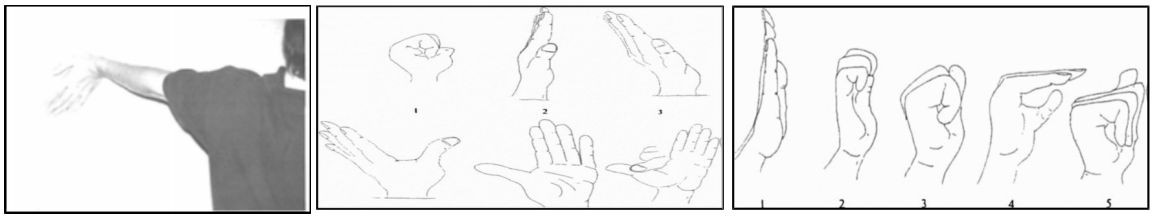


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.

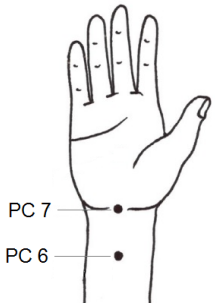


Figure 3. Acupuncture points.

Patient evaluation

In order to evaluate the response to treatment the parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment and compared between the three groups.

The maximum grip force (in kg) was measured using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was held from the top and the bottom in order to prevent the measurement to be affected by the weight of the device. All the measurements were evaluated by the same device both before and after the treatment (38). To evaluate the range of motion (ROM) the wrist flexion and extension were measured by using goniometer.

None of the participants dropped out in this study. Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In the other word, neither the patient nor the therapist and study investigator was aware of which groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent intra and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age, sex, height, weight, job, the presence of systemic disease, involved hand and disease severity was seen in three treatment groups (P>0.05).

The current study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist was significantly improved in CTS patients at the end of 6 weeks in all three groups (P<0.05). Although using brace alone (control group) did not have any significant effect on the binding of the wrist (P=0.098) (table 2).

Table 1- Participant characteristics at baseline*

Variable	Brace+ acupuncture (n=20)	Brace+ Exercise therapy (n=20)	Control (n=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Sex	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)

**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value
Grip force	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	<0.004
	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025

Pinch force	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	<0.001
	Brace+ Exercise therapy	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001
Flexion	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001
	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002
Extension	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.001
	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015

SD = standard deviation.

Discussion

The aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

In the current study, no significant statistical difference existed between age, sex, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups which shows that these factors do not affect our study results. Also, there was no significant difference between variables of pinch and grip force, flexion and extension of the wrist in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment was increased significantly. But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it can recover normal griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (23, 25, 39-41). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for

treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power compared to the beginning of the study, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (42).

Yao et al reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (42). These results are not consistent with the finding of the current study. Although all three groups showed significant improvement in pinching power in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be related to the difference in intervention methods, a number of acupuncture sessions and primary characteristics of patients. Fr example, in Goetez et al study, the pinch strength would decrease. Due to the effect of lidocaine-like on the flexor pollicis longus which is located under the PC-7 acupoint that is caused by electroacupuncture (43, 44).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al results (27). Moreover, In Akalin, *et al*. study the effectiveness of nerve and tendon gliding exercises along with splinting compared with splinting alone was evaluated in the treatment of CTS. Results showed an improvement in pinching power in both groups after treatment but the improvement in mobilization group was higher than splint alone. These results consistent with the results of the current study (26). In another study by Madenci, *et al*. (2012) was also reported than tendon and nerve gliding exercises with night splint significantly improved the gripping power in CTS patients (38). Results of Penas, *et al*. study (2017) in Spain also show that exercise therapy is effective in improving pinching and gripping power in CTS patients (45).

The results of the current study showed significant improvement in range of motion (binding and opening) of the wrist in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of binding of the hand. On the other hand, exercise therapy had the most effect on increasing the range of motion (binding and opening) of the wrist. To confirm these results, Chung, *et al.* (2016) also showed that functional performance of wrist of mild to moderate CTS patients in the acupuncture+splint group was better than the control group (splinting alone) (23). In another study, Tal-Akabi and Rushton (2000)

studied and compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups was better than the control group but the difference was not significant so carpal bone mobilization for 3 weeks improves CTS patients function but the results were not statistically significant because of the small sample size (46).

CTS give arises to lose the physiologic mobility of the median nerve. According to Wright et al and Szabo et al study, during flexion to an extension, the median nerve glides 19.6 mm and during fingers flexion, it would be 9 mm. Also, the flexor digitorum superficialis tendons glide 30 mm during fingers flexion in the CT (47, 48). Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (49).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a larger sample and long-term monitoring.

Conclusion

The results of this study showed that all three treatment methods could provide an overall functional improvement in patients with CTS but when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also a range of motion in the wrist was more than using splint alone. Also, the effectiveness of exercise therapy in most cases was better than electroacupuncture. Finally, these treatment interventions are effective, inexpensive, safe and accessible treatment options and can be applied to the management of patients with mild to

moderate CTS.

Acknowledgment

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**** Reviewer 2:

Dear author/s,
The writing of paper needs to be checked by a native. Sentences are too long and difficult to follow.

Introduction *is written so general and has not focused on topic accurately. In your introduction, you are talking about CTS and there is not enough explanation about acupuncture and exercise therapy for it. Your references are also mostly about CTS. Novelty of paper is not clear for me.*

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Method:
If it is a RCT, you have to add your IRCT number clearly and also explain about ethic approval and ethic number.
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color. The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Your method section is not following a standard format and it is not acceptable in current form (follow CONSORT checklist).
Allocation and randomization are not explained accurately.
It is not clear how you recognized 237 patients??

There are some general sentences and need to be explained clearly. For example "At first, all patients were under full clinical examination".
How you defined the locations of acupuncture?

In evaluation section you mentioned that evaluations were done in baseline and after treatment but this time is different for different groups.

ROM evaluation is not explained correctly. The techniques should be explained accurately. Details of goniometer are necessary to be written. It is not clear if it was active or passive?

Response:
Done. We appreciate this concern. We have now rewritten the method section and write all reviewer's suggestion in above with red color.

How you recognized symptoms of atrophy or muscle weakness?
Response:
We appreciate this concern. It recognized by neurologist based on clinical criteria and comparisons with the opposite hand

Figure 2. You are not allowed to use other pictures. You have to use your own pictures. Duration of therapy for different groups seems different. Is it correct?? In my view, it is not acceptable. Your study design does not seem correct

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now replaced the pictures by the own pictures.

There is no detail about blinding. It is not clear if the assessor was blind
Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Table 1: why here you have 15 participants???????

Response:
We appreciate this concern. Pardon us, it was a miswritten and have now changed the word "15" to "20" have now edited with red color.

Your results should be written based on within group and between group comparison and talk about the effect size.

Response:

Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data, and we added the results in the section with red color.

Discussion *in current form is very general and not acceptable.*
The theory behind your findings should be mentioned clearly and then compare with opposite and similar studies.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

Your ***conclusion*** *is a repetition of your results.*

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

Please use from real pictures.
Please replace patient with participant in whole paper.
Please replace sex with gender in whole paper.

Response:
Done. We appreciate this concern and have now changed the word "sex" to "gender" and the word "participant" to "patient" have now edited with red color.

Abstract

Background and aim: Carpal tunnel syndrome (CTS) is the most prevalent form of peripheral neuropathy. The efficacy of acupuncture and exercise therapy in the treatment of carpal tunnel syndrome (CTS) has been investigated in limited studies with controversial results. The aim of this study was to compare the short-term efficacy of acupuncture and exercise therapy in patients with mild to moderate CTS.
Materials and Methods: This is a randomized controlled clinical trial study conducted on 60 patients with mild to moderate CTS referring to Imam Hossein Hospital in Tehran in 2017. The patients were randomly divided in to 3 equal groups (20 patients in each group) In the first group only night splint was used for 6 weeks (control), in the second group splint and tendon and nerve gliding exercises (2 times a day for 6 weeks) were applied, and the third group splint and

electroacupuncture was performed for 12 sessions of 40- minute duration (2 sessions/week). The parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment.
Results: In this study, 55 women and 5 men with the average age of 49.23±8.96 were enrolled. At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of the wrist in the control group ($p=0.098$). Our findings indicate that exercises therapy had more effect on ROM of flexion than acupuncture and acupuncture had more effect on pinching than exercise therapy but the effect sizes were weak. Also, the efficacy of splint alone was less than intervention groups in all parameters.
Conclusion: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in the management of these patients.

Keywords: Carpal Tunnel syndrome, Splint, Exercise, Acupuncture.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). The entrapment of the median nerve within the carpal tunnel which is limited by carpal bones and the transverse carpal ligament is the main cause of CTS (3). Physiologic evidence shows the increased pressure in the carpal tunnel and therefore decrease of middle nerve function in that surface (2, 4). CTS found in 3.8% of the general population and can occur in all ages (4), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (4, 5). CTS risk factors include job conditions such as repeating movements of the hand when using the computer, medical conditions, and other factors (1). Repeated striking due to intense flexion and extension of the wrist such as working with machines creating vibration or long flexion is also known as factors worsening carpal tunnel syndrome (6, 7). Considering the above risk factors and fast use of the computer in the society, we face to increasing prevalence of CTS and this disease reduces the quality of an individual's life. Moreover, the late treatment of CTS sometimes causes permanent damage to the median nerve (some or all nerve fibers are damaged) and therefore permanent sensory or motor damage occurs in affected patients (8).

Different treatments methods for CTS which are divided into two group: conservative treatment and surgery (9). Conservative treatment is usually selected for CTS patients with mild to moderate symptoms (10), which include: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint. (9). Although the effectiveness of using splints and steroids as primary treatments to improve the patient's symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (11). Also, each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (12, 13). In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (4, 14, 15). Also although National Institute of Health (NIH) has approved the use of acupuncture for management of mild to moderate CTS there is controversy about its effectiveness (16).

The studies over a couple decade have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (17-20). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that "acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression." (21) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (17, 22). Vincent et al (2016)'s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (23). On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization. They concluded that adding nerve mobilization to standard care does not cause improvement in outcome of CTS patients. They also determined several reasons for the lack of acceptable result in nerve gliding group including more than 50% rate of exclusion of patients which is common in hospitals and weak conformity of symptom severity in both groups

(24). So it is recommended that more controlled studies on using mobilization techniques in CTS treatment be done.

Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improve wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (23). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (25).

Akalin et al study on 28 CTS patients indicate that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (26). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (27).

Carpal tunnel syndrome is the most common neuropathy of upper limbs. In many guidelines, including National Institute for Health and Care Excellence (NIHCE) (28), American Academy of Orthopedic Surgeons (AMOS) (29) and American College of Occupational and Environmental Medicine (ACOEM), wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (30). Also among different management options for this disease using acupuncture and exercise therapy is increasing. But there is no specific recommendation about the use of acupuncture and effectiveness of exercise therapy (23, 31, 32). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

Methods

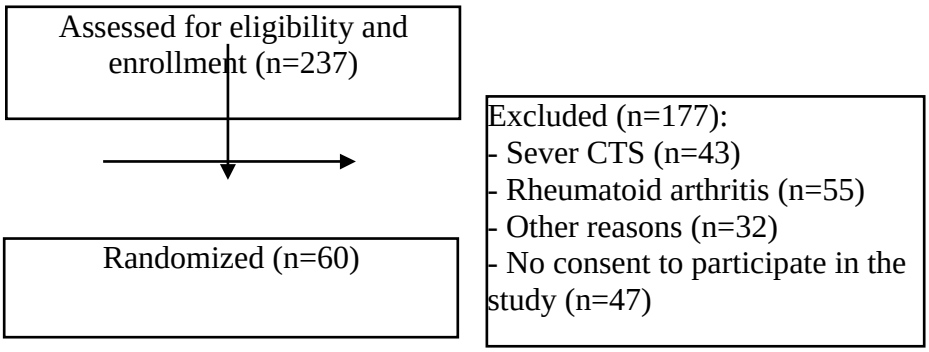
The present study is a randomized, controlled clinical trial which is performed on 60 CTS patients referring to the Sports Medicine Clinic of Imam Hossein Hospital in Tehran in 2017. The whole patients with CTS at the Hospital in 2017 were assessed in the study was 237 and after screened for eligibility at the Clinic 177 patients excluded and 60 remains to included (Figure 1).

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV. Patients enrolled in the study after receiving explanations by researchers regarding the purpose of the study and by obtaining informed consent.

The inclusion criteria for the study including: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of atrophy or muscle weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment regarding CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, non-performing of the exercises requested, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as bleeding tendency, local infection, or a history of needling shock.

At first, all patients were under full clinical examination which explained in following at the Patient evaluation subsection. The demographic and history profiles were also completed for all patients. This form includes demographic characteristics (age, gender, place of living, marital status), medical history and clinical information including smoking and alcohol consumption, underlying diseases, weight, height, drugs used and characteristics of CTS including pain severity, affected hand, and duration of CTS.



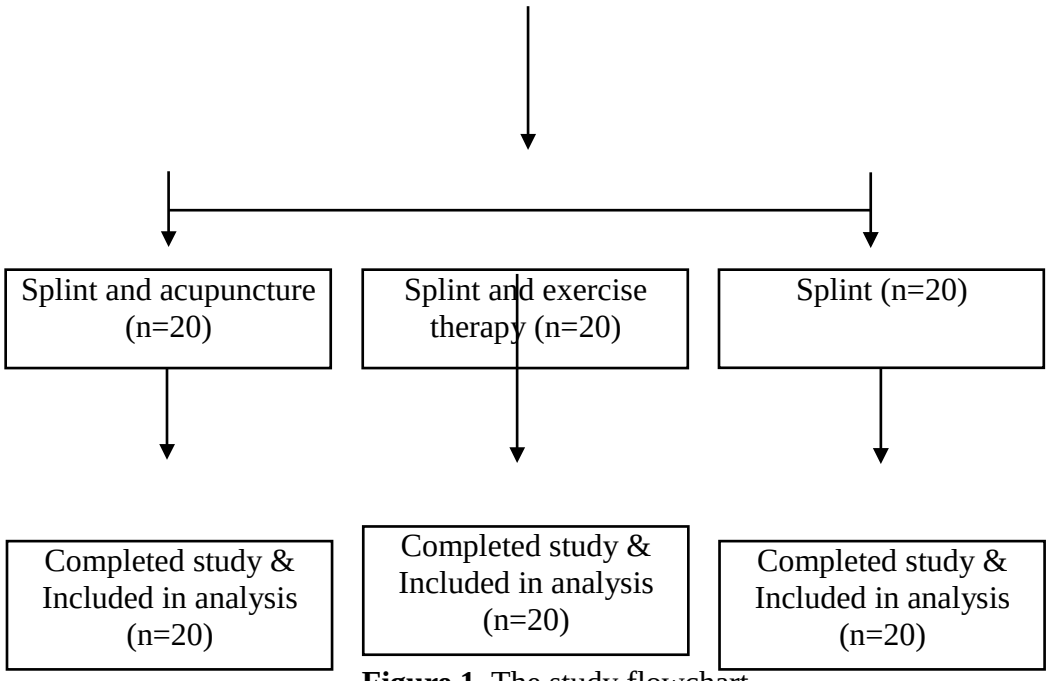


Figure 1. The study flowchart.

Intervention

Block randomization which used by Random Allocation Software random was applied to allocate patients to groups after eligibility confirmation (38, 39). Patients were randomly divided into three equal groups (20 patients in each group) with an adjusted age of 10 years. In the first group, the patients received only night splint for a period of 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes electroacupuncture was performed (2 times a week) in two points of PC-7 (Daling) and PC-6 (Neiguan) using the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz up to patient's pain threshold (Figure 3). The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

To find acupoints the examiner asks patients to press the thumb and little finger together for the better presentation of the tendon of the flexor carpi radialis and tendon of the palmaris longous. After appearing of the tendons, the needle located at between the tendons on the flexor aspect of the forearm which are between the two tendons. The distance between PC-7 and PC-6 is two thumbs wide. PC-6 (Neiguan) is located at 2 cun above the transverse crease of the wrist PC-7, between palmaris longus and flexor carpi radialis tendons, on the line connecting

PC-3 and PC-7. PC-7 (Daling) is located at in the middle of the transverse crease of the wrist between palmaris longus and flexor carpi radialis tendons (Figure 3) (40). These acupoints chose because of their efficiency which is reported in previous studies (41).

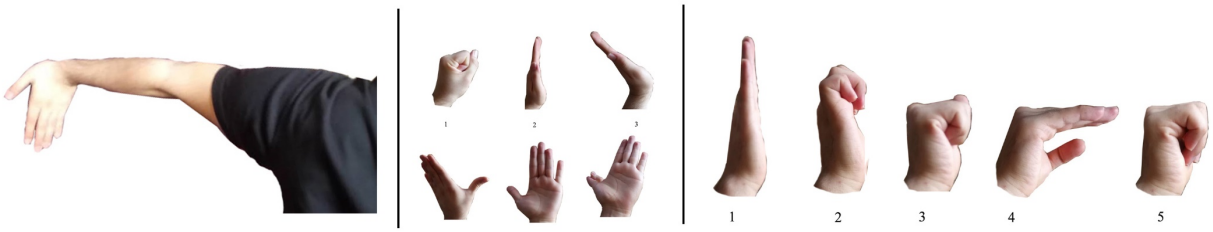


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.



Figure 3. Acupuncture points.

Patient evaluation

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV.

In order to evaluate the response to treatment the parameters of pinch force, grip force, ROM (flexion and extension) quality of life (symptoms and functional status), and pain intensity were evaluated at baseline and 6 weeks later after treatment and compared between the three groups.

We used Carpal Tunnel Questionnaires to evaluate the response to treatment quality of life (symptoms and functional status) which is recommended by the

American Academy of Orthopedic Surgeons (42, 43) and visual analogue scale (VAS) for pain intensity of patients. The first one was The Boston Carpet Tunnel Questionnaire (BCTQ) which used to evaluate the patients' performance and the severity of symptoms. It is consist of 11 questions about the severity of the symptoms (BCTQ SYMPT) and 8 question about functional status (BCTQ FUNCT). The items of each scale were scored from 1 (mildest) to 5 (most severe). The reliability and sensitivity of the Persian version which used in the current study were confirmed in a previous study (16). Pain intensity measured using the visual analogue scale (VAS). The patient evaluated their pain intensity from zero (complete analgesia) to 10 (the most experienced patient's pain).

The Physical examination which used in the current study was made based on at least one of the following clinical criteria were included: Tinel sign test, Phalen maneuver test, numbness or tingling in ≥ 2 of 4 radial fingers, median nerve compression and wrist flexion tests (44, 45). Patients that diagnosed with CTS was confirmed by the presence of at least one of EMG/NCV criteria which were included: DML ≥ 4.2 ms, DSL ≥ 3.6 ms, and W-P SNCV < 40 ms (46).

The maximum grip force (in kg) was measured using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was held from the top and the bottom in order to prevent the measurement to be affected by the weight of the device. All the measurements were evaluated by the same device both before and after the treatment (47). To evaluate the range of motion (ROM) the active wrist flexion and extension were measured by using goniometer (Plastic goniometer MSD). All the measurements were performed in a sitting position, which the patients sitting next to a supporting surface with shoulder abducted to 90º, the elbow flexed to 90º, and the palm of the hand facing the ground. The forearm was midway between supination and pronation. The examiner was a caution to avoid radial or ulnar deviation of the wrist and flexion of the fingers. The examiner put the center fulcrum of goniometer on the lateral aspect of the wrist over the triquetrum and aligned proximal and distal arm with the lateral midline of the ulna and fifth metacarpal respectively.

Then the examiner asked the patients to flex the wrist. The examiner used one hand to align the distal arm of the goniometer with the 5th metacarpal at the end of the flexion while the patients maintaining the wrist in that position and the ROM degrees was recorded. To measure active wrist extension the examiner performed all process like active wrist flexion except in extension movements (48). None of the patients dropped out in this study.

Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In the other word, neither the patient nor the therapist and study investigator was aware of which groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent intra and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Ethics approval

The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152) and was registered in IRCT under the code IRCT20180212038693N1.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age, gender, height, weight, job, the presence of systemic disease, involved hand and disease severity was seen in three treatment groups ($P>0.05$).

The current study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist was significantly improved in CTS patients at the end of 6 weeks in all three groups ($P<0.05$). Although using brace alone (control group)

did not have any significant effect on the binding of the wrist (P=0.098) (table 2).

The between groups analysis indicate that acupuncture affected the pinch force more than exercise therapy and it was statistically significant F(df=2)=0.035, P=0.0001 but weak (P Eta Squared=0.001). Also, the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension) but just ROM of flexion was statistically significant F(df=2)=0.000, P=0.0001 but weak (P Eta Squared=0.012).

Table 1- Patient characteristics at baseline*

Variable	Brace+ acupuncture (n=20)	Brace+ Exercise therapy (n=20)	Control (n=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Gender	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)

**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value	Effect Size
Grip force	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	<0.004	0.103
	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001	0.359
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025	0.249
Pinch force	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	<0.001	0.201
	Brace+ Exercise	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001	0.447

	therapy					
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001	0.573
Flexion	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098	0.044
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001	0.490
	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002	0.209
Extension	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.001	0.114
	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001	0.702
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015	0.194

SD = standard deviation.

Discussion

The aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

In the current study, no significant statistical difference existed between age, gender, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups which shows that these factors do not affect our study results. Also, there was no significant difference between variables of pinch and grip force, flexion and extension of the wrist in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment was increased significantly. But exercises had an effect on ROM of flexion and acupuncture had an effect on pinching but the effect sizes were weak. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it can recover normal griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (23, 25, 49-51). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for

treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power compared to the beginning of the study, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52).

Yao et al reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52). These results are not consistent with the finding of the current study. Although all three groups showed significant improvement in pinching power in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be related to the difference in intervention methods, a number of acupuncture sessions and primary characteristics of patients. Fr example, in Goetez et al study, the pinch strength would decrease. Due to the effect of lidocaine-like on the flexor pollicis longus which is located under the PC-7 acupoint that is caused by electroacupuncture (41, 53).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al results (27). Moreover, In Alkalin, *et al*. study the effectiveness of nerve and tendon gliding exercises along with splinting compared with splinting alone was evaluated in the treatment of CTS. Results showed an improvement in pinching power in both groups after treatment but the improvement in mobilization group was higher than splint alone. These results consistent with the results of the current study (26). In another study by Madenci, *et al*. (2012) was also reported than tendon and nerve gliding exercises with night splint significantly improved the gripping power in CTS patients (47). Results of Penas, *et al*. study (2017) in Spain also show that exercise therapy is effective in improving pinching and gripping power in CTS patients (54).

The results of the current study showed significant improvement in range of motion (binding and opening) of the wrist in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of binding of the hand. On the other hand, exercise therapy had the most effect on increasing the range of motion (binding and opening) of the wrist. To confirm these results, Chung, *et al*. (2016) also showed that functional performance of wrist of mild to moderate CTS patients in the acupuncture+splint group was better than the control group (splinting alone) (23). In another study, Tal-Akabi and Rushton (2000)

studied and compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups was better than the control group but the difference was not significant so carpal bone mobilization for 3 weeks improves CTS patients function but the results were not statistically significant because of the small sample size (55).

CTS give arises to lose the physiologic mobility of the median nerve. According to Wright et al and Szabo et al study, during flexion to an extension, the median nerve glides 19.6 mm and during fingers flexion, it would be 9 mm. Also, the flexor digitorum superficialis tendons glide 30 mm during fingers flexion in the CT (56, 57). Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (58).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved.

Conclusion

The results of this study indicate that conservative groups were better than the control group, but the difference was statistically significant and weak just in an efficacy of exercise therapy on ROM of flexion and an efficacy of acupuncture on pinch force. Probably because of the limited case data. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a larger sample and long-term monitoring.

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Competing interests: None declared

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**** Reviewer 3:

HI
This manuscript needs major revision.
Title: The effectiveness of exercise therapy and acupuncture on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Relevant topic nevertheless, some points should be improved.

Abstract
Question 1. In the abstract of result part please explain; At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of wrist in control group ($p=0.098$);??
Please make your point clear.

Response:
We appreciate this concern. Pardon us, it was a miswritten there is no exception, all parameters had significant improvements. the authors eliminate the sentence.

Question 2. In the abstract of result part please explain; our findings indicate that acupuncture affected the pinch force more than exercise therapy;
There was no between groups analyses, how did you make that judgment?

Question 3. In the abstract of result part please explain; But the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension).

There was no between groups analyses, how did you make that judgment?

Question 4. In the abstract of result part please explain; Also the efficacy of splint alone was less than intervention groups in all parameters;
There was no between groups analyses, how did you make that judgment?

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data and we added the results in the section with red color

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Methods
Question 5.Please define mild, moderate and severe CTS with details

Response:
Done. We appreciate this concern. We have now rewritten that method section with red colour.

Question 6. Please mention the ethical code

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red colour.

Ethics approval
The trial was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Question 7. Please give complete information about the exact anatomic location of two points of acupuncture including PC-6 (Daling) and PC-7 (Neiguan).

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Question 8. Please explain why you selected PC-6 (Daling) and PC-7 (Neiguan) points among other points.

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Discussion
Question 9. please explain ;But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients;
According to your analyses which did not include between groups difference, you can not make that judgment.

Conclusion
Question 10. please explain ; when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also range of motion in wrist was more than using splint alone. Also the effectiveness of exercise therapy in most cases was better than electroacupuncture.
Either omit this information or do a complementary analysis between groups.

Response:
Done. We appreciate this concern. and in accordance with reviewer’s suggestion We have now rewritten the section with red colour.

Abstract

Background and aim: Carpal tunnel syndrome (CTS) is the most prevalent form of peripheral neuropathy. The efficacy of acupuncture and exercise therapy in the treatment of carpal tunnel syndrome (CTS) has been investigated in limited studies with controversial results. The aim of this study was to compare the short-term efficacy of acupuncture and exercise therapy in patients with mild to moderate CTS.

Materials and Methods: This is a randomized controlled clinical trial study conducted on 60 patients with mild to moderate CTS referring to Imam Hossein Hospital in Tehran in 2017. The patients were randomly divided in to 3 equal groups (20 patients in each group) In the first group only night splint was used for 6 weeks (control), in the second group splint and tendon and nerve gliding exercises (2 times a day for 6 weeks) were applied, and the third group splint and electroacupuncture was performed for 12 sessions of 40- minute duration (2 sessions/week). The parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment.

Results: In this study, 55 women and 5 men with the average age of 49.23±8.96 were enrolled. At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of the wrist in the control group ($p=0.098$). Our findings indicate that exercises therapy had more effect on ROM of flexion than acupuncture and acupuncture had more effect on pinching than exercise therapy but the effect sizes were weak. Also, the efficacy of splint alone was less than intervention groups in all parameters.

Conclusion: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in the management of these patients.

Keywords: Carpal Tunnel syndrome, Splint, Exercise, Acupuncture.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). The entrapment of the median nerve within the carpal tunnel which is limited by carpal bones and the transverse carpal ligament is the main cause of CTS (3). Physiologic evidence shows the increased pressure in the carpal tunnel and therefore decrease of middle nerve function in that surface (2, 4). CTS found in 3.8% of the general population and can occur in all ages (4), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (4, 5). CTS risk factors include job conditions such

as repeating movements of the hand when using the computer, medical conditions, and other factors (1). Repeated striking due to intense flexion and extension of the wrist such as working with machines creating vibration or long flexion is also known as factors worsening carpal tunnel syndrome (6, 7). Considering the above risk factors and fast use of the computer in the society, we face to increasing prevalence of CTS and this disease reduces the quality of an individual's life. Moreover, the late treatment of CTS sometimes causes permanent damage to the median nerve (some or all nerve fibers are damaged) and therefore permanent sensory or motor damage occurs in affected patients (8).

Different treatments methods for CTS which are divided into two group: conservative treatment and surgery (9). Conservative treatment is usually selected for CTS patients with mild to moderate symptoms (10), which include: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint. (9). Although the effectiveness of using splints and steroids as primary treatments to improve the patient’s symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (11). Also, each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (12, 13). In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (4, 14, 15). Also although National Institute of Health (NIH) has approved the use of acupuncture for management of mild to moderate CTS there is controversy about its effectiveness (16).

The studies over a couple decade have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (17-20). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that “acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression.” (21) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (17, 22). Vincent et al (2016)’s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (23). On the other hand, Heebner and Roddney

(2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization. They concluded that adding nerve mobilization to standard care does not cause improvement in outcome of CTS patients. They also determined several reasons for the lack of acceptable result in nerve gliding group including more than 50% rate of exclusion of patients which is common in hospitals and weak conformity of symptom severity in both groups (24). So it is recommended that more controlled studies on using mobilization techniques in CTS treatment be done.

Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improve wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (23). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (25).

Akalin et al study on 28 CTS patients indicate that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (26). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (27).

Carpal tunnel syndrome is the most common neuropathy of upper limbs. In many guidelines, including National Institute for Health and Care Excellence (NIHCE) (28), American Academy of Orthopedic Surgeons (AMOS) (29) and American College of Occupational and Environmental Medicine (ACOEM), wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (30). Also among different management options for this disease using acupuncture and exercise therapy is increasing. But there is no specific recommendation about the use of acupuncture and effectiveness of exercise therapy (23, 31, 32). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture

and exercise therapy.

Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

Methods

The present study is a randomized, controlled clinical trial which is performed on 60 CTS patients referring to the Sports Medicine Clinic of Imam Hossein Hospital in Tehran in 2017. The whole patients with CTS at the Hospital in 2017 were assessed in the study was 237 and after screened for eligibility at the Clinic 177 patients excluded and 60 remains to included (Figure 1).

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV. Patients enrolled in the study after receiving explanations by researchers regarding the purpose of the study and by obtaining informed consent.

The inclusion criteria for the study including: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of atrophy or muscle weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment regarding CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, non-performing of the exercises requested, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as bleeding tendency, local infection, or a history of needling shock.

At first, all patients were under full clinical examination which explained in following at the Patient evaluation subsection. The demographic and history profiles were also completed for all patients. This form includes demographic characteristics (age, gender, place of living, marital status), medical history and clinical information including smoking and alcohol consumption, underlying

diseases, weight, height, drugs used and characteristics of CTS including pain severity, affected hand, and duration of CTS.

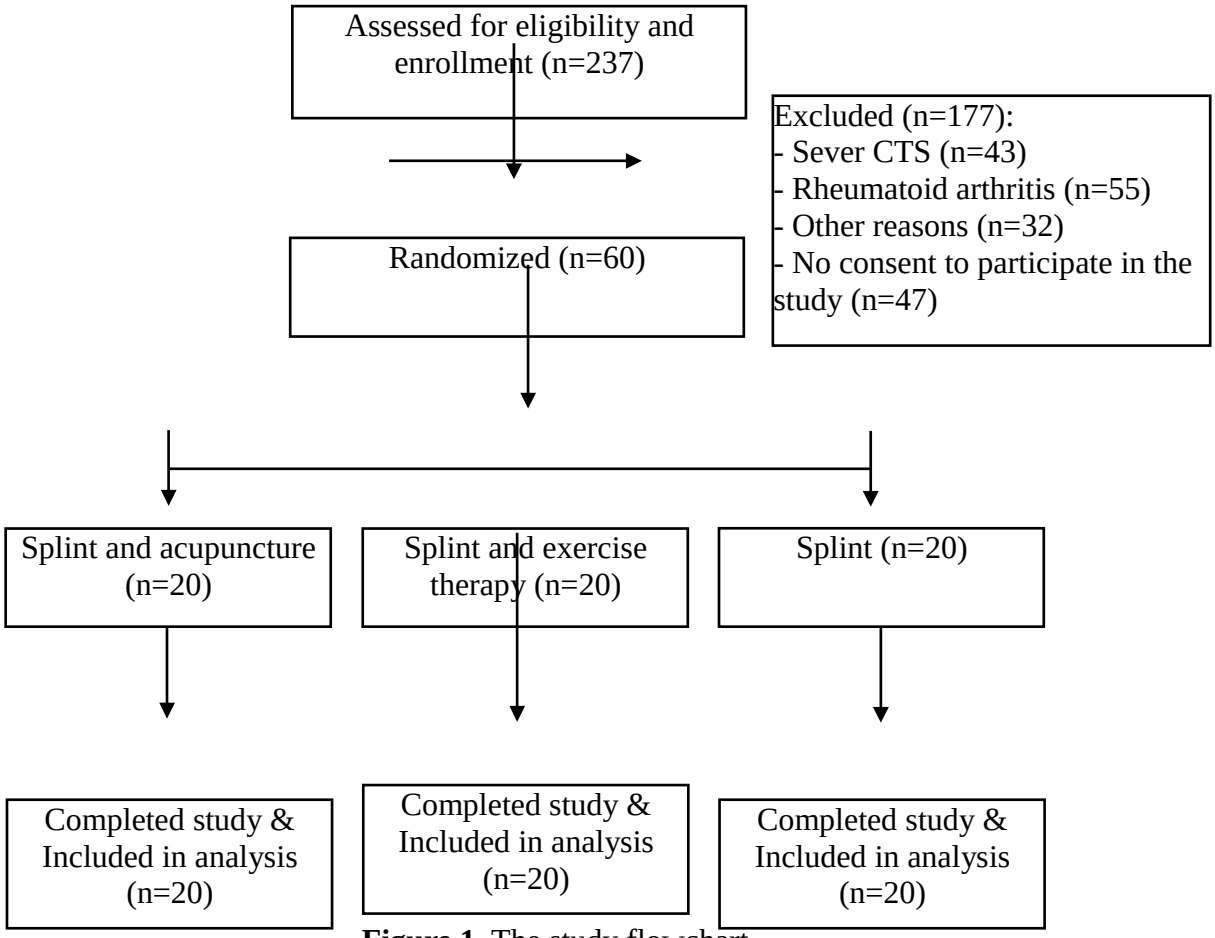


Figure 1. The study flowchart.

Intervention

Block randomization which used by Random Allocation Software random was applied to allocate patients to groups after eligibility confirmation (38, 39). Patients were randomly divided into three equal groups (20 patients in each group) with an adjusted age of 10 years. In the first group, the patients received only night splint for a period of 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes electroacupuncture was performed (2 times a week) in two points of PC-7 (Daling) and PC-6 (Neiguan) using the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz up to patient's pain

threshold (Figure 3). The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

To find acupoints the examiner asks patients to press the thumb and little finger together for the better presentation of the tendon of the flexor carpi radialis and tendon of the palmaris longous. After appearing of the tendons, the needle located at between the tendons on the flexor aspect of the forearm which are between the two tendons. The distance between PC-7 and PC-6 is two thumbs wide. PC-6 (Neiguan) is located at 2 cun above the transverse crease of the wrist PC-7, between palmaris longus and flexor carpi radialis tendons, on the line connecting PC-3 and PC-7. PC-7 (Daling) is located at in the middle of the transverse crease of the wrist between palmaris longus and flexor carpi radialis tendons (Figure 3) (40). These acupoints chose because of their efficiency which is reported in previous studies (41).

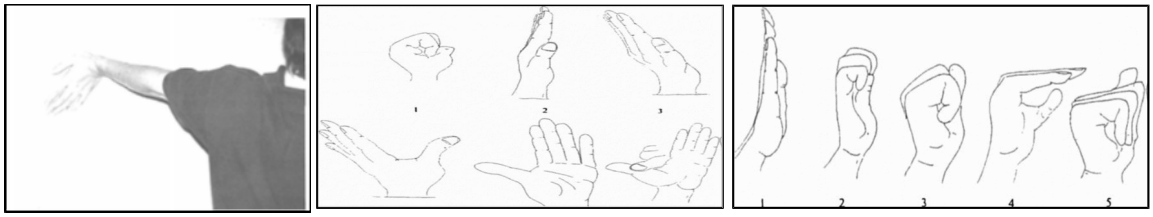


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.

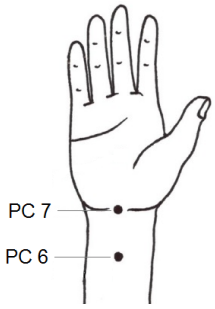


Figure 3. Acupuncture points.

Patient evaluation

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV.

In order to evaluate the response to treatment the parameters of pinch force, grip

force, ROM (flexion and extension) quality of life (symptoms and functional status), and pain intensity were evaluated at baseline and 6 weeks later after treatment and compared between the three groups.

We used Carpal Tunnel Questionnaires to evaluate the response to treatment quality of life (symptoms and functional status) which is recommended by the American Academy of Orthopedic Surgeons (42, 43) and visual analogue scale (VAS) for pain intensity of patients. The first one was The Boston Carpet Tunnel Questionnaire (BCTQ) which used to evaluate the patients' performance and the severity of symptoms. It is consist of 11 questions about the severity of the symptoms (BCTQ SYMPT) and 8 question about functional status (BCTQ FUNCT). The items of each scale were scored from 1 (mildest) to 5 (most severe). The reliability and sensitivity of the Persian version which used in the current study were confirmed in a previous study (16). Pain intensity measured using the visual analogue scale (VAS). The patient evaluated their pain intensity from zero (complete analgesia) to 10 (the most experienced patient's pain).

The Physical examination which used in the current study was made based on at least one of the following clinical criteria were included: Tinel sign test, Phalen maneuver test, numbness or tingling in ≥ 2 of 4 radial fingers, median nerve compression and wrist flexion tests (44, 45). Patients that diagnosed with CTS was confirmed by the presence of at least one of EMG/NCV criteria which were included: DML ≥ 4.2 ms, DSL ≥ 3.6 ms, and W-P SNCV < 40 ms (46).

The maximum grip force (in kg) was measured using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was held from the top and the bottom in order to prevent the measurement to be affected by the weight of the device. All the measurements were evaluated by the same device both before and after the treatment (47). To evaluate the range of motion (ROM) the active wrist flexion and extension were measured by using goniometer (Plastic goniometer MSD). All the measurements were performed in a sitting position, which the patients sitting next to a supporting surface with shoulder abducted to 90º, the elbow flexed to 90º, and the palm of the

hand facing the ground. The forearm was midway between supination and pronation. The examiner was a caution to avoid radial or ulnar deviation of the wrist and flexion of the fingers. The examiner put the center fulcrum of goniometer on the lateral aspect of the wrist over the triquetrum and aligned proximal and distal arm with the lateral midline of the ulna and fifth metacarpal respectively. Then the examiner asked the patients to flex the wrist. The examiner used one hand to align the distal arm of the goniometer with the 5^{th} metacarpal at the end of the flexion while the patients maintaining the wrist in that position and the ROM degrees was recorded. To measure active wrist extension the examiner performed all process like active wrist flexion except in extension movements (48). None of the patients dropped out in this study.

Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In the other word, neither the patient nor the therapist and study investigator was aware of which groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent intra and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Ethics approval

The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152) and was registered in IRCT under the code IRCT20180212038693N1.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age,

gender, height, weight, job, the presence of systemic disease, involved hand and disease severity was seen in three treatment groups (P>0.05).

The current study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist was significantly improved in CTS patients at the end of 6 weeks in all three groups (P<0.05). Although using brace alone (control group) did not have any significant effect on the binding of the wrist (P=0.098) (table 2).

The between groups analysis indicate that acupuncture affected the pinch force more than exercise therapy and it was statistically significant F(df=2)=0.035, P=0.0001 but weak (P Eta Squared=0.001). Also, the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension) but just ROM of flexion was statistically significant F(df=2)=0.000, P=0.0001 but weak (P Eta Squared=0.012).

Table 1- Patient characteristics at baseline*

Variable	Brace+ acupuncture (n=20)	Brace+ Exercise therapy (n=20)	Control (n=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Gender	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)

**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value	Effect Size
Grip force	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	<0.004	0.103

	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001	0.359
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025	0.249
Pinch force	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	<0.001	0.201
	Brace+ Exercise therapy	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001	0.447
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001	0.573
Flexion	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098	0.044
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001	0.490
	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002	0.209
Extension	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.001	0.114
	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001	0.702
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015	0.194

SD = standard deviation.

Discussion

The aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

In the current study, no significant statistical difference existed between age, gender, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups which shows that these factors do not affect our study results. Also, there was no significant difference between variables of pinch and grip force, flexion and extension of the wrist in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment was increased significantly. But exercises had an effect on ROM of flexion and acupuncture had an effect on pinching but the effect sizes were weak. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it

can recover normal griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (23, 25, 49-51). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power compared to the beginning of the study, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52).

Yao et al reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52). These results are not consistent with the finding of the current study. Although all three groups showed significant improvement in pinching power in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be related to the difference in intervention methods, a number of acupuncture sessions and primary characteristics of patients. Fr example, in Goetez et al study, the pinch strength would decrease. Due to the effect of lidocaine-like on the flexor pollicis longus which is located under the PC-7 acupoint that is caused by electroacupuncture (41, 53).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al results (27). Moreover, In Alkalin, *et al*. study the effectiveness of nerve and tendon gliding exercises along with splinting compared with splinting alone was evaluated in the treatment of CTS. Results showed an improvement in pinching power in both groups after treatment but the improvement in mobilization group was higher than splint alone. These results consistent with the results of the current study (26). In another study by Madenci, *et al*. (2012) was also reported than tendon and nerve gliding exercises with night splint significantly improved the gripping power in CTS patients (47). Results of Penas, *et al*. study (2017) in Spain also show that exercise therapy is effective in improving pinching and gripping power in CTS patients (54).

The results of the current study showed significant improvement in range of motion (binding and opening) of the wrist in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of binding of the hand. On the other hand, exercise therapy had the most effect on increasing

the range of motion (binding and opening) of the wrist. To confirm these results, Chung, *et al.* (2016) also showed that functional performance of wrist of mild to moderate CTS patients in the acupuncture+splint group was better than the control group (splinting alone) (23). In another study, Tal-Akabi and Rushton (2000) studied and compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups was better than the control group but the difference was not significant so carpal bone mobilization for 3 weeks improves CTS patients function but the results were not statistically significant because of the small sample size (55).

CTS give arises to lose the physiologic mobility of the median nerve. According to Wright et al and Szabo et al study, during flexion to an extension, the median nerve glides 19.6 mm and during fingers flexion, it would be 9 mm. Also, the flexor digitorum superficialis tendons glide 30 mm during fingers flexion in the CT (56, 57). Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (58).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved.

Conclusion

The results of this study indicate that conservative groups were better than the control group, but the difference was statistically significant and weak just in an efficacy of exercise therapy on ROM of flexion and an efficacy of acupuncture on pinch force. Probably because of the limited case data. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a

larger sample and long-term monitoring.

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OPEN PEER REVIEW

Revision (3)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: EIC | **Revision** (3) 29 Dec 2018

Dear Author,
The list of authors in this revision is different from the previous version. One Author has been added to the Authors' list in new version. According to our journal policy, we cannot accept new author after first submission.
Thanks.

OPEN PEER REVIEW

Revision (4)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

The effectiveness of exercise therapy and dry needling on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

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**** Reviewer 1:

This is a respectable manuscript, it is written straightforward and concise, but I believe it can be improved with some changes. some general comments first:

1.justification of doing the study is my main concern here. I was looking for the justification in its introduction, but it has failed to demonstrate the need for conducting a new study , their reference for controversy about using acupuncture for CTS dates back to 2009, there has been a number of reviews about Effects of acupuncture therapy on the carpal tunnel syndrome. are the authors familiar with this systematic review of 2011:
https://www.ncbi.nlm.nih.gov/pubmed/21093382

Response:
We appreciate this concern and in accordance with reviewer's suggestion, the following explanation have now edited in the last part of introduction section now with red colour.

There is limited evidence regarding the efficacy of acupuncture (even according to reviewer's systematic review on 2011) and exercise therapy. Moreover, According to newest a systematic and meta-analysis on 2018 most of studies (10 trails) compare the surgical treatment versus conservative treatment (manual therapy, injection, and splint) and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones. The specific questions which drive the research is which to comparison and determining the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

https://www.ncbi.nlm.nih.gov/pubmed/20490348

https://www.ncbi.nlm.nih.gov/pubmed/27117725

https://www.ncbi.nlm.nih.gov/pubmed/30015499

https://www.ncbi.nlm.nih.gov/pubmed/27749538

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2. There is no Sham acupuncture group which compromises the quality of the study. it would be acceptable if there hasn't been a vast number of studies with sham acupuncture arm for studying acupuncture for CTS.

Response:
We appreciate this concern. As the reviewer said there hasn't been a vast number of studies with sham for CTS even in the reviewers systematic reviews of 2011 suggestion there were only 2 studies with sham.

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3. there is a dissociation between the results, discussion and abstract. according to the results, there is no significant difference between treatment groups, but the authors have suggested in the discussion that Acupuncture has shown better results in pinching force and the exercise has had a better effect on the gripping force, they have also suggested adding exercise and acupuncture to the splinting based on these findings:

results: Results of ANOVA test showed no statistical difference in gripping force (P=0.398), pinching force (P=0.233), bending (P=0.089) and opening the wrist (P=0.250) before treatment among three groups of brace, brace + exercise therapy and brace+acupuncture,

discussion: But exercises had the most effect on gripping and acupuncture had the most effect on pinching.

Abstract: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in [THE] management of these patients.

Response:
We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It's about the P-value of before treatment among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

I have also some specific comments:

4. The manuscript needs some English improvement: (just a number from Abstract)

The efficacy of acupuncture and exercise therapy in [THE] treatment of carpal tunnel syndrome (CTS) has been

The aim of this study was to comparison [compare] the short-term efficacy of acupuncture

(2 times a day for 6 week [s])

except [THE] flexion of wrist in [THE] control group

Also [,] the efficacy of splint

be adopted in [THE] management of these patients

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with yellow highlight.

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5. The introduction is not focused on the main question of study and it has mentioned other methods of treatment like massage therapy which is unrelated to the scope of this study. it can be rewritten in a standard form of introduction (3-4 paragraphs in the order of known>unknown>the question)

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

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6. Methods: "the study was completely blinded", the blindness should be described.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

---

7. results: "which these results shows[s is redundent] the complete randomization of samples and the absence of bias in sample selection" this assumption is beyond my understanding, would the authors elaborate on that?

Response:
We appreciate this concern. Pardon us, misunderstanding has occurred with the paragraph which the reviewer mention it. It's about the P-value of before treatment among three groups which these results show the complete randomization of samples and the absence of bias in sample selection. For preventing the future misunderstanding for audience the authors eliminate the paragraph.

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8. Discussion: the first sentence of discussion usually describe the main finding of the study, and the discussion should also show how proposed treatment can affect the results (physiologically), it should be more than just referencing previous studies.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

Abstract

Background and aim: Carpal tunnel syndrome (CTS) is the most prevalent form of peripheral neuropathy. The efficacy of acupuncture and exercise therapy in the treatment of carpal tunnel syndrome (CTS) has been investigated in limited studies with controversial results. The aim of this study was to compare the short-term efficacy of acupuncture and exercise therapy in patients with mild to moderate CTS.

Materials and Methods: This is a randomized controlled clinical trial study conducted on 60 patients with mild to moderate CTS referring to Imam Hossein Hospital in Tehran in 2017. The patients were randomly divided in to 3 equal groups (20 patients in each group) In the first group only night splint was used for 6 weeks (control), in the second group splint and tendon and nerve gliding exercises (2 times a day for 6 weeks) were applied, and the third group splint and electroacupuncture was performed for 12 sessions of 40- minute duration (2 sessions/week). The parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment.

Results: In this study, 55 women and 5 men with the average age of 49.23±8.96 were enrolled. At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of the wrist in the control group ($p=0.098$). Our findings indicate that acupuncture affected the pinch force more than exercise therapy. But the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension). Also, the efficacy of splint alone was less than intervention groups in all parameters.

Conclusion: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in the management of these patients.

Keywords: Carpal Tunnel syndrome, Splint, Exercise, Acupuncture.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). The entrapment of the median nerve within the carpal tunnel which is limited by carpal bones and the transverse carpal ligament is the main cause of CTS (3). Physiologic evidence shows the increased pressure in the carpal tunnel and therefore decrease of middle nerve function in that surface (2, 4). CTS found in 3.8% of the general population and can occur in all ages (4), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (4, 5). CTS risk factors include job conditions such as repeating movements of the hand when using the computer, medical conditions, and other factors (1). Repeated striking due to intense flexion and extension of the wrist such as working with machines creating vibration or long flexion is also known as factors worsening carpal tunnel syndrome (6, 7). Considering the above risk factors and fast use of the computer in the society, we face to increasing prevalence of CTS and this disease reduces the quality of an individual's life. Moreover, the late treatment of CTS sometimes causes permanent damage to the median nerve (some or all nerve fibers are damaged) and therefore permanent sensory or motor damage occurs in affected patients (8).

Different treatments methods for CTS which are divided into two group: conservative treatment and surgery (9). Conservative treatment is usually selected for CTS patients with mild to moderate symptoms (10), which include: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint. (9). Although the effectiveness of using splints and steroids as primary treatments to improve the patient’s symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (11). Also, each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (12, 13). In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or

alternative treatment which showed very different results on symptoms and function of CTS patient (4, 14, 15). Also although National Institute of Health (NIH) has approved the use of acupuncture for management of mild to moderate CTS there is controversy about its effectiveness (16).

The studies over a couple decade have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (17-20). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that "acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression." (21) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (17, 22). Vincent et al (2016)'s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (23). On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization. They concluded that adding nerve mobilization to standard care does not cause improvement in outcome of CTS patients. They also determined several reasons for the lack of acceptable result in nerve gliding group including more than 50% rate of exclusion of patients which is common in hospitals and weak conformity of symptom severity in both groups (24). So it is recommended that more controlled studies on using mobilization techniques in CTS treatment be done.

Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improve wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (23). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (25).

Akalin et al study on 28 CTS patients indicate that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (26). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (27).

Carpal tunnel syndrome is the most common neuropathy of upper limbs. In many guidelines, including National Institute for Health and Care Excellence (NIHCE) (28), American Academy of Orthopedic Surgeons (AMOS) (29) and American College of Occupational and Environmental Medicine (ACOEM), wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (30). Also among different management options for this disease using acupuncture and exercise therapy is increasing. But there is no specific recommendation about the use of acupuncture and effectiveness of exercise therapy (23, 31, 32). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

Methods

The present study is a randomized, controlled clinical trial which is performed on 60 CTS patients referring to the Sports Medicine Clinic of Imam Hossein Hospital in Tehran in 2017. The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV. Patients enrolled in the study after receiving explanations by researchers regarding the purpose of the study and by obtaining informed consent.

The inclusion criteria for the study including: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of atrophy or muscle weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment regarding CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, non-performing of the exercises requested, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as bleeding tendency, local infection, or a history of needling shock.

At first, all patients were under full clinical examination. The demographic and history profiles were also completed for all patients. This form includes demographic characteristics (age, sex, place of living, marital status), medical history and clinical information including smoking and alcohol consumption, underlying diseases, weight, height, drugs used and characteristics of CTS including pain severity, affected hand, and duration of CTS. The diagram of the study process is presented in Figure 1.

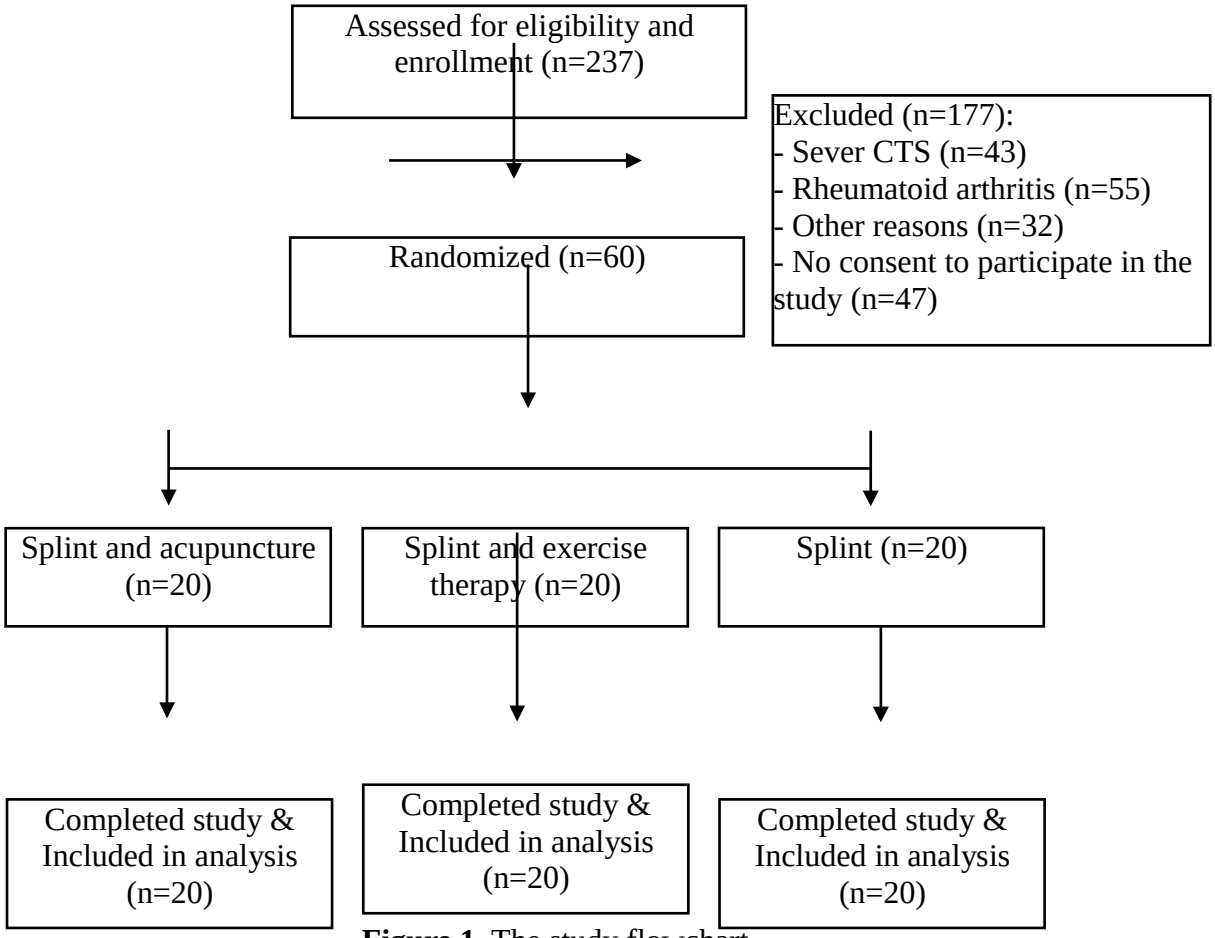


Figure 1. The study flowchart.

Intervention

Patients were randomly divided into three equal groups (20 patients in each group) with an adjusted age of 10 years. In the first group, the patients received only night splint for a period of 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes electroacupuncture was performed (2 times a week) in two points of PC-6 (Daling) and PC-7 (Neiguan) using the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz up to patient's pain threshold (Figure 3). The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

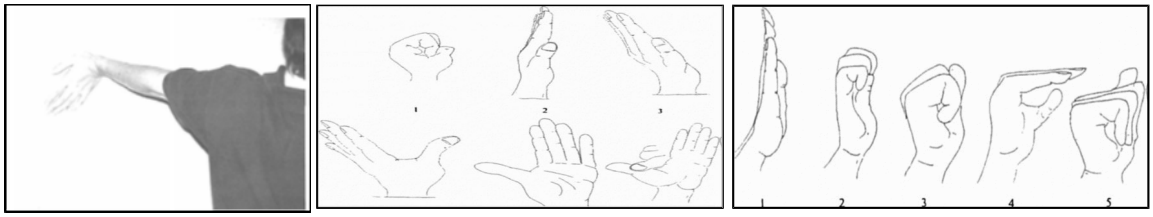


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.

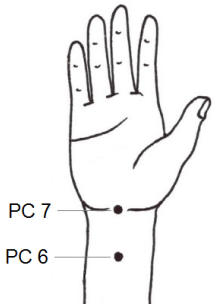


Figure 3. Acupuncture points.

Patient evaluation

In order to evaluate the response to treatment the parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment and compared between the three groups.

The maximum grip force (in kg) was measured using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was held from the top and the bottom in order to prevent the measurement to be affected by the weight of the device. All the measurements were evaluated by the same device both before and after the treatment (38). To evaluate the range of motion (ROM) the wrist flexion and extension were measured by using goniometer.

None of the participants dropped out in this study. Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In the other word, neither the patient nor the therapist and study investigator was aware of which groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent intra and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age, sex, height, weight, job, the presence of systemic disease, involved hand and disease severity was seen in three treatment groups (P>0.05).

The current study showed the grip force, pinch force and range of motion (flexion

and extension) of the wrist was significantly improved in CTS patients at the end of 6 weeks in all three groups (P<0.05). Although using brace alone (control group) did not have any significant effect on the binding of the wrist (P=0.098) (table 2).

Table 1- Participant characteristics at baseline*

Variable	Brace+ acupuncture (n=20)	Brace+ Exercise therapy (n=20)	Control (n=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Sex	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)
**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value
Grip force	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	<0.004
	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025
Pinch force	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	<0.001
	Brace+ Exercise therapy	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001
Flexion	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001

	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002
Extension	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.001
	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015

SD = standard deviation.

Discussion

The aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

In the current study, no significant statistical difference existed between age, sex, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups which shows that these factors do not affect our study results. Also, there was no significant difference between variables of pinch and grip force, flexion and extension of the wrist in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment was increased significantly. But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it can recover normal griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (23, 25, 39-41). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power compared to the beginning of the study, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (42).

Yao et al reported that acupuncture with bracing has no significant effect on the

treatment of mild to moderate CTS (42). These results are not consistent with the finding of the current study. Although all three groups showed significant improvement in pinching power in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be related to the difference in intervention methods, a number of acupuncture sessions and primary characteristics of patients. Fr example, in Goetez et al study, the pinch strength would decrease. Due to the effect of lidocaine-like on the flexor pollicis longus which is located under the PC-7 acupoint that is caused by electroacupuncture (43, 44).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al results (27). Moreover, In Akalin, *et al*. study the effectiveness of nerve and tendon gliding exercises along with splinting compared with splinting alone was evaluated in the treatment of CTS. Results showed an improvement in pinching power in both groups after treatment but the improvement in mobilization group was higher than splint alone. These results consistent with the results of the current study (26). In another study by Madenci, *et al*. (2012) was also reported than tendon and nerve gliding exercises with night splint significantly improved the gripping power in CTS patients (38). Results of Penas, *et al*. study (2017) in Spain also show that exercise therapy is effective in improving pinching and gripping power in CTS patients (45).

The results of the current study showed significant improvement in range of motion (binding and opening) of the wrist in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of binding of the hand. On the other hand, exercise therapy had the most effect on increasing the range of motion (binding and opening) of the wrist. To confirm these results, Chung, *et al.* (2016) also showed that functional performance of wrist of mild to moderate CTS patients in the acupuncture+splint group was better than the control group (splinting alone) (23). In another study, Tal-Akabi and Rushton (2000) studied and compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups was better than the control group but the difference was not significant so carpal bone mobilization for 3 weeks improves CTS patients function but the results were not statistically significant because of the small

sample size (46).

CTS give arises to lose the physiologic mobility of the median nerve. According to Wright et al and Szabo et al study, during flexion to an extension, the median nerve glides 19.6 mm and during fingers flexion, it would be 9 mm. Also, the flexor digitorum superficialis tendons glide 30 mm during fingers flexion in the CT (47, 48). Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (49).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a larger sample and long-term monitoring.

Conclusion

The results of this study showed that all three treatment methods could provide an overall functional improvement in patients with CTS but when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also a range of motion in the wrist was more than using splint alone. Also, the effectiveness of exercise therapy in most cases was better than electroacupuncture. Finally, these treatment interventions are effective, inexpensive, safe and accessible treatment options and can be applied to the management of patients with mild to moderate CTS.

Acknowledgment

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****** Reviewer 2:**

Dear author/s,
The writing of paper needs to be checked by a native. Sentences are too long and difficult to follow.

Introduction *is written so general and has not focused on topic accurately. In your introduction, you are talking about CTS and there is not enough explanation about acupuncture and exercise therapy for it. Your references are also mostly about CTS. Novelty of paper is not clear for me.*

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Method:
If it is a RCT, you have to add your IRCT number clearly and also explain about ethic approval and ethic number.
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color. The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Your method section is not following a standard format and it is not acceptable in current form (follow CONSORT checklist).
Allocation and randomization are not explained accurately.
It is not clear how you recognized 237 patients??

There are some general sentences and need to be explained clearly. For example "At first, all patients were under full clinical examination".
How you defined the locations of acupuncture?

In evaluation section you mentioned that evaluations were done in baseline and after treatment but this time is different for different groups.

ROM evaluation is not explained correctly. The techniques should be explained accurately. Details of goniometer are necessary to be written. It is not clear if it was active or passive?

Response:
Done. We appreciate this concern. We have now rewritten the method section and write all reviewer's suggestion in above with red color.

How you recognized symptoms of atrophy or muscle weakness?
Response:
We appreciate this concern. It recognized by neurologist based on clinical criteria and comparisons with the opposite hand

Figure 2. You are not allowed to use other pictures. You have to use your own pictures. Duration of therapy for different groups seems different. Is it correct?? In my view, it is not acceptable. Your study design does not seem correct

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now replaced the pictures by the own pictures.

There is no detail about blinding. It is not clear if the assessor was blind
Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red color.

Table 1: why here you have 15 participants???????

Response:
We appreciate this concern. Pardon us, it was a miswritten and have now changed the word "15" to "20" have now edited with red color.

Your results should be written based on within group and between group comparison and talk about the effect size.

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data, and we added the results in the section with red color.

Discussion *in current form is very general and not acceptable.*
The theory behind your findings should be mentioned clearly and then compare with opposite and similar studies.

Response:

Done. We appreciate this concern and in accordance with reviewer's suggestion, have now explain more that issue in the discussion section of our revised manuscript with red color.

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*Your **conclusion** is a repetition of your results.*

Response:
Done. We appreciate this concern. We have now rewritten that section with red color.

Please use from real pictures.
Please replace patient with participant in whole paper.
Please replace sex with gender in whole paper.

Response:
Done. We appreciate this concern and have now changed the word "sex" to "gender" and the word "participant" to "patient" have now edited with red color.

Abstract

Background and aim: Carpal tunnel syndrome (CTS) is the most prevalent form of peripheral neuropathy. The efficacy of acupuncture and exercise therapy in the treatment of carpal tunnel syndrome (CTS) has been investigated in limited studies with controversial results. The aim of this study was to compare the short-term efficacy of acupuncture and exercise therapy in patients with mild to moderate CTS.

Materials and Methods: This is a randomized controlled clinical trial study conducted on 60 patients with mild to moderate CTS referring to Imam Hossein Hospital in Tehran in 2017. The patients were randomly divided in to 3 equal groups (20 patients in each group) In the first group only night splint was used for 6 weeks (control), in the second group splint and tendon and nerve gliding exercises (2 times a day for 6 weeks) were applied, and the third group splint and electroacupuncture was performed for 12 sessions of 40- minute duration (2 sessions/week). The parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment.

Results: In this study, 55 women and 5 men with the average age of 49.23±8.96 were enrolled. At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of the wrist in the control group ($p=0.098$). Our findings indicate that exercises therapy had more effect on ROM of flexion than acupuncture and acupuncture had more effect on pinching than exercise therapy but the effect sizes were weak. Also, the efficacy of splint alone was less than intervention groups in all parameters.

Conclusion: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in the management of these patients.

Keywords: Carpal Tunnel syndrome, Splint, Exercise, Acupuncture.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). The entrapment of the median nerve within the carpal tunnel which is limited by carpal bones and the transverse carpal ligament is the main cause of CTS (3). Physiologic evidence shows the increased pressure in the carpal tunnel and therefore decrease of middle nerve function in that surface (2, 4). CTS found in 3.8% of the general population and can occur in all ages (4), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (4, 5). CTS risk factors include job conditions such as repeating movements of the hand when using the computer, medical conditions, and other factors (1). Repeated striking due to intense flexion and extension of the wrist such as working with machines creating vibration or long flexion is also known as factors worsening carpal tunnel syndrome (6, 7). Considering the above risk factors and fast use of the computer in the society, we face to increasing prevalence of CTS and this disease reduces the quality of an individual's life. Moreover, the late treatment of CTS sometimes causes permanent damage to the median nerve (some or all nerve fibers are damaged) and therefore permanent sensory or motor damage occurs in affected patients (8).

Different treatments methods for CTS which are divided into two group: conservative treatment and surgery (9). Conservative treatment is usually selected for CTS patients with mild to moderate symptoms (10), which include: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint. (9). Although the effectiveness of using splints and steroids as primary treatments to improve the patient’s symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (11). Also,

each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (12, 13). In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (4, 14, 15). Also although National Institute of Health (NIH) has approved the use of acupuncture for management of mild to moderate CTS there is controversy about its effectiveness (16).

The studies over a couple decade have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (17-20). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that “acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression.” (21) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (17, 22). Vincent et al (2016)’s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (23). On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization. They concluded that adding nerve mobilization to standard care does not cause improvement in outcome of CTS patients. They also determined several reasons for the lack of acceptable result in nerve gliding group including more than 50% rate of exclusion of patients which is common in hospitals and weak conformity of symptom severity in both groups (24). So it is recommended that more controlled studies on using mobilization techniques in CTS treatment be done.

Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improve wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (23). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (25).

Akalin et al study on 28 CTS patients indicate that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (26). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (27).

Carpal tunnel syndrome is the most common neuropathy of upper limbs. In many guidelines, including National Institute for Health and Care Excellence (NIHCE) (28), American Academy of Orthopedic Surgeons (AMOS) (29) and American College of Occupational and Environmental Medicine (ACOEM), wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (30). Also among different management options for this disease using acupuncture and exercise therapy is increasing. But there is no specific recommendation about the use of acupuncture and effectiveness of exercise therapy (23, 31, 32). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

Methods

The present study is a randomized, controlled clinical trial which is performed on 60 CTS patients referring to the Sports Medicine Clinic of Imam Hossein Hospital in Tehran in 2017. The whole patients with CTS at the Hospital in 2017 were assessed in the study was 237 and after screened for eligibility at the Clinic 177 patients excluded and 60 remains to included (Figure 1).

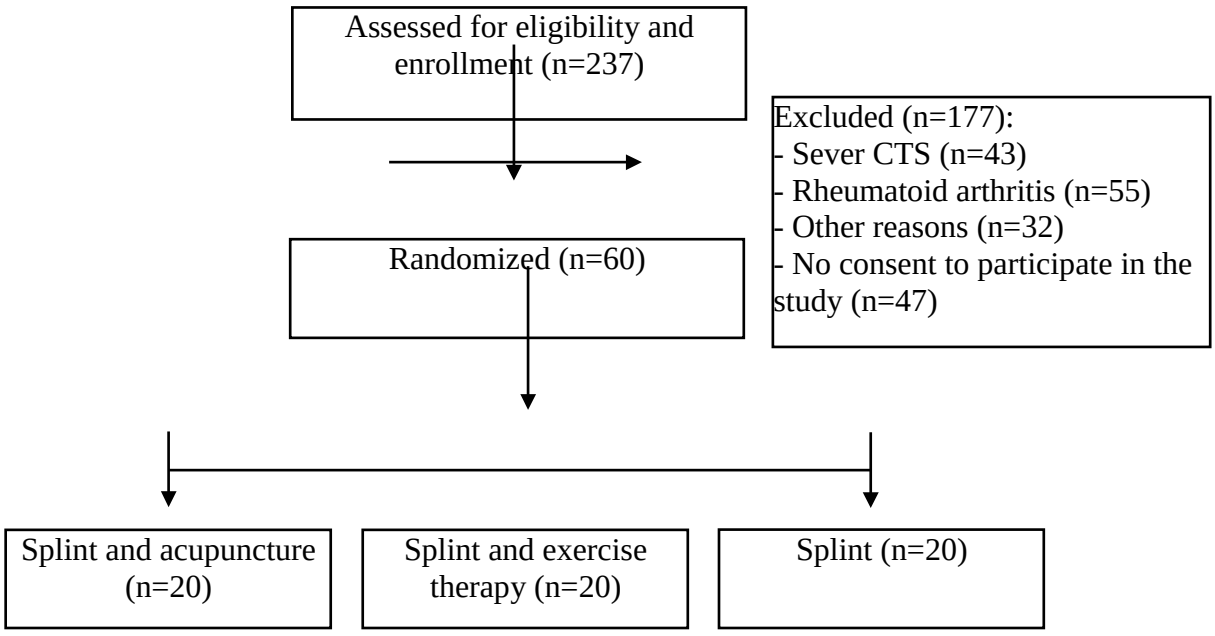
The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV.

Patients enrolled in the study after receiving explanations by researchers regarding the purpose of the study and by obtaining informed consent.

The inclusion criteria for the study including: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of atrophy or muscle weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment regarding CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, non-performing of the exercises requested, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as bleeding tendency, local infection, or a history of needling shock.

At first, all patients were under full clinical examination which explained in following at the Patient evaluation subsection. The demographic and history profiles were also completed for all patients. This form includes demographic characteristics (age, gender, place of living, marital status), medical history and clinical information including smoking and alcohol consumption, underlying diseases, weight, height, drugs used and characteristics of CTS including pain severity, affected hand, and duration of CTS.



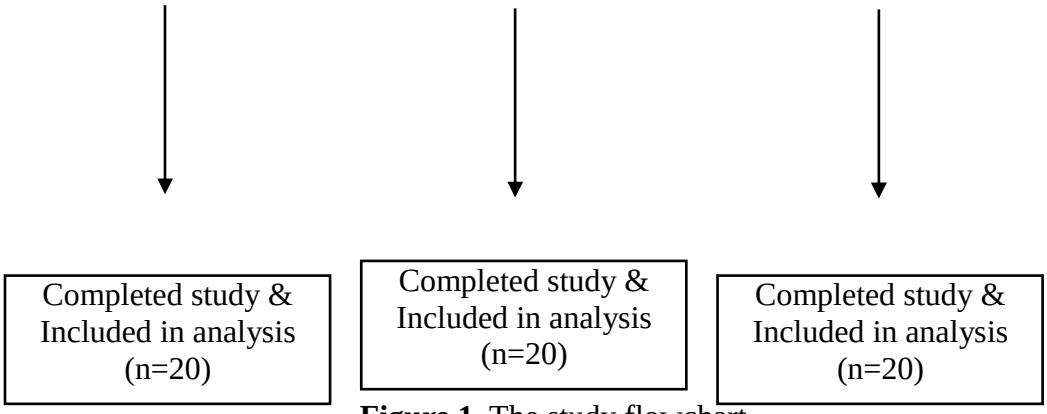


Figure 1. The study flowchart.

Intervention

Block randomization which used by Random Allocation Software random was applied to allocate patients to groups after eligibility confirmation (38, 39). Patients were randomly divided into three equal groups (20 patients in each group) with an adjusted age of 10 years. In the first group, the patients received only night splint for a period of 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes electroacupuncture was performed (2 times a week) in two points of PC-7 (Daling) and PC-6 (Neiguan) using the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz up to patient's pain threshold (Figure 3). The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

To find acupoints the examiner asks patients to press the thumb and little finger together for the better presentation of the tendon of the flexor carpi radialis and tendon of the palmaris longous. After appearing of the tendons, the needle located at between the tendons on the flexor aspect of the forearm which are between the two tendons. The distance between PC-7 and PC-6 is two thumbs wide. PC-6 (Neiguan) is located at 2 cun above the transverse crease of the wrist PC-7, between palmaris longus and flexor carpi radialis tendons, on the line connecting PC-3 and PC-7. PC-7 (Daling) is located at in the middle of the transverse crease of the wrist between palmaris longus and flexor carpi radialis tendons (Figure 3) (40). These acupoints chose because of their efficiency which is reported in previous studies (41).

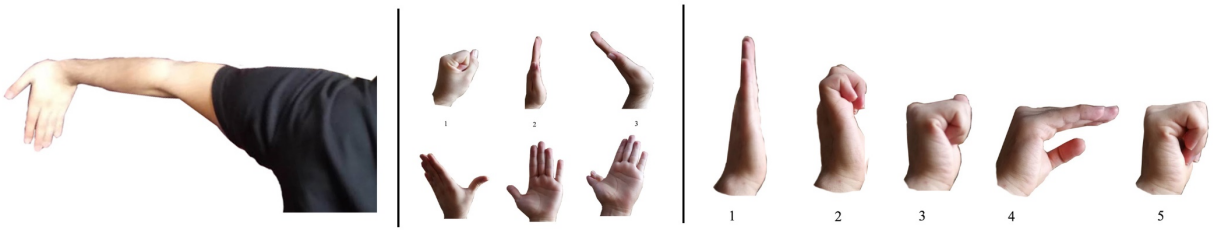


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.



Figure 3. Acupuncture points.

Patient evaluation

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV.

In order to evaluate the response to treatment the parameters of pinch force, grip force, ROM (flexion and extension) quality of life (symptoms and functional status), and pain intensity were evaluated at baseline and 6 weeks later after treatment and compared between the three groups.

We used Carpal Tunnel Questionnaires to evaluate the response to treatment quality of life (symptoms and functional status) which is recommended by the American Academy of Orthopedic Surgeons (42, 43) and visual analogue scale (VAS) for pain intensity of patients. The first one was The Boston Carpet Tunnel Questionnaire (BCTQ) which used to evaluate the patients' performance and the severity of symptoms. It is consist of 11 questions about the severity of the symptoms (BCTQ SYMPT) and 8 question about functional status (BCTQ FUNCT). The items of each scale were scored from 1 (mildest) to 5 (most severe).

The reliability and sensitivity of the Persian version which used in the current study were confirmed in a previous study (16). Pain intensity measured using the visual analogue scale (VAS). The patient evaluated their pain intensity from zero (complete analgesia) to 10 (the most experienced patient's pain).

The Physical examination which used in the current study was made based on at least one of the following clinical criteria were included: Tinel sign test, Phalen maneuver test, numbness or tingling in ≥ 2 of 4 radial fingers, median nerve compression and wrist flexion tests (44, 45). Patients that diagnosed with CTS was confirmed by the presence of at least one of EMG/NCV criteria which were included: DML ≥ 4.2 ms, DSL ≥ 3.6 ms, and W-P SNCV < 40 ms (46).

The maximum grip force (in kg) was measured using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was held from the top and the bottom in order to prevent the measurement to be affected by the weight of the device. All the measurements were evaluated by the same device both before and after the treatment (47). To evaluate the range of motion (ROM) the active wrist flexion and extension were measured by using goniometer (Plastic goniometer MSD). All the measurements were performed in a sitting position, which the patients sitting next to a supporting surface with shoulder abducted to 90º, the elbow flexed to 90º, and the palm of the hand facing the ground. The forearm was midway between supination and pronation. The examiner was a caution to avoid radial or ulnar deviation of the wrist and flexion of the fingers. The examiner put the center fulcrum of goniometer on the lateral aspect of the wrist over the triquetrum and aligned proximal and distal arm with the lateral midline of the ulna and fifth metacarpal respectively. Then the examiner asked the patients to flex the wrist. The examiner used one hand to align the distal arm of the goniometer with the 5^{th} metacarpal at the end of the flexion while the patients maintaining the wrist in that position and the ROM degrees was recorded. To measure active wrist extension the examiner performed all process like active wrist flexion except in extension movements (48). None of the patients dropped out in this study.

Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In the other word, neither the patient nor the therapist and study investigator was aware of which groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent intra and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Ethics approval

The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152) and was registered in IRCT under the code IRCT20180212038693N1.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age, gender, height, weight, job, the presence of systemic disease, involved hand and disease severity was seen in three treatment groups ($P>0.05$).

The current study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist was significantly improved in CTS patients at the end of 6 weeks in all three groups ($P<0.05$). Although using brace alone (control group) did not have any significant effect on the binding of the wrist ($P=0.098$) (table 2).

The between groups analysis indicate that acupuncture affected the pinch force more than exercise therapy and it was statistically significant $F(df=2)=0.035$, $P=0.0001$ but weak (P Eta Squared=0.001). Also, the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension) but just ROM of flexion was statistically significant $F(df=2)=0.000$, $P=0.0001$ but weak (P Eta Squared=0.012).

Table 1- Patient characteristics at baseline*

Variable	Brace+ acupuncture (n=20)	Brace+ Exercise therapy (n=20)	Control (n=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Gender	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)

**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value	Effect Size
Grip force	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	<0.004	0.103
	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001	0.359
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025	0.249
Pinch force	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	<0.001	0.201
	Brace+ Exercise therapy	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001	0.447
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001	0.573
Flexion	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098	0.044
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001	0.490
	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002	0.209
Extension	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.001	0.114

	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001	0.702
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015	0.194

SD = standard deviation.

Discussion

The aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

In the current study, no significant statistical difference existed between age, gender, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups which shows that these factors do not affect our study results. Also, there was no significant difference between variables of pinch and grip force, flexion and extension of the wrist in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment was increased significantly. But exercises had an effect on ROM of flexion and acupuncture had an effect on pinching but the effect sizes were weak. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it can recover normal griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (23, 25, 49-51). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power compared to the beginning of the study, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52).

Yao et al reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52). These results are not consistent with the

finding of the current study. Although all three groups showed significant improvement in pinching power in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be related to the difference in intervention methods, a number of acupuncture sessions and primary characteristics of patients. Fr example, in Goetez et al study, the pinch strength would decrease. Due to the effect of lidocaine-like on the flexor pollicis longus which is located under the PC-7 acupoint that is caused by electroacupuncture (41, 53).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al results (27). Moreover, In Alkalin, *et al*. study the effectiveness of nerve and tendon gliding exercises along with splinting compared with splinting alone was evaluated in the treatment of CTS. Results showed an improvement in pinching power in both groups after treatment but the improvement in mobilization group was higher than splint alone. These results consistent with the results of the current study (26). In another study by Madenci, *et al*. (2012) was also reported than tendon and nerve gliding exercises with night splint significantly improved the gripping power in CTS patients (47). Results of Penas, *et al*. study (2017) in Spain also show that exercise therapy is effective in improving pinching and gripping power in CTS patients (54).

The results of the current study showed significant improvement in range of motion (binding and opening) of the wrist in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of binding of the hand. On the other hand, exercise therapy had the most effect on increasing the range of motion (binding and opening) of the wrist. To confirm these results, Chung, *et al.* (2016) also showed that functional performance of wrist of mild to moderate CTS patients in the acupuncture+splint group was better than the control group (splinting alone) (23). In another study, Tal-Akabi and Rushton (2000) studied and compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups was better than the control group but the difference was not significant so carpal bone mobilization for 3 weeks improves CTS patients function but the results were not statistically significant because of the small sample size (55).

CTS give arises to lose the physiologic mobility of the median nerve. According to Wright et al and Szabo et al study, during flexion to an extension, the median nerve glides 19.6 mm and during fingers flexion, it would be 9 mm. Also, the flexor digitorum superficialis tendons glide 30 mm during fingers flexion in the CT (56, 57). Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (58).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved.

Conclusion

The results of this study indicate that conservative groups were better than the control group, but the difference was statistically significant and weak just in an efficacy of exercise therapy on ROM of flexion and an efficacy of acupuncture on pinch force. Probably because of the limited case data. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a larger sample and long-term monitoring.

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Competing interests: None declared

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**** Reviewer 3:

HI
This manuscript needs major revision.
Title: The effectiveness of exercise therapy and acupuncture on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Relevant topic nevertheless, some points should be improved.

Abstract
Question 1. In the abstract of result part please explain; At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of wrist in control group ($p=0.098$);??
Please make your point clear.

Response:
We appreciate this concern. Pardon us, it was a miswritten there is no exception, all parameters had significant improvements. the authors eliminate the sentence.

Question 2. In the abstract of result part please explain; our findings indicate that acupuncture affected the pinch force more than exercise therapy;
There was no between groups analyses, how did you make that judgment?

Question 3. In the abstract of result part please explain; But the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension).

There was no between groups analyses, how did you make that judgment?

Question 4. In the abstract of result part please explain; Also the efficacy of splint alone was less than intervention groups in all parameters;
There was no between groups analyses, how did you make that judgment?

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion; we reanalysed the data and we added the results in the section with red color

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Methods
Question 5.Please define mild, moderate and severe CTS with details

Response:
Done. We appreciate this concern. We have now rewritten that method section with red colour.

Question 6. Please mention the ethical code

Response:
Done. We appreciate this concern and in accordance with reviewer's suggestion, have now edited with red colour.

Ethics approval
The trial was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152), and was registered in IRCT under the code IRCT20180212038693N1.

Question 7. Please give complete information about the exact anatomic location of two points of acupuncture including PC-6 (Daling) and PC-7 (Neiguan).

Response:

Done. We appreciate this concern. We have now rewritten with red colour.

Question 8. Please explain why you selected PC-6 (Daling) and PC-7 (Neiguan) points among other points.

Response:
Done. We appreciate this concern. We have now rewritten with red colour.

Discussion
Question 9. please explain; But exercises had the most effect on gripping and acupuncture had the most effect on pinching. Also splint alone had the least effect on gripping and pinching of CTS patients;
According to your analyses which did not include between groups difference, you can not make that judgment.

Conclusion
Question 10. please explain; when exercise or acupuncture was used with night splinting improvement in pinch and grip force and also range of motion in wrist was more than using splint alone. Also the effectiveness of exercise therapy in most cases was better than electroacupuncture.
Either omit this information or do a complementary analysis between groups.

Response:
Done. We appreciate this concern. and in accordance with reviewer's suggestion We have now rewritten the section with red colour.

Abstract

Background and aim: Carpal tunnel syndrome (CTS) is the most prevalent form of peripheral neuropathy. The efficacy of acupuncture and exercise therapy in the treatment of carpal tunnel syndrome (CTS) has been investigated in limited studies with controversial results. The aim of

this study was to compare the short-term efficacy of acupuncture and exercise therapy in patients with mild to moderate CTS.
Materials and Methods: This is a randomized controlled clinical trial study conducted on 60 patients with mild to moderate CTS referring to Imam Hossein Hospital in Tehran in 2017. The patients were randomly divided in to 3 equal groups (20 patients in each group) In the first group only night splint was used for 6 weeks (control), in the second group splint and tendon and nerve gliding exercises (2 times a day for 6 weeks) were applied, and the third group splint and electroacupuncture was performed for 12 sessions of 40- minute duration (2 sessions/week). The parameters of pinch force, grip force, ROM (flexion and extension) were evaluated at baseline and after the treatment.
Results: In this study, 55 women and 5 men with the average age of 49.23±8.96 were enrolled. At the final follow up, significant improvements in all parameters were found in third groups ($p<0.05$), except flexion of the wrist in the control group ($p=0.098$). Our findings indicate that exercises therapy had more effect on ROM of flexion than acupuncture and acupuncture had more effect on pinching than exercise therapy but the effect sizes were weak. Also, the efficacy of splint alone was less than intervention groups in all parameters.
Conclusion: Results of this study demonstrated that adding exercise or acupuncture to nocturnal splinting, the functional improvement is more in patients with mild to moderate carpal tunnel syndrome and these interventions could be adopted in the management of these patients.

Keywords: Carpal Tunnel syndrome, Splint, Exercise, Acupuncture.

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). The entrapment of the median nerve within the carpal tunnel which is limited by carpal bones and the transverse carpal ligament is the main cause of CTS (3). Physiologic evidence shows the increased pressure in the carpal tunnel and therefore decrease of middle nerve function in that surface (2, 4). CTS found in 3.8% of the general population and can occur in all ages (4), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (4, 5). CTS risk factors include job conditions such as repeating movements of the hand when using the computer, medical conditions, and other factors (1). Repeated striking due to intense flexion and extension of the wrist such as working with machines creating vibration or long flexion is also known as factors worsening carpal tunnel syndrome (6, 7). Considering the above risk factors and fast use of the computer in the society, we face to increasing

prevalence of CTS and this disease reduces the quality of an individual's life. Moreover, the late treatment of CTS sometimes causes permanent damage to the median nerve (some or all nerve fibers are damaged) and therefore permanent sensory or motor damage occurs in affected patients (8).

Different treatments methods for CTS which are divided into two group: conservative treatment and surgery (9). Conservative treatment is usually selected for CTS patients with mild to moderate symptoms (10), which include: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint. (9). Although the effectiveness of using splints and steroids as primary treatments to improve the patient’s symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (11). Also, each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (12, 13). In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (4, 14, 15). Also although National Institute of Health (NIH) has approved the use of acupuncture for management of mild to moderate CTS there is controversy about its effectiveness (16).

The studies over a couple decade have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (17-20). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that “acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression.” (21) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (17, 22). Vincent et al (2016)’s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (23). On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization. They concluded that adding nerve

mobilization to standard care does not cause improvement in outcome of CTS patients. They also determined several reasons for the lack of acceptable result in nerve gliding group including more than 50% rate of exclusion of patients which is common in hospitals and weak conformity of symptom severity in both groups (24). So it is recommended that more controlled studies on using mobilization techniques in CTS treatment be done.

Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improve wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (23). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (25).

Akalin et al study on 28 CTS patients indicate that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (26). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (27).

Carpal tunnel syndrome is the most common neuropathy of upper limbs. In many guidelines, including National Institute for Health and Care Excellence (NIHCE) (28), American Academy of Orthopedic Surgeons (AMOS) (29) and American College of Occupational and Environmental Medicine (ACOEM), wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (30). Also among different management options for this disease using acupuncture and exercise therapy is increasing. But there is no specific recommendation about the use of acupuncture and effectiveness of exercise therapy (23, 31, 32). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy.

Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve

and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

Methods

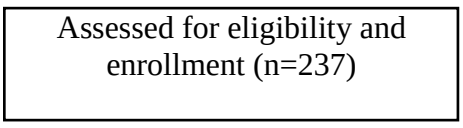
The present study is a randomized, controlled clinical trial which is performed on 60 CTS patients referring to the Sports Medicine Clinic of Imam Hossein Hospital in Tehran in 2017. The whole patients with CTS at the Hospital in 2017 were assessed in the study was 237 and after screened for eligibility at the Clinic 177 patients excluded and 60 remains to included (Figure 1).

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV. Patients enrolled in the study after receiving explanations by researchers regarding the purpose of the study and by obtaining informed consent.

The inclusion criteria for the study including: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of atrophy or muscle weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment regarding CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, non-performing of the exercises requested, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as bleeding tendency, local infection, or a history of needling shock.

At first, all patients were under full clinical examination which explained in following at the Patient evaluation subsection. The demographic and history profiles were also completed for all patients. This form includes demographic characteristics (age, gender, place of living, marital status), medical history and clinical information including smoking and alcohol consumption, underlying diseases, weight, height, drugs used and characteristics of CTS including pain severity, affected hand, and duration of CTS.



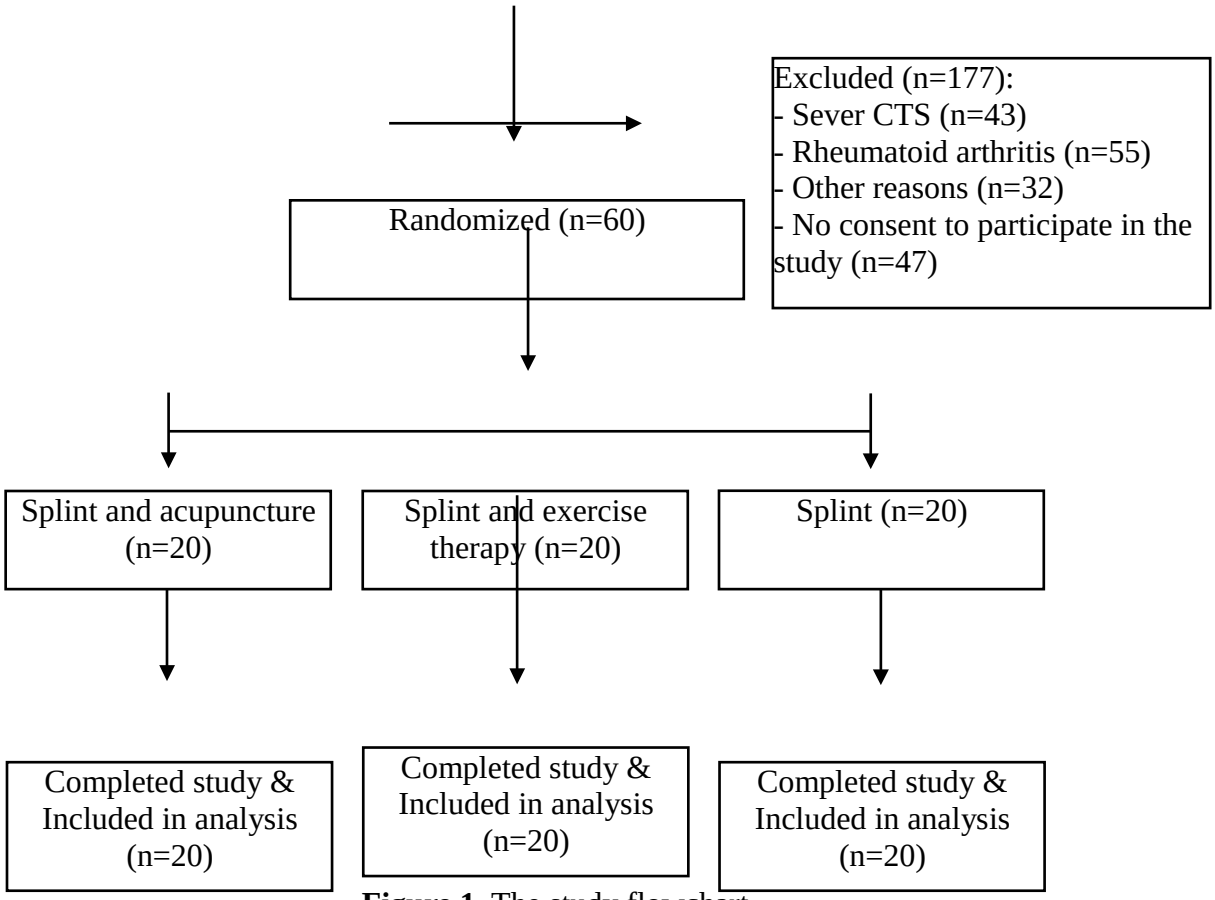


Figure 1. The study flowchart.

Intervention

Block randomization which used by Random Allocation Software random was applied to allocate patients to groups after eligibility confirmation (38, 39). Patients were randomly divided into three equal groups (20 patients in each group) with an adjusted age of 10 years. In the first group, the patients received only night splint for a period of 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes electroacupuncture was performed (2 times a week) in two points of PC-7 (Daling) and PC-6 (Neiguan) using the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz up to patient's pain threshold (Figure 3). The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

To find acupoints the examiner asks patients to press the thumb and little finger together for the better presentation of the tendon of the flexor carpi radials and tendon of the palmaris longous. After appearing of the tendons, the needle located

at between the tendons on the flexor aspect of the forearm which are between the two tendons. The distance between PC-7 and PC-6 is two thumbs wide. PC-6 (Neiguan) is located at 2 cun above the transverse crease of the wrist PC-7, between palmaris longus and flexor carpi radials tendons, on the line connecting PC-3 and PC-7. PC-7 (Daling) is located at in the middle of the transverse crease of the wrist between palmaris longus and flexor carpi radials tendons (Figure 3) (40). These acupoints chose because of their efficiency which is reported in previous studies (41).

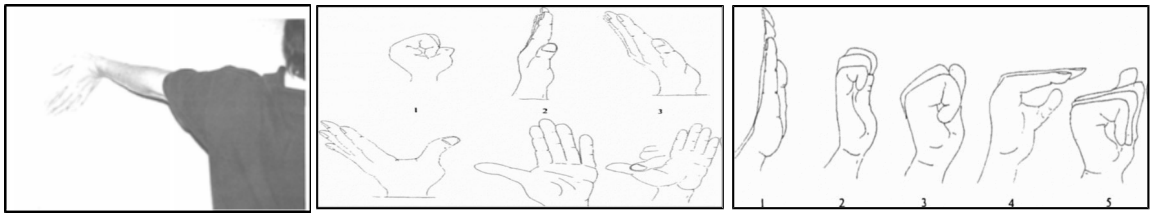


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.

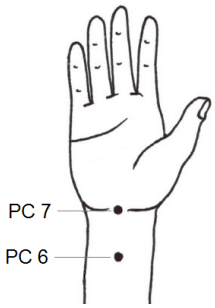


Figure 3. Acupuncture points.

Patient evaluation

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV.

In order to evaluate the response to treatment the parameters of pinch force, grip force, ROM (flexion and extension) quality of life (symptoms and functional status), and pain intensity were evaluated at baseline and 6 weeks later after treatment and compared between the three groups.

We used Carpal Tunnel Questionnaires to evaluate the response to treatment quality of life (symptoms and functional status) which is recommended by the

American Academy of Orthopedic Surgeons (42, 43) and visual analogue scale (VAS) for pain intensity of patients. The first one was The Boston Carpet Tunnel Questionnaire (BCTQ) which used to evaluate the patients' performance and the severity of symptoms. It is consisting of 11 questions about the severity of the symptoms (BCTQ SYMPT) and 8 question about functional status (BCTQ FUNCT). The items of each scale were scored from 1 (mildest) to 5 (most severe). The reliability and sensitivity of the Persian version which used in the current study were confirmed in a previous study (16). Pain intensity measured using the visual analogue scale (VAS). The patient evaluated their pain intensity from zero (complete analgesia) to 10 (the most experienced patient's pain).

The Physical examination which used in the current study was made based on at least one of the following clinical criteria were included: Tinel sign test, Phalen maneuver test, numbness or tingling in ≥ 2 of 4 radial fingers, median nerve compression and wrist flexion tests (44, 45). Patients that diagnosed with CTS was confirmed by the presence of at least one of EMG/NCV criteria which were included: DML ≥ 4.2 ms, DSL ≥ 3.6 ms, and W-P SNCV < 40 ms (46).

The maximum grip force (in kg) was measured using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was held from the top and the bottom in order to prevent the measurement to be affected by the weight of the device. All the measurements were evaluated by the same device both before and after the treatment (47). To evaluate the range of motion (ROM) the active wrist flexion and extension were measured by using goniometer (Plastic goniometer MSD). All the measurements were performed in a sitting position, which the patients sitting next to a supporting surface with shoulder abducted to 90º, the elbow flexed to 90º, and the palm of the hand facing the ground. The forearm was midway between supination and pronation. The examiner was a caution to avoid radial or ulnar deviation of the wrist and flexion of the fingers. The examiner put the center fulcrum of goniometer on the lateral aspect of the wrist over the triquetrum and aligned proximal and distal arm with the lateral midline of the ulna and fifth metacarpal respectively.

Then the examiner asked the patients to flex the wrist. The examiner used one hand to align the distal arm of the goniometer with the 5th metacarpal at the end of the flexion while the patients maintaining the wrist in that position and the ROM degrees was recorded. To measure active wrist extension the examiner performed all process like active wrist flexion except in extension movements (48). None of the patients dropped out in this study.

Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In the other word, neither the patient nor the therapist and study investigator was aware of which groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent intra and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Ethics approval

The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152) and was registered in IRCT under the code IRCT20180212038693N1.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age, gender, height, weight, job, the presence of systemic disease, involved hand and disease severity was seen in three treatment groups ($P>0.05$).

The current study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist was significantly improved in CTS patients at the end of 6 weeks in all three groups ($P<0.05$). Although using brace alone (control group)

did not have any significant effect on the binding of the wrist (P=0.098) (table 2).

The between groups analysis indicate that acupuncture affected the pinch force more than exercise therapy and it was statistically significant F(df=2)=0.035, P=0.0001 but weak (P Eta Squared=0.001). Also, the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension) but just ROM of flexion was statistically significant F(df=2)=0.000, P=0.0001 but weak (P Eta Squared=0.012).

Table 1- Patient characteristics at baseline*

Variable	Brace+ acupuncture (n=20)	Brace+ Exercise therapy (n=20)	Control (n=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Gender	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)

**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value	Effect Size
Grip force	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	<0.004	0.103
	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001	0.359
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025	0.249
Pinch force	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	<0.001	0.201
	Brace+ Exercise	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001	0.447

	therapy					
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001	0.573
Flexion	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098	0.044
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001	0.490
	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002	0.209
Extension	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.001	0.114
	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001	0.702
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015	0.194

SD = standard deviation.

Discussion

The aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

In the current study, no significant statistical difference existed between age, gender, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups which shows that these factors do not affect our study results. Also, there was no significant difference between variables of pinch and grip force, flexion and extension of the wrist in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment was increased significantly. But exercises had an effect on ROM of flexion and acupuncture had an effect on pinching but the effect sizes were weak. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it can recover normal griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (23, 25, 49-51). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for

treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power compared to the beginning of the study, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52).

Yao et al reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (52). These results are not consistent with the finding of the current study. Although all three groups showed significant improvement in pinching power in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be related to the difference in intervention methods, a number of acupuncture sessions and primary characteristics of patients. Fr example, in Goetez et al study, the pinch strength would decrease. Due to the effect of lidocaine-like on the flexor pollicis longus which is located under the PC-7 acupoint that is caused by electroacupuncture (41, 53).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al results (27). Moreover, In Alkalin, *et al*. study the effectiveness of nerve and tendon gliding exercises along with splinting compared with splinting alone was evaluated in the treatment of CTS. Results showed an improvement in pinching power in both groups after treatment but the improvement in mobilization group was higher than splint alone. These results consistent with the results of the current study (26). In another study by Madenci, *et al*. (2012) was also reported than tendon and nerve gliding exercises with night splint significantly improved the gripping power in CTS patients (47). Results of Penas, *et al*. study (2017) in Spain also show that exercise therapy is effective in improving pinching and gripping power in CTS patients (54).

The results of the current study showed significant improvement in range of motion (binding and opening) of the wrist in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of binding of the hand. On the other hand, exercise therapy had the most effect on increasing the range of motion (binding and opening) of the wrist. To confirm these results, Chung, *et al.* (2016) also showed that functional performance of wrist of mild to moderate CTS patients in the acupuncture+splint group was better than the control group (splinting alone) (23). In another study, Tal-Akabi and Rushton (2000)

studied and compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups was better than the control group but the difference was not significant so carpal bone mobilization for 3 weeks improves CTS patients function but the results were not statistically significant because of the small sample size (55).

CTS give arises to lose the physiologic mobility of the median nerve. According to Wright et al and Szabo et al study, during flexion to an extension, the median nerve glides 19.6 mm and during fingers flexion, it would be 9 mm. Also, the flexor digitorum superficialis tendons glide 30 mm during fingers flexion in the CT (56, 57). Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (58).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved.

Conclusion

The results of this study indicate that conservative groups were better than the control group, but the difference was statistically significant and weak just in an efficacy of exercise therapy on ROM of flexion and an efficacy of acupuncture on pinch force. Probably because of the limited case data. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a larger sample and long-term monitoring.

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OPEN PEER REVIEW

Revision (4)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (4) 29 Jan 2019

Dear AE,
I believe the article is in the scope of AsJSM. but still, some changes are required.
1. I am happy to say, the English are better now but it still needs improvement:
including but not limited to:
which are divided into two groups [s]:
and 8 question[s] about functional status
2. The introduction should follow this pattern: a. What's known b. What's unknown (limitations and gaps in previous studies) c. Your burning question/hypothesis/aim d. Your experimental approach e. Why your experimental approach is new and different and important (fills in the gaps) in 3-4 paragraphs, please take the reader step by step from what is known to what is unknown. End with your specific question. please summarize at a high level! Leave detailed descriptions, speculations, and criticisms of particular studies for the discussion.
Thanks.

REFEREE: Reviewer | **Revision** (4) 30 Jan 2019

Dear AE,
The authors have done my comment nicely and the paper is improved but it is not acceptable in current form.
- The tense used in your paper should be checked and it is better if you use past tense. For example, "To find acupoints the examiner asks patients…"
- There are many typos in your paper and the writing is not acceptable.
For example one time you write same this: "Vincent et al (2016)'s study.."
- Other times you write the same this: "Akalin et al study on.."
- Another example is, "The whole patients with CTS at the Hospital in 2017 were assessed in the study was 237 and after screened for eligibility at the Clinic 177 patients excluded and 60 remains to included (Figure 1)".
- Another example, "After appearing of the tendons, the needle located at between the…"
- Total number of participants should be shown with "N" not "n".
- Many times, you talked about studies, but you have just reported one study,
For example, "These acupoints chose because of their efficiency which is reported in previous studies
(41)".

- Please omit this sentence: “None of the patients dropped out in this study”.
- Units are missing in tables.
- In Table 2, we can see a meaningful P-value for Grip Force and Extension in control group. Please justify it.
- In Table2, in differences section, in some section, SD is bigger than the mean. Could you please double check it with a statistician?
Thanks.

REFEREE: Associate Editor | **Revision (4)** 14 Feb 2019

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

REFEREE: EIC | **Revision (4)** 16 Feb 2019

Dear Author,
The third round of peer review of your manuscript is completed. I now have the reports of the Referees, which suggest that your manuscript needs more correction.
Thanks.

OPEN PEER REVIEW

Revision (5)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

The effectiveness of exercise therapy and dry needling on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

**** Reviewer 1:

The authors have done my comment nicely and the paper is improved but it is not acceptable in current form.

1. The tense used in your paper should be checked and it is better if you use past tense.

For example, "To find acupoints the examiner asks patients…"
There are many typos in your paper and the writing is not acceptable.
For example one time you write same this: "Vincent et al (2016)'s study.."
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Other example, "The whole patients with CTS at the Hospital in 2017 were assessed in the study was 237 and after screened for eligibility at the Clinic 177 patients excluded and 60 remains to included (Figure 1)".
Other example, "After appearing of the tendons, the needle located at between the…"
Total number of participants should be shown with "N" not "n".

Response:
Done. We appreciate this concern and in accordance with the reviewer's suggestion. We have now rewritten it with Yellow Highlight.

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2. Many times, you talked about studies, but you have just reported one study, For example, "These acupoints chose because of their efficiency which is reported in previous studies (41)".

Response:
Done. We appreciate this concern. Pardon us, it was a miswriting in the sentence which the reviewer mentions it and now rewritten it with Yellow highlight. And in the other sentence which we use the "previous studies," we cited to 5 articles and we have colored with red in page 3 the last paragraph:

There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (33-37)

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3. Please omit this sentence: "None of the patients dropped out in this study".

Response:
Done. We appreciate this concern.

---

4. Units are missing in tables.

Response:
Done. We appreciate this concern.

---

5. In Table 2, we can see a meaningful P value for Grip Force and Extension in the control group. Please justify it.

6. In Table2, in differences section, in some section, SD is bigger than mean. Could you please double check it with a statistician?

Response:
Done. We appreciate this concern. Pardon us, some numbers have been moved during the translation of articles to English and now table 2 rewritten it with Yellow highlight.

The effectiveness of exercise therapy and dry needling on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). CTS found in 3.8% of the general population and can occur in all ages (3), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain,

numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms often get worse at night, and During the day, activities that require hand bending are difficult to handle (3, 4).

Different treatments methods for CTS exist. they are divided into two groups: conservative treatment and surgery (5). Conservative treatments are usually used for patients with mild to moderate CTS (6), These treatments include the following: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint (5). Although the effectiveness of using splints and steroids as primary treatments to improve the patient's symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (7). Also, each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (8, 9).

In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (3, 10, 11). Also although the National Institute of Health (NIH) has approved the use of acupuncture for the management of mild to moderate CTS there is controversy about its effectiveness (12). The studies over a couple of decades have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (13-16). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that "acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression." (17) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (13, 18). Vincent et al (2016)'s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (19). Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improves wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (19). Zavela,

et al. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (20).

On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization (21). Akalin et al. (2002) study on 28 CTS patients indicates that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (22). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (23). In many guidelines, wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (24-26).

Our study differs from previous studies in that instead of comparing acupuncture, exercise therapy, and splint treatments. We chose this trail because there is no specific recommendation about the use of acupuncture and the effectiveness of exercise therapy (19, 27, 28). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with Comparison of acupuncture and exercise therapy effectiveness on ones (29-33).

The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy. Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

Methods

The present study is a randomized, controlled clinical trial which is performed on 60 patients with Carpal tunnel syndrome, referring to the Sports Medicine Clinic of

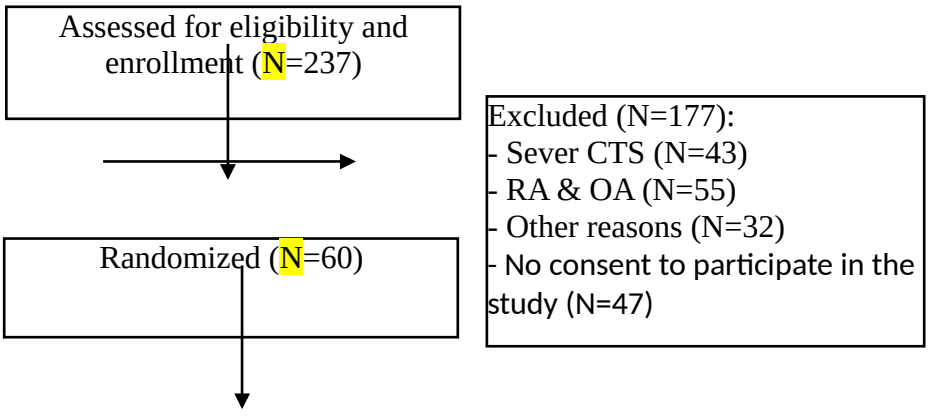
Imam Hossein Hospital in Tehran in 2017. Of the 237 patients evaluated, only 60 patients had the required conditions for entry into the study (Figure 1).

The definitive diagnosis of patients and disease severity was made by the neurologist based on the history and physical examination and using EMG/NCV. Patients enrolled in the study after giving explanations and obtaining informed consent.

The following were criteria for the inclusion of patients to study: mild to moderate CTS, the lack of severe limitation in upper extremities that inhibit the desired exercise from the patient (such as wrist fracture, deep scarring, burning, presence of cyst or tumors in the area of wrists, and history of wrist surgery), no symptoms of muscle atrophy or weakness, absence of autoimmune or inflammatory diseases, no previous taking steroidal drugs, using splint and any treatment for CTS.

Exclusion criteria were as follows: severe stage of the disease during the study, Refusal to perform exercises, no referring at the requested time for acupuncture, using acetaminophen for more than 7 days because of severe pain, pregnancy, diabetes mellitus, using NSAID or gabapentin or any other medication or any contraindication for needling such as, local infection, bleeding tendency or a history of needling shock.

At first, all patients were under full clinical examination that has been explained in the Patients evaluation subsection. The demographic and history profiles were also completed for all patients. This form included demographic characteristics (age, gender, place of living, marital status), medical history and Clinical information such as smoking history and alcohol consumption, underlying diseases, weight, height, drugs used and clinical characteristics of CTS including pain severity, affected hand, and duration of CTS.



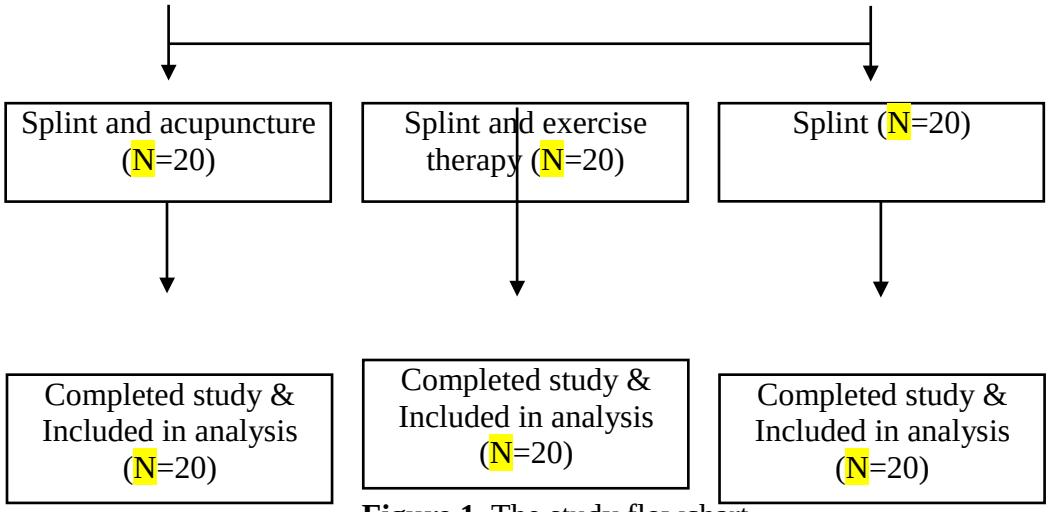


Figure 1. The study flowchart.

Intervention

Block randomization is a commonly used method in clinical trial design to reduce bias (34). Random Allocation Software is a very good and free software to control different attributes of the random allocation sequence. (35)Patients were randomly divided into three equal groups (20 patients in each group). In the first group, the patients received only night splint for 6 weeks (control). In the second group, the splint and exercise therapy were used. Exercise therapy included tendon gliding and median nerve gliding, two times a day for 6 weeks (Figure 2). In the third group, splint and 12 sessions of 40 minutes' electroacupuncture were performed (2 times a week) in two points of PC-7 (Daling) and PC-6 (Nei Guan). PC-7 was located on the flexor area of the forearm in the middle transverse crease between palmaris longus and flexor carpi radialis tendons and PC-6 is 5 cm proximal to PC-7. (36) (Figure 3). These acupoints were chosen because of their efficiency which had been reported in a previous study (37). To find acupoints we asked patients to press the little and thumb finger together for the better presentation of the tendons. We used the thin sterile needle (0.25×25mm size gauge) with the frequency of 60-100 Hz and the intensity of the flow went up to the threshold of pain tolerance. The needles were inserted vertically into specific points in the depth of 2-5 mm. Acetaminophen was used in all three groups if needed.

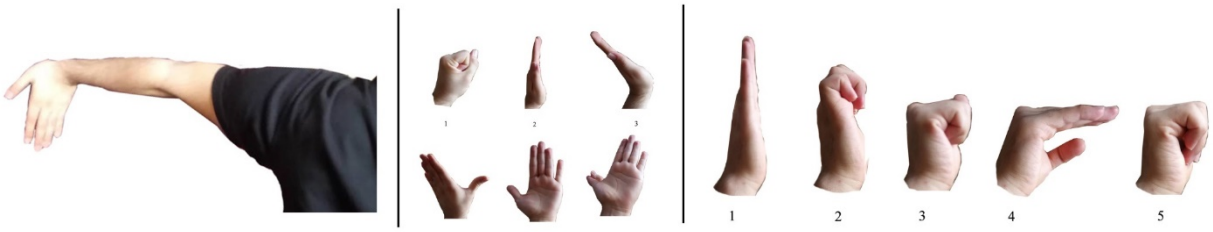


Figure 2. Tendon gliding (Right) and median nerve gliding exercise (middle and left). The patients were asked to do each position for 5 seconds, and repeat each position 10 times for at least two times a day.



Figure 3. Acupuncture points.

Patient evaluation

The definitive diagnosis was given by the neurologist based on the history and physical examination and using EMG/NCV.

To evaluate the response to treatment, the following parameters were measured in all groups: pinch and grip forces, ROM (flexion and extension), quality of life (symptoms and functional status) and pain intensity

We used Carpal Tunnel Questionnaires to evaluate the response to treatment quality of life (symptoms and functional status) which is recommended by the American Academy of Orthopedic Surgeons (38, 39) and visual analog scale (VAS) for pain intensity of patients. The first one was The Boston Carpet Tunnel Questionnaire (BCTQ) which used to evaluate the patients' performance and the severity of symptoms. BCTQ has 11 questions about the severity of the symptoms (BCTQ SYMPT) and 8 questions about functional status (BCTQ FUNCT). The items of each scale were scored from 1 (mildest) to 5 (most severe). The reliability and sensitivity of the Persian version which used in the current study were confirmed in a previous study(40) Pain intensity measured by using the visual

analog scale (VAS). The patients evaluated their pain intensity from zero (complete analgesia) to 10 (the most experienced patient's pain).

The Physical examination which used in the current study was made based on at least one of the following clinical criteria: Tinel sign test, Phalen maneuver test, numbness or tingling in fingers, median nerve compression (41). Patients that diagnosed with CTS were confirmed by the presence of at least one of EMG/NCV criteria which were included: DML ≥ 4.2 ms, DSL ≥ 3.6 ms, and W-P SNCV < 40 ms (42).

The maximum grip force (in kg) was measured by using Jamar hand hydraulic dynamometer. Moreover, pinch dynamometer was used to evaluate the pinch force. All the measurements were performed when the patient was in a sitting position, shoulder in adduction and neutral rotation, elbow in 90º flexion, forearm in a neutral position, wrist in 0º to 30º dorsiflexion and 0º to 15º ulnar flexion. The patients were asked to maintain maximum grip strength. Measurements were repeated for three times and their mean was calculated. During measurement, Jamar dynamometer was kept from the top and the bottom in order to prevent from affecting device weight to the measurement. All the measurements were evaluated by the same device both before and after the treatment (43). To evaluate the range of motion (ROM) the active wrist flexion and extension were measured by using goniometer (Plastic goniometer MSD). All the measurements were performed in a sitting position with shoulder abducted to 90º, the elbow flexed to 90º, and the palm of the hand facing the ground. The forearm was midway between supination and pronation. The examiner was a caution to avoid radial or ulnar deviation of the wrist and flexion of the fingers. The examiner put the center fulcrum of goniometer on the lateral aspect of the wrist over the triquetrum and aligned proximal and distal arm with the lateral midline of the ulna and fifth metacarpal respectively. Then the examiner asked the patients to flex the wrist. The examiner used one hand to align the distal arm of the goniometer with the 5^{th} metacarpal at the end of the flexion while the patients maintaining the wrist in that position and the ROM degrees was recorded. To measure active wrist extension, the examiner performed all process like active wrist flexion except in extension movements (44). At this stage, none of the patients were excluded from the study.

Entrance and evaluation of information after the end of treatment was carried out by a researcher who did not know about grouping the patients. In another word, neither the patient nor the therapist and study investigator was aware of which

groups is treatments or a control (triple-blind, randomized clinical trial). However, the sports medicine specialist and student were aware of the procedure and groups in order to prevent the inadvertent pre and post-intervention events.

Statistical Analysis

Version 22 of SPSS software was used to statistical analysis. Normality for variables was assessed using the Kolmogorov Smirnov test. Obtained data were analyzed by descriptive statistics including frequency, mean, standard deviation, frequency percentage and inferential statistics including paired sample t-test, Chi-square, and analysis of variance (ANOVA). A p-value < 0.05 was considered statistically significant.

Ethics approval

The protocol of this study was approved by the Ethics and Research Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1395.152) and was registered in IRCT under the code IRCT20180212038693N1.

Results

In the current study, 55 females and 5 males with the mean age of 49.23 ± 8.96 (29-70) participated. Demographic and clinical information of the patients is provided in table1. There was no statistically significant difference between age, gender, height, weight, job, the presence of systemic disease, involved hand and disease severity were seen in three treatment groups ($P>0.05$).

The current study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist were significantly improved in CTS patients at the end of 6 weeks in all three groups ($P<0.05$). Although using brace alone (control group) did not have any significant effect on the wrist flexion and extension ($P=0.098$ & 0.093) (table 2).

The between groups analysis indicate that acupuncture affected the pinch force more than exercise therapy and it was statistically significant $F(df=2) =0.035$, $P=0.001$ but weak (P Eta Squared=0.001). Also, the efficacy of exercise therapy was more than acupuncture in parameters of grip force and ROM (both flexion and extension) but just ROM of flexion was statistically significant $F(df=2) =0.000$, $P=0.001$ but weak (P Eta Squared=0.012).

Table 1- Patient characteristics at baseline*

Variable	Brace+ acupuncture (N=20)	Brace+ Exercise therapy (N=20)	Control (N=20)	P-value**
Age (year)	50.75±9.59	49.55±8.41	47.4±8.96	0.495
Gender	Female: 18 (90) Male: 2 (10)	Female: 19 (95) Male: 1 (5)	Female: 19 (95) Male: 1 (5)	0.804
Weight (kg)	77.5±12.85	78.78±10.8	77.9±9.4	0.933
Height (cm)	159.35±5.3	160.2±5.8	163.5±7.8	0.098
Job	Employed: 18 (90) Housewife: 2 (10)	Employed: 15 (75) Housewife: 5 (25)	Employed: 12 (60) Housewife: 8 (40)	0.077
systemic disease (yes)	9 (11)	5 (25)	6 (30)	0.377
Affected hand	Right: 9 (45) Left: 11 (52)	Right: 8 (40) Left: 12 (60)	Right: 12 (60) Left: 8 (40)	0.420
Disease severity	Mild: 13 (65) Moderate: 7 (35)	Mild: 12 (60) Moderate: 8 (40)	Mild: 13 (65) Moderate: 7 (35)	0.931

*Data are presented as mean±SD or frequency (%)
**Significance at p≤0.05.

Table 2. Mean scores of grip and pinch force and range of motion (flexion and extension) in CTS patients

Variable	Group	Baseline (mean±SD)	After treatment (mean±SD)	difference	P-value	Effect Size
Grip force (kg)	Control	16.9 ± 5	17.95 ± 5.1	1.05 ± 1.43	0.054	0.103
	Brace+ Exercise therapy	18.78 ± 5.7	22.95 ± 5.1	4.15 ± 4.1	<0.001	0.359
	Brace+ acupuncture	18.8 ± 4.32	21.15 ± 4.78	2.35 ± 4.33	0.025	0.249
Pinch force (kg)	Control	6.03 ± 1.4	6.67 ± 1.7	0.65 ± 0.52	0.082	0.201
	Brace+ Exercise therapy	5.26 ± 1.23	6.58 ± 1.4	1.05 ± 1	<0.001	0.447
	Brace+ acupuncture	5.45 ± 0.66	6.57 ± 0.92	1.12 ± 1.08	<0.001	0.573
Flexion (cm)	Control	83.28 ± 3.8	83.62 ± 3.89	0.34 ± 0.89	0.098	0.044
	Brace+ Exercise therapy	77.57 ± 6.15	83.17 ± 3.42	5.6 ± 4.21	<0.001	0.490
	Brace+ acupuncture	82.47 ± 4.31	84.13 ± 3.39	1.67 ± 2.01	0.002	0.209
Extension (cm)	Control	66.2 ± 5.39	67.37 ± 4.77	1.16 ± 1.28	0.093	0.114
	Brace+ Exercise therapy	64.77 ± 3.69	71.32 ± 2.9	6.55 ± 2.97	<0.001	0.702
	Brace+ acupuncture	68.36 ± 3.14	69.75 ± 3.84	1.39 ± 2.34	0.015	0.194

SD = standard deviation.

Discussion

The aim of the current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function, including gripping, pinching, and range of motion of the wrist in patients with mild to moderate CTS.

In the current study, no significant statistical difference existed between age, gender, height, weight, job, systemic disease, involved hand and disease severity in three treatment groups. Also, there was no significant difference between variables of pinch and grip force, wrist flexion and extension in the three groups before treatment which shows the randomization of samples and the absence of bias in sample selection.

Based on this study's findings, in all three groups gripping and pinching force of the wrist after treatment were increased significantly. But exercises had an effect on ROM of flexion and acupuncture had an effect on pinching but the effect sizes were weak. Also splint alone had the least effect on gripping and pinching of CTS patients.

The results of the current study indicate that the effectiveness of electroacupuncture with night splinting is more than splinting alone. In addition, it can improve griping power in CTS patients and increase hand grip strength. These results are consistent with the results of other studies (19, 20, 45-47). On the other hand, Yao et al. (2012) in a randomized controlled study investigated the effectiveness of 6 sessions of acupuncture compared to placebo acupuncture for treating patients with CTS. Night splinting was also used in both groups. After 6 weeks both treatment and placebo groups had significant improvement in pinching power In comparison with the baseline, but there was no significant difference between the groups so it was reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (48).

Yao et al reported that acupuncture with bracing has no significant effect on the treatment of mild to moderate CTS (48). These results are not consistent with the finding of the current study. Although all three groups showed significant improvement in pinching force in the current study but the improvement in the acupuncture group was higher than the control group. This difference could be

related to the diversity in intervention methods, a number of acupuncture sessions and primary characteristics of patients.in hessami et al study showed that use of splint alone in mild CTS is a suitable and adequate treatment; however, in moderate CTS, taking gabapentin along with splinting and exercise indicated better treatment results compared to splinting alone (49).

The current study found that nerve and tendon gliding exercises can improve grip and pinch strength which is consistent with Pinar et al. (2005) results (23). Moreover, In Alkalin, *et al*. (2002) study the effectiveness of nerve and tendon gliding exercises along with splinting was compared with splinting alone. Results showed an improvement in pinching force in both groups after treatment but the improvement in the mobilization group was higher than splint alone. These results are consistent with the results of the current study (22). In another study by Madenci, *et al*. (2012) was also reported that tendon and nerve gliding exercises with night splint significantly improved the gripping force in CTS patients (43). Results of Penas, *et al*. study (2017) in Spain also showed that exercise therapy is effective in improving pinching and gripping power in CTS patients (50).

The results of the current study showed significant improvement in wrist range of motion in both acupuncture and exercise therapy group but using splint alone had no effect on the improvement of them. On the other hand, exercise therapy had the most effect on increasing the range of motion. To confirm these results, Chung, *et al.* (2016) also showed that wrist functional performance in patients with mild to moderate CTS in the acupuncture+splint group was better than the control group (splinting alone) (19). In another study, Tal-Akabi and Rushton (2000) compared the effectiveness of two treatment methods of carpal bone mobilization and neurodynamic mobilization with the control group in CTS patients. Results showed that wrist range of motion (flexion and extension) in both treatment groups were better than the control group but the difference was not statistically significant because of the small sample size (51).

CTS is caused by the loss of the physiological movements of the median nerve. Excursion of the wrist flexor tendons required for full finger flexion changed from 23 to 31 mm also Median nerve displacement changed from 9 to 14 mm. (52). during wrist extension to flexion, the median nerve at wrist glides 19.6 mm approximately (53) Hence, the nerve and tendon gliding exercises could help to an increased relative excursion of the median nerve in the CT which leads to improvement in the grip and pinch strength (54).

Lastly it should be noted that the current study was done for the first time in comparing the effectiveness of two methods of exercise therapy and acupuncture in treating mild to moderate CTS and achieved valuable information on the effectiveness of exercise therapy and acupuncture in treating these patients which were in line with the results of other similar studies.

Limitations of the present study include the relatively small sample size and the lack of mid-term and long-term monitoring of patients, a limited number of therapeutic sessions in the acupuncture group and if treatment sessions are added, better treatment outcomes might be achieved.

Conclusion

this study showed the grip force, pinch force and range of motion (flexion and extension) of the wrist were significantly improved in CTS patients at the end of 6 weeks in all three groups. Although using brace alone (control group) did not have any significant effect on the wrist flexion and extension. Probably because of the limited case data. Since there has been no study comparing the effectiveness of acupuncture with exercises in the treatment of CTS, it is not possible to compare the findings of this study with the results of other studies. Therefore, our results need to be confirmed in future studies with a larger sample and long-term monitoring.

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****** Reviewer 2:**

Response:

Done. We appreciate this concern and in accordance with the reviewer's suggestion. We omitted some sentences and have now rewritten the introduction section with Yellow Highlight.

The effectiveness of exercise therapy and dry needling on wrist range of motion, pinch and grip force in carpal tunnel syndrome: a randomized clinical Trial

Introduction

Carpal Tunnel Syndrome (CTS) is the most common peripheral nerve entrapment and also the most common pressure neuropathy in upper limbs (1, 2). CTS found in 3.8% of the general population and can occur in all ages (3), although it mostly influences the 40-60 years old (2). Clinical characteristics of CTS include pain, numbness, pain or paresthesia in distal parts of the median nerve (thumb, pointing finger, middle finger and radial part of the ring finger) and a decrease of gripping power and hand function. These symptoms worsen at night, and it causes a problem during the day activities needing hand bending (3, 4).

Different treatments methods for CTS exist which are divided into two groups: conservative treatment and surgery (5). Conservative treatments are usually used for patients with mild to moderate CTS (6), These treatments include the following: oral steroids, injection of corticosteroids, vitamins B6 and B12, nonsteroidal anti-inflammatory drugs (NSAIDs), ultrasound, yoga, carpal bone mobilization and using hand splint (5). Although the effectiveness of using splints and steroids as primary treatments to improve the patient's symptoms has been shown in recent studies the effects of these methods are usually temporary and transient (7). Also, each of these methods has some complication and side effects. For example, gastrointestinal, renal and liver side effects in using nonsteroidal or steroidal drugs, tendon rupture, and the probability of damage to the nerve after localized injection of corticosteroids (8, 9).

In some studies, the effect of acupuncture and massage therapy and stretching exercises have been evaluated as a complementary or alternative treatment which showed very different results on symptoms and function of CTS patient (3, 10, 11). Also although the National Institute of Health (NIH) has approved the use of

acupuncture for the management of mild to moderate CTS there is controversy about its effectiveness (12). The studies over a couple of decades have been conducted using acupuncture and electroacupuncture after a peripheral nerve injury can promote nerve repair and blood supply (13-16). Yang et al determine the effectiveness of acupuncture and oral steroids on CTS. Their results show that "acupuncture treatment can be considered as an alternative therapy for those who do not opt for early surgical decompression." (17) Using full-time splints are effective but there is a limitation in patients daily activities which cause the ones to complain (13, 18). Vincent et al (2016)'s study on 181 CTS patients with chronic mild to moderate symptoms shows that combining electroacupuncture with nocturnal splints treatments provide small improvements in symptoms (19). Chung, *et al*. studies (2016) showed that the use of acupuncture with splinting or splint alone significantly improves wrist skills and pinching force of mild to moderate CTS patients without the need to surgery, but the effectiveness of electroacupuncture with night splinting is more than splinting alone (19). Zavela, *et al*. (2010) also reported the effectiveness of acupuncture in recovering normal griping power in CTS patients (20).

On the other hand, Heebner and Roddney (2008) in a study evaluated the effect of adding nerve mobilization exercises (nerve gliding) to standard care (splint and tendon gliding) in patients with carpal tunnel syndrome. Evaluating the results of a range of motion extension of elbow and wrist in an upper limb median nerve tension test in the first and sixth month after treatment showed no significant difference in results between two group of standard care and nerve mobilization (21). Akalin et al. (2002) study on 28 CTS patients indicates that the nerve and tendon gliding exercise have a better effect but it was not statistically significant and they suggest for further research on the topic (22). Pinar et al compared the nerve gliding exercise combined with conservative therapy with a splint on 26 women with CTS. They found that nerve gliding exercise can improve functional, especially in grip strength, and more pain reduction (23). In many guidelines, wrist splinting is recommended as the primary treatment option for CTS patients despite no promise in its effectiveness (24-26).

Our study differs from previous studies in that instead of comparing acupuncture, exercise therapy, and splint treatments. We chose this trail because there is no specific recommendation about the use of acupuncture and the effectiveness of exercise therapy (19, 27, 28). There is limited evidence regarding the efficacy of acupuncture and exercise therapy and previous studies of CTS have not dealt with

Comparison of acupuncture and exercise therapy effectiveness on ones (29-33). The specific controversy which drives the research in which to compare and determine the effectiveness of between the conservative treatments, acupuncture and exercise therapy. Because of the low cost and non-invasive nature of acupuncture and exercise therapy and relative acceptance of these treatments in the society and presence of limited studies about their effectiveness in CTS patients, so the aim of current study was comparing the short-term effects (6 weeks) of acupuncture and nerve and tendon gliding exercises on patients' function including gripping, pinching, and range of motion of the wrist of mild to moderate CTS patients.

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OPEN PEER REVIEW

Revision (5)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (5) 9 Sep 2019

Dear EIC,
The authors have modified the manuscript accordingly and have provided specific answers in an accurate manner. I suggest that this version is suitable for publication.
Thanks.

REFEREE: EIC | **Revision** (5) 9 Sep 2019

Dear Authors,
The second round of peer review of your manuscript has been completed, and I am pleased to inform you that your manuscript has now been accepted for publication in our journal.
We look forward to working with you again in the future.
Thanks.