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Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9170-review.doc).

Title: Eccentric training as a new approach for rotator cuff tendinopathy – review and perspectives

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The comments of reviewers surely contributed for a better quality of the paper. Each of the comments of the review team is addressed below and alterations were made to the manuscript. We have highlighted the corresponding alterations to the manuscript.

The focus of the review is eccentric training for shoulder tendinopathy including pathology. I think there are two important points in order that readers understand this topic clearly.

First, we should use main terms carefully (i.e. shoulder tendinopathy, rotator cuff tendinopathy, painful tendon, tendon lesion, tendinosis, tendon injury, tendon disorders, etc...). What is your main topic? Training for shoulder tendinopathy (including deltoid and biceps tendinopathies)? Or just focus on rotator cuff tendinopathy? And please reconsider and refine these terms (I refer to " Knee Surg Sports Traumatol Arthrosc. 2011 May;19(5):835-41. Terminology for Achilles tendon related disorders").

Second, each section is well organized. Some of them, however, seem to be a little bit vague. We should focus on shoulder (or rotator cuff) tendinopathy concretely in addition to general tendon and tendopathy explanations.

We agree with the reviewer. After a careful reading we chose as the main topic rotator cuff tendinopathy. As such, other terms (shoulder tendinopathy, rotator cuff tendinopathy, painful tendon, tendon lesion, tendinosis, tendon injury, tendon disorders, etc...) were replaced when appropriate. Also, we now bring more information about rotator cuff tendons instead of general tendon. Considering the rotator cuff tendons, more information is provided about the supraspinatus tendon as this muscle is the most commonly involved.

#Abstract

1-1

"but less evidence exists about its effectiveness for the rotator cuff tendons."

"the rotator cuff tendons" → "rotator cuff tendinopathy" or "shoulder tendinopathy"?

"Rotator cuff tendons" was replaced by "rotator cuff tendinopathy" (page 2).

1-2

Few studies were done on eccentric training for people with shoulder pain.

“shoulder pain” → “shoulder tendinopathy”?

“shoulder” was replaced by “rotator cuff tendinopathy” (page 2).

#INTRODUCTION

1-3

“Although tendon problems are very frequent, they are not always easy to manage. Rehabilitation of the tendon can take several months and conservative treatment is usually used as it can help the healing of the tendon by changing its metabolism and their structural and mechanical properties^[5].”

“Rehabilitation of the tendon” → “Rehabilitation of shoulder tendinopathy”?

“Rehabilitation of the tendon” was replaced by “Rehabilitation of shoulder tendinopathy” (page 4).

1-4

take several months and conservative treatment is usually used as it can help the healing of the tendon by changing its metabolism and their structural and mechanical properties^[5].

(Please add a definition; “What is eccentric exercise? And what is difference with conventional training regimen?” here) There is some evidence that eccentric training may be effective in the management of tendinopathy of the Achilles and patellar tendons ^[6-8].

Done as suggested (page 4).

1-5

“Histological changes in the supraspinatus tendon have been found to have similarities with those of the Achilles and patellar tendons^[9,10].”

“tendon” → “tendinosis”? What kind of pathological change? What are histological similarities in these tendinosis? Please explain it with detail.

“tendon” was replaced by “tendinosis”. Pathological changes and similarities in these tendinosis are now described on page 4.

1-6

“Rotator cuff tendinopathy is one of the most common causesthe supraspinatus tendon have already been described in subjects who were treated with subacromial decompression.”

This section is an explanation of shoulder impingement syndrome. It is better to move this section into other section, for example “*Etiology and pathologic processes of tendinopathies*” section.

Done as suggested (page 8).

1-7

The purpose of this paper is to review the studies that used eccentric training program in the treatment of shoulder impingement as well as the tendon structure, the healing process and the possible mechanisms for why eccentric exercises can be effective in treating tendinopathy.

“shoulder impingement” → “shoulder tendinopathy”?

“shoulder impingement” was replaced by “rotator cuff tendinopathy” (page 4).

Tendon structure

1-8

This section is explained about tendon structure in general point of view. We would like to know information about shoulder tendons (or rotator cuff tendons) and somewhat differences between shoulder tendons and other tendons (i.e. Achilles tendon and patellar tendon) with detail. Please add information about shoulder tendon structure.

Information about shoulder tendon structure is now added to the manuscript (pages 5 and 6).

Tendon composition

1-9

This section is also explained in general tendon composition. We would like to know information about shoulder tendons and somewhat difference between other tendons (i.e. Achilles tendon and patellar tendon) and shoulder tendons with detail.

Information about composition of shoulder tendons is now provided on pages 7 and 8.

Tenocytes biology: mechanotransduction

1-10

This section is presenting important effects of exercise in terms of basic science. For better understanding, I recommend you to revise this title “*Tenocytes biology: mechanotransduction in exercise*”.

The title was changed as suggested (page 10).

Tendon lesion and healing processes

1-11

This section is explained in general point of view. We would like to know information about tendon healing process in the shoulder as well. Please add information about shoulder tendons.

Information about shoulder tendons was added (pages 11-14).

1-12

“The changes in cellular activity in the extracellular matrix have been identified as a precursor of tendon lesion^[44].”

What kind of change can we see? Please describe it concretely.

Changes in the extracellular matrix are now described in the manuscript (page 11).

1-13

“Another interesting point associated to rehabilitation process is the deterioration of the tendon after immobilization. A decrease of protein synthesis^[49] and an increase of collagenase activity in damaged and not damaged fascicles^[50] degenerate the immobilized tendon. Curiously, these deleterious processes have been stopped through cyclic stretching in *in vitro* studies^[51,52].”

I think this section should be composed in “Introduction” or “Conservative treatment” section as a demerit of the conventional rehabilitation regime. Please consider to move this section into “Introduction” or “Conservative treatment” section

This section was moved into “Conservative Treatment” (page 16).

Etiology and pathologic processes of tendinopathies

1-14

I think it is better to move this section just after “Tendon composition” section. This section is very important explaining terminology of “tendiopathy” and “tendinosis”. We should show this section to readers earlier.

Done as suggested (page 8).

1-15

“Rotator cuff tendinopathy is one of the most common causes of shoulder pain^[15,16] and is frequently labeled as shoulder impingement^[17].”

This sentence does not make sense. Tendinopathy is a clinical condition with pain (Feeling pain in a tendon site despite histological findings, is “tendinopathy”). “Shoulder impingement is one of the most common causes of shoulder tendinopathy.” sounds better.

Done as suggested (page 8).

Clinical assessment of shoulder tendinopathy

1-16

Why do you use “the painful tendon”? If you have any reason, please let me know. If not, please revise this title “Clinical assessment of shoulder tendinopathy”. And, please describe concrete explanation. For example, VAS score, DASH score, and some pain provocative tests (i.e. SSP test, ISP test, Lift off test, Speed test, etc) in the shoulder.

The title was changed to “Clinical assessment of shoulder tendinopathy” as suggested by the reviewer. The use of questionnaires and special tests is now described in the manuscript (pages 14 and 15).

1-17

“To diagnose a painful tendon, the anamnesis should include questions that allow the

clinician to recognize if there is increase in inactivity and to identify which are the aggravating activities and also the relieving factors.”

“a painful tendon” → “tendinopathy”?

“a painful tendon” was replaced by “tendinopathy” (page 15)

1-18

“Imaging assessment (ultrasound and magnetic resonance) improves the diagnosis of tendinopathy as it provides morphological information^[70] about the tendon leading to a better clinician’s make-decision.”

What kind of findings can we see in ultrasound and MRI? Please describe it concretely.

This information is now added in the manuscript (page 15).

Conservative treatment of the painful tendon

1-19

Again, why do you use “the painful tendon”? If you have any reason, please let me know. If not, please revise this title “*Conservative treatment of shoulder tendinopathy*”.

Done as suggested by the reviewer (page 15).

1-20

“The presence and the size of the rotator cuff tears could limit the therapeutic capacity of the exercises that underline the necessity of a correct diagnostic^[8,72].”

Do you mean the therapeutic capacity of exercise is limited by the presence and the size of the rotator cuff tear? If so, please describe the short algorithm (With >XX mm partial tear in MRI, we should not perform exercise, for example).

There is no information in the literature with regards to the size of the rotator cuff tear that exercise should not be performed. However, massive chronic rotator cuff tears are often associated to restricted or loss of active shoulder range of motion. This information was added on page 15.

Also, definition of massive rotator cuff tear is not clear in the literature. Cofield et al (1982) defined a massive tear as being >5 cm in diameter, whereas Gerber et al (2000) defined a massive tear as having 2 or more tendons involved.

1-21

“Relative rest and stretching techniques must be applied in the correct doses because its capacity of turnover the collagen synthesis.”

“the correct dose”; How much dose should we perform in general?

Information added on page 16.

Eccentric training

1-22

“This technique has been advocated as a treatment of painful tendons, such as chronic Achilles tendinosis, patellar tendinosis, lateral humeral epicondylagia and rotator cuff tendinosis^[26].”

“painful tendons” → “tendinopathy”?

And, please recheck “tendinosis” is correct?

“painful tendons” and “tendinosis” were replaced by “tendinopathy” (page 16).

1-23

“In fact, it has been hypothesized that the resolution of the tendinosis neovascularisation by eccentric training, closely associated with new nerve endings, will be disturbed or even destroyed due to a lack of perfusion by their nutrient neovessels.”

Please add a reference here.

A reference was added on page 18 (**Knobloch K**. The role of tendon microcirculation in Achilles and patellar tendinopathy. *J Orthop Surg Res* 2008; 3: 18).

1-24

The influence of sex in eccentric training effects has been studied, but there are no clear answers on whether sex differences exist in muscle after either submaximal or maximal exercise protocols^[89].

This sentence is too vague. What is a main message of this paper? Please note it clearly.

We agree with the reviewer that this sentence was too vague. We have decided to delete it from the manuscript.

*Negative effects of eccentric training*

1-25

This section is well organized. Please integrate this section into “Eccentric training” section.

Done as suggested.

*Rotator cuff tendinopathy*

1-26

Your “Rotator cuff tendinopathy” section is explaining eccentric trainings for shoulder tendinopathy as well. I think this is a main section in this review article. Please integrate this section into “Eccentric training” section.

Done as suggested.

Thank you.