

# Italian consensus conference on guidelines for conservative treatment on lower limb muscle injuries in athlete

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## ABSTRACT

Provide the state of the art concerning (1) biology and aetiology, (2) classification, (3) clinical assessment and (4) conservative treatment of lower limb muscle injuries (MI) in athletes. Seventy international experts with different medical backgrounds participated in the consensus conference. They discussed and approved a consensus composed of four sections which are presented in these documents. This paper represents a synthesis of the consensus conference, the following four sections are discussed: (i) The biology and aetiology of MIs. A definition of MI was formulated and some key points concerning physiology and pathogenesis of MIs were discussed. (ii) The MI classification. A classification of MIs was proposed. (iii) The MI clinical assessment, in which were discussed anamnesis, inspection and clinical examination and are provided the relative guidelines. (iv) The MI conservative treatment, in which are provided the guidelines for conservative treatment based on the severity of the lesion. Furthermore, instrumental therapy and pharmacological treatment were discussed. Knowledge of the aetiology and biology of MIs is an essential prerequisite in order to plan and conduct a rehabilitation plan. Another important aspect is the use of a rational MI classification on prognostic values. We propose a classification based on radiological investigations performed by ultrasonography and MRI strongly linked to prognostic factors. Furthermore, the consensus conference results will be able to provide fundamental guidelines for diagnostic and rehabilitation practice, also considering instrumental therapy and pharmacological treatment of MI. Expert opinion, level IV.

## INTRODUCTION

Muscle injuries (MI) are the most common trauma both in team and individual sports and are responsible for most of the time lost in both training and competition.<sup>1-3</sup> In professional football (soccer), they account for 30%<sup>4</sup> and in track and field 48% of all injuries recorded.<sup>1</sup> In soccer, the muscle groups most prone to injury are the hamstrings (37% of all the MIs),<sup>1-5</sup> followed by the adductors (23%),<sup>4</sup> rectus femoris (19%)<sup>4</sup> and calf muscles (13%).<sup>4,6</sup> However, despite the strong interest of clinicians and researchers in this topic, there is still no consensus conference (CC) which simultaneously covered the aetiopathogenesis, classification, clinical examination and treatment of MIs.<sup>3,6</sup>

## BACKGROUND OF ITALIAN CONSENSUS CONFERENCE ON GUIDELINES FOR CONSERVATIVE TREATMENT ON LOWER LIMB INJURIES IN ATHLETE

The first 'Italian Consensus Conference on Guidelines for Conservative Treatment on Lower Limb Injuries in Athlete' was organised by the Italian Society of Arthroscopy in Milan, on 8 April 2017, with the participation of 70 national experts with different

medical backgrounds: orthopaedic surgeons (25), sports physicians (8), radiologists (5), rehabilitation physicians (3), sport physiologists (3), general surgeons (2), family physicians (2), physiotherapists (11) and physical trainers (11). The selection was based on their Hirsch index, the number of publications concerning MI and experience in the clinical evaluation, medical treatment and rehabilitation of MI. The experts did not represent any organisations. All experts who participated in the CC are included as authors of this report. Three authors (EC, KC and ZV) though not present at CC were invited to give their intellectual contribution to the study.

*This paper represents the synthesis of the Italian Consensus Conference on Guidelines for Conservative Treatment on Lower Limb Injuries in Athlete, while the complete document (about 200 pages in Italian language) can be consulted at the official website of the Italian Society of Arthroscopy (www.siaonline.net).*

### CC LITERATURE REVIEW PROCESS

Prior to the CC, two senior authors (GNB and PV) performed a systematic literature review on the biology and aetiology, classification, clinical evaluation and conservative treatment of MI. The review process was conducted as follows:

1. An independent research was performed independently by two authors, with no language limitation applied.
2. Databases used were MEDLINE, EMBASE, EXCERPTA MEDICA, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Review. The so-called 'grey literature' (ie, conferences, abstracts, thesis and unpublished reports) was not taken into consideration.

Following the review, all studies that did not report relevant information to the above-mentioned four specific clinical points were excluded.

After the review, the authors provided a comprehensive summary document divided into four distinct sections: (1) biology and aetiology; (2) classification; (3) clinical evaluation; and (4) conservative treatment regarding MI. This document was delivered in advance (7 days) to each expert participating at the CC and was considered as a starting point for the discussion. The two senior authors had the role of facilitator (GNB) and chairman (PV) during the CC.

**Table 1** The results of the different voting rounds concerning document 1 (biology and aetiology of muscle injury document consensus)

Voting (n=3)	Score
Voting 1	9.2±0.5
Voting 2	9.6±0.4
Voting 3	9.4±0.5

**Table 2** The results of the different voting rounds concerning document 2 (muscle injury classification document consensus)

Voting (n=17)	Score
Voting 1	9.4±0.5
Voting 2	9±0.6
Voting 3	8.8±0.6
Voting 4	9±0.5
Voting 5	9.2±0.4
Voting 6	9.2±0.5
Voting 7	9±0.6
Voting 8	9.2±0.3
Voting 9	9.2±0.5
Voting 10	9.2±0.5
Voting 11	9.2±0.5
Voting 12	9.2±0.5
Voting 13	9.2±0.5
Voting 14	9.2±0.5
Voting 15	9.2±0.5
Voting 16	9.4±0.4
Voting 17	9.2±0.5

### CC PRESENTATION

All the CC participants approved the four following sections of the summary document:

1. Biology and aetiology of MI.
2. MI classification.
3. MI clinical assessment.
4. MI conservative treatment.

During the discussion, each document was initially presented by the facilitator (GNB), followed by a plenary discussion guided by the chairman (PV), and finally approved by a vote.

The CC participants voted for each document, utilising a Likert scale of 0–10, where 0 reflected complete disagreement, 5 neither agreement nor disagreement and 10 complete agreement. The discussions continued until a mean score of >7.5 was reached<sup>7,8</sup> and the voting process enabled the chairman to interrupt the discussion if in his opinion final decision could not be reached. The first document required three separate discussions and three voting rounds, while the second, third and fourth documents required 17, 1 and 4 discussions of subparts and voting rounds, respectively. During the discussions, the document was modified and then the final version was voted on. Consensus was reached in all cases at the end of each discussion phase, where the majority of participants reached an agreement (ie, when a mean score of >7.5 was reached). The voting results are shown in tables 1–4.

**Table 3** The results of the different voting rounds concerning document 3 (muscle injury clinical assessment document consensus)

Voting (n=1)	Score
Voting 1	9.5±0.4

## SECTION 1. SUMMARY OF BIOLOGY AND AETIOLOGY OF MI DOCUMENT CONSENSUS

Few authors have explicitly defined the term ‘muscular injury’, although some have attempted to correlate the concept of injury to that of loss of proper muscle functions.<sup>9 10</sup> However, identifying MI with the simple loss of function is not entirely correct, since muscle function can be affected by events such as fatigue or atrophy, which has nothing to do with the injury mechanism. For these reasons, during the CC, we formulated the following definition of muscle lesion:

*‘MI is a loss of function caused by a damage of the anatomical structure that generates (muscle) and transmits (tendon) force.’*

### Key points

The central role of eccentric contraction in the pathogenesis of indirect MI (indMI; ie, a lesion due to an overstretching of the muscle fibres) was underlined.<sup>9 11–15</sup> Furthermore, the significance of overlapping mechanical causes<sup>11–18</sup> and metabolic pathways was discussed.<sup>19–21</sup> The importance of the calcium overload stage and the consequent self-aggravation of the lesion in the immediate postinjury period was stressed.<sup>21–23</sup> Finally, the importance of the role of stem cells (SC) in skeletal muscle repair and regeneration processes was also discussed<sup>24–29</sup> and, in agreement with other studies,<sup>28 29</sup> the use of stem cells as treatment for MIs was disapproved because scientific evidence does not confirm its effectiveness and safety.

The importance of three different phases when planning conservative treatment programmes was acknowledged: (1) destruction phase, (2) repair phase and (3) remodelling phase.<sup>27 30–32</sup>

## SECTION 2. SUMMARY OF MI CLASSIFICATION DOCUMENT CONSENSUS

We provide guidance on:

- The classification of indMI.
- The classification of direct MI (dirMI; ie, an injury caused by a blunt trauma at muscle belly level).
- The timing of imaging exams.

### The classification of MI

Classification should respect the following points:

- It must be reproducible.
- It must provide a clear distinction between different categories.
- It must be easy to remember.
- It must be concise and easily understandable.
- It must be linked to prognostic factors.

**Table 4** The results of the different voting rounds concerning document 4 (muscle injury conservative treatment document consensus)

Voting (n=4)	Score
Voting 1	9.0±0.5
Voting 2	9.0±0.5
Voting 3	9.0±0.6
Voting 4	9.0±0.5

The CC, carrying out a synthesis of the main and most recent classifications in literature,<sup>33–48</sup> proposed the following classification for the indMI, subdividing it in accordance with the radiological investigation performed by ultrasonography (US) or MRI.

### Staging of indMI by US examination

#### Delayed muscle soreness

The delayed-onset muscle soreness (DOMS) does not give any US abnormalities. Diagnosis should therefore be based on the clinical examination, and imaging is not recommended for 48 hours. DOMS is to be considered as a substructural (ie, not detectable by radiological examination) lesion of the muscle, although due to a physiological adaptation.<sup>49</sup>

#### Clinical-history criteria

- The athlete has no recollection of any injury event.
- The pain appears about 24–48 hours after the triggering event (training or competition).
- The pain is usually bilateral.
- The athlete does not indicate a specific point of pain, but rather the entire muscle belly.
- Usually, the athlete feels pain at rest as well as during the activity which includes minimal muscle activation.
- Usually, the pain decreases after warm-up and during training sessions.
- The triggering event is usually a high-intensity training session or competition, related to unusual exercises often with high eccentric loading, or from unfavourable environmental conditions such as particularly heavy playing grounds.

#### Prognosis

The usual return to full participation to training and competition (RFPTC) prognosis for DOMS (with optimal treatment) is between 48 and 72 hours. In case of extremely severe DOMS, the prognosis for RFPTC is subjective.

#### Fatigue-induced muscular disorder

Fatigue-induced muscular disorder (FIMD) is a substructural lesion normally not causing US abnormalities, although occasionally there may be a slight change in structural echogenicity.

*Clinical-anamnesic criteria*

- i. In FIMD the athlete does not correlate onset of pain to a precise movement and/or situation.
- ii. In opposite to DOMS, symptomatology is usually monolateral.
- iii. In opposite to DOMS, initial cramping is often perceived during the game, or the symptoms are perceived at the end of the activity.
- iv. In opposite to DOMS, pain is not perceived at rest but only during activity.
- v. The athlete does not indicate a precise point of pain, rather an extensive muscle area but still less than the entire muscular belly.

*Prognosis*

The prognosis for RFPTC in the case of FIMD (with optimal treatment) is 3–5 days.

*Grade 0 lesion (indMI 0°)*

Given the difficulty of detecting objective oedema through US examination and especially given the impossibility of differentiating an oedema from a haemorrhagic zone, especially in small lesions, the 'grade 0' staging via US examination is not advisable.

*Grade I lesion (indMI I°)*

The indMI I° is as macroscopic (ie, detectable by radiological examination) structural damage.

*Clinical-anamnesic criteria*

- i. The onset is acute and can be referred to a precise event.
- ii. In most cases, the athlete is unable to continue the sporting activity he is engaged in.
- iii. Pain, localised and well reproducible, is perceived during activity only.

*US imaging criteria*

The US shows a lesion at the primary and secondary muscle fascicles and the presence of a haematoma. The lesion extension has a diameter smaller than that of a secondary fascicle (ie, less than 5 mm). Perifascial liquid can be present.

*Prognosis*

The prognosis for RFPTC (with optimal treatment) is about 15 days.

*Grade II lesion (indMI II°)*

The indMI II° is as a macroscopic structural damage.

*Clinical-anamnesic criteria*

- i. The onset is acute and can be traced back to a very precise event.
- ii. In almost all cases, the athlete fails to continue the sporting activity in which he is engaged, and often has to stop immediately.
- iii. Localised and well-reproducible pain is often perceived at rest. Sports activities are impossible.

*US imaging criteria*

There is a substantial muscle discontinuity area, associated with a visible haematoma distal and proximal to the lesion. The extension of the lesion involves more than one secondary fascicle (ie, greater than 5 mm). Muscle areas adjacent to the injured zone appear to be hyperechogenic. Commonly, a considerable amount of intermuscular, perifascial and subcutaneous fluid collection is observed.

Often, a heterogeneous haematoma may overshadow the terminal tendon area, increasing the difficulty in reaching a precise diagnosis. In these cases, the terminal tendon area is better observed by MRI exam.

Sometimes, it is objectively difficult to differentiate an indMI grade I from II by MRI exam.<sup>50</sup> In these cases, the US exam is a valuable complementary tool to confirm the accuracy of the lesion<sup>18 45 50</sup> with the possibility that the US itself allows to highlight the macroscopic structural alterations of the muscle at the level of the lesion site occurring during an eccentric dynamic contraction (during which the US imaging shows an increase in the lesion gap) typical of the grade II lesions.<sup>45 50</sup>

*Prognosis*

The prognosis for RFPTC (with optimal treatment) has been estimated to be between 20 and 60 days.

*Grade III lesion (indMI III°)*

IndMI III° is a macroscopic structural damage.

*Clinical-anamnesic criteria*

- i. The onset is acute and can be traced back to a very precise event by the athlete.
- ii. In all cases, the athlete is forced to stop the sporting activity in which he is engaged, at the time of the injury.
- iii. The pain, localised and well reproducible, is also perceived at rest.
- iv. Sports activities are impossible.

*US imaging criteria*

In US examination, an indMI III° involves more than 85% of the total muscle diameter. Muscle areas adjacent to the lesion zone are hyperechogenic. Commonly, a considerable amount of intermuscular, perifascial and subcutaneous fluid collection is observed.

*Prognosis*

With optimal treatment the prognosis for RFPTC can be estimated between 60 and 90 days (in cases of serious injuries of muscles particularly involved in the sporting activity).

**Staging of indMI by MRI examination***Delayed-onset muscle soreness**Clinical-anamnesic criteria*

The criteria stated for the US exam remain valid.

*MRI criteria*

A low-grade DOMS does not involve alterations of the MRI signal either in the anatomic or fluid-sensitive sequences.



There may sometimes be transient oedema with no trace of blood. On the contrary, in the case of extremely severe DOMS, oedema in fluid-sensitive sequences appears to be superimposable to the one present in the case of indMI I°–II° (without fascicle damages) and persist for a period that may last even for 80 days.

#### Fatigue-induced muscular disorder

##### *Clinical-anamnestic criteria*

The criteria stated for the US exam remain valid.

##### *MRI criteria*

FIMD generally does not result in alteration of the MRI signal neither in the anatomic nor in fluid-sensitive sequences. Transient oedema with no trace of blood may occasionally be present. The difference between DOMS and DMFI is therefore in principal basically based on the clinical-anamnestic investigation.

##### *Prognosis*

The criteria given for the US examination remain valid.

#### Grade 0 lesion (indMI 0°)

The indMI 0° is a substructural MI with functional consequences and not a macroscopic structural damage.

##### *Clinical-anamnestic criteria*

- i. The athlete can recall of a traumatic event in a reproducible anatomically well-located point.
- ii. The athlete is often able to continue the sports activity.
- iii. Pain is not felt at rest but only during the activity.

##### *MRI criteria*

No macroscopic alterations in the muscular architecture are visible. There is a muscle oedema without discontinuity of the fibres and without the presence of blood. The absence of blood is the comparative parameter that allows differentiating indMI 0° from an indMI I°.

##### *Prognosis*

With optimal treatment the prognosis for RFPTC is about 8 days.

#### Grade I lesion (indMI I°)

The indMI I° is a macroscopic structural damage.

##### *Clinical-anamnestic criteria*

The clinical-anamnestic criteria identified for the US exam remain valid.

##### *MRI criteria*

An increased signal within the lesion zone is visible in high-contrast gradient sequences (STIR Short-tau inversion recovery (STIR) and T2 weighted image). The signal increase is due to oedema and blood flow, usually from the muscle-tendon junction, which expands along the muscular fascicles producing a classic 'bird pen' pattern. The lesion extension has a maximum diameter,

however, smaller than that of a secondary bundle (ie, less than 5 mm). In the indMI I° perifascial fluid is also visible.

##### *Prognosis*

With optimal treatment the prognosis for RFPTC is about 15 days.

#### Grade II lesion (indMI II°)

In opposite to US, MRI examination, thanks to its high-contrast gradient, allows to differentiate indMI II° in three variants: types A, B and C. The indMI II° (in its variants A, B and C) must be considered a macroscopic structural damage.

##### *Clinical-anamnestic criteria*

The clinical-anamnestic criteria identified for the US exam remain valid.

##### *MRI criteria*

Macroscopic alterations of muscular architecture can be observed within the lesion zone. The extension of the lesion involves more than one secondary bundle (ie, greater than 5 mm). Frequently, the perifascial liquid may be very abundant and may expand in accordance to the anatomical structure of the injured muscle, allowing to easily see the secondary fascicles remaining structurally intact.

A further classification of the grade II lesions can be performed by staging the extension of the lesion (and indirectly the number of secondary fascicles)<sup>36 43</sup>:

- i. Grade II lesion A-type (indMI II° A) injury involving less than one-third (ie, less than ~35%) of the muscular cross-sectional area (CSA).
- ii. Grade II lesion B-type (indMI II° B) injury involving more than one-third but less than two-thirds (ie, between ~35% and ~65%) of CSA.
- iii. Grade II lesion C-type (indMI II° C) injury involving more than two-thirds (ie, between ~65% and ~85%) of CSA.

The prognosis for RFPTC (with optimum treatment) is ~20 days for an indMI II° A, ~40 days for an indMI II° B and ~60 days for an indMI II° C.

#### Grade III lesion (indMI III°)

Generally, third-degree lesions are observed more frequently at the origin of the free proximal tendon, while they are less frequent distally. Grade III lesions are rare and represent on average 3% of all lesions observed.<sup>51</sup> Surgery is rarely needed and is normally performed in the case of avulsion trauma with a retraction greater than 2–3 cm.<sup>3 6 45</sup> IndMI III° is a macroscopic structural damage.

##### *Clinical-anamnestic criteria*

The clinical-anamnestic criteria identified for the US exam remain valid.

### MRI criteria

A third-degree injury involves more than 85% of the CSA with a haematoma that fully fills the gap of the lesion. The secondary bundles show a clear ripple and retraction.

### Prognosis

With optimal treatment the prognosis for RFPTC is on average between 60 and 90 days.

### Direct MI

DirMIs are divided into contusions and lacerations. The contusions are caused by the impact of a generally rounded foreign body on the muscle surface. The lacerations are the result of the effect of a sharp body (cutting wounds) or the penetration of a pointed body (tip injuries) in the muscle.

As far as the second case is concerned, for the tears, CC does not propose a specific classification of their gravity. In this category only contusions were considered.

The CC adopted a classification of dirMI divided into three categories: minor, moderate and severe; this classification is mainly based on functional (clinical) evaluation. All the three categories of dirMI are to be considered a structural lesion.

- i. Minor dirMI (dirMI GMi) where movement is possible for more than half of the range of motion (ROM) of the involved joints is possible. The US and MRI exam show the presence of a limited haematoma. The prognosis (with optimal treatment) is between 3 and 10 days.
- ii. Moderate dirMI (dirMI GMo) where movement is possible for less than half but more than one-third of the entire ROM of the involved joints is possible. The US and MRI exams show the presence of a diffuse haematoma. The prognosis (with optimal treatment) ranges from 10 to 50 days depending on the extension of the haematoma itself.
- iii. Severe dirMI (dirMI GS) where the movement is possible for less than one-third of the total range of movement of the involved joints is allowed. The US and MRI exam show the presence of widespread haematoma and muscle fibre crushing. The prognosis (with optimal treatment) is between 50 and 70 days.

On examination of US and MRI, the dirMI does not differ significantly from the indMI, showing a more or less circumscribed oedema or haematoma, with a possible discontinuity of the secondary fascicles. In the US examination, the appearance of a haematoma is quite variable and depends on the trauma dating. A recent and high-pressure haematoma is sometimes more echogenic because of its high cellular content and can, therefore, remain difficult to differentiate from muscle tissue. In any case, it is important to note that a haematoma in the first 24 hours post-trauma may have a very variable appearance, from not echogenic at all or hypoechogenic to a frankly hyperechogenic appearance. Finally, in the following 2–3

days the haematoma moves to hypoechogenicity or not echogenicity appearance.<sup>52</sup>

It should be noted that in dirMI the extent of haematoma is not necessarily correlated, as opposed to indMI, with the severity of the lesion and consequently with the severity of the prognosis. In fact, a direct trauma causes vascular damage and internal bleeding. Structural fibre lesion is rare since the contusing force tends to crush them.<sup>43</sup> In other words, a diffused haematoma can only be caused by a rupture of the vessels and not necessarily by the loss of continuity of muscle fibres, as it is the case with indMI. For this reason, in dirMI the prognosis is usually better than the indMI of equal size.<sup>43 45</sup>

### The timing of the imaging exam

There is no consensus in the literature as to the optimal timing to perform the MRI or the US after the injury event.<sup>42 53</sup> As far as the US examination is concerned, the timing of the exam execution that is more consensual would seem to be ~48 hours from the injury.<sup>41 50 54</sup> Therefore, this is the indication provided by the CC.

Regarding MRI examination, some authors<sup>55</sup> demonstrated the signal invariance in the fluid-sensitive sequences within the so-called 'acute phase', that is, during the first 7 days after injury. However, in the present study, the MRI signal recorded in the fluid-sensitive sequences is considered in its entirety, that is, without differentiating the oedema from the blood. Indeed, one of the most important parameters regarding the choice of timing of the imaging is that it can accurately discern whether the fluid content inside and around the area is oedema and/or haematic in nature. This aspect is fundamental when it comes to differentiating an indMI 0° from an indMI I°, given in particular the important prognostic difference between the two different types of lesion (8 days vs 15 days) and the resulting obvious diversity of the rehabilitation programmes to be adopted. As already mentioned, such differentiation is only possible through MRI assessment, provided that it is carried out within a proper 'time window'. Based on studies performed on brain bleeding states, and in absence of any study concerning muscle haematoma in different states,<sup>56–61</sup> this CC suggests that the ideal observation window lies between the third and fifth postlesion days. During this period, it is possible to differentiate the oedema from the blood by comparing the T1 and the T2 sequences.<sup>56–61</sup> In any case, it is important to note that muscle haematoma sometimes shows, at MRI examination, a rather variable appearance compared with the lesion dating; therefore, the appearance may sometimes differ from that observed in a haematoma at the cerebral tissue level.<sup>56 57 61</sup> It is, therefore, advisable to exercise caution in data interpretation.

## SECTION 3. SUMMARY OF MI CLINICAL ASSESSMENT DOCUMENT CONSENSUS

Despite the increasing imaging utilisation in MI diagnostics, clinical skills remain a fundamental point. According

to the CC conclusion, clinical evaluation must basically consist of three distinct, but highly complementary phases:

- i. Anamnesis (AN; history).
- ii. Inspection (IS).
- iii. Clinical examination.

### Anamnesis

AN is a fundamental part of the clinical evaluation. In order to rationalise the anamnestic examination, the CC recommends to follow the key points below:

- i. Pay attention whether in the past or recent AN similar lesion to the one currently evaluated has occurred, or in an anatomically adjacent area: this finding is crucial to identify possible recent or late reinjuries.
- ii. The fact that the patient can easily recall of the moment of trauma and indicates with exact accuracy the precise area of pain is highly suggestive of a structural muscular injury. This diagnostic suspicion could be confirmed by the fact that the athlete has failed to complete the rest of training session or competition.
- iii. Conversely, a cramping sensation, though progressive, would be strongly suggestive of an ultrastructural lesion.
- iv. The young age and the particular anatomic location of the pain site (anterior superior iliac spine, anterior inferior iliac spine, ischial tuberosity) may be highly suggestive of the diagnosis of an apophyseal injury.

### Inspection

IS is the second phase of the clinical evaluation. The CC recommends the following key points to be respected during the IS:

- i. Check for swelling.
- ii. Check for the presence of haematoma (strongly suggestive of the indirect lesion) or ecchymosis (strongly suggestive of direct trauma).
- iii. Check for the presence of gap or clear muscle retraction.
- iv. Check for changes in the muscular profile in the region of the suspected lesion in comparison to the contralateral muscle.

### Clinical examination

A proper clinical examination must be based on the following points:

- i. Palpation.
- ii. Checking of ROM.
- iii. Stretching.
- iv. Functional manoeuvres.

### Palpation

The palpation exam (PE) requires specific skill set and experience of the clinician. The PE shall be conducted in two ways:

- i. PE mode 1: The patient is positioned in a way that the examined muscle is in a slightly elongated position (hence slightly contracted eccentrically).

- ii. PE mode 2: The muscle to be examined must be completely relaxed. The PE should be repeated several times, according to the two above-mentioned modalities, both on the entire muscle belly and on the area/point of pain indicated by the patient. The clinician should get information, obviously subjective, from the skin, subcutaneous tissue, fascia and muscle. The PE should be performed, when applicable, in a comparative manner and in both modalities described above, exerting a moderate pressure, and in a proximal-distal direction and vice versa, always following the orientation of the fibres.

The PE aims to verify:

- i. The tone of the muscles affected by the alleged lesion compared with the contralateral one. In addition, it is of utmost importance to check the tone of the muscles adjacent to the presumably injured one, as a tone alteration may suggest a high-grade lesion.<sup>18 32</sup>
- ii. The presence of gap or clear muscle retraction.
- iii. The existence of stiff zones.
- iv. The existence of previous fibrotic areas or altered myofascial adhesion.
- v. The existence of painful areas or otherwise impaired perception by the patient.

### Checking of ROM

The ROM of the proximal and distal joints (when applicable) to the injured muscle should be checked (eg, hip and knee in case of a rectus femoris lesion).

### Stretching

A stretching of the injured muscle should be performed in the following modalities:

- i. Active modality.
- ii. Passive modality.

Generally, a structural lesion results in pain on both passive and active stretching, while in a functional pathology (such as the DOMS) stretching may provide a pleasant feeling to the patient.

### Functional manoeuvres

The injured muscle should be tested in three ways:

- i. Maximum isometric contraction.
- ii. Concentric contraction of medium intensity against the operator's resistance.
- iii. Medium effort eccentric contraction against operator's resistance with no pain.

Quantification (from 0 to 10) of the perceived pain in accordance with the visual analogue scale<sup>62</sup> will be required for each type of contraction.

Finally, in order to facilitate a summary of the main information of the clinical evaluation exam, CC proposes the adoption of two dedicated tabs of which we provide an example in online supplementary annex 1 and annex 2.

## SECTION 4. SUMMARY OF MI CONSERVATIVE TREATMENT DOCUMENT CONSENSUS

In the fourth document, all the non-surgical treatments of MI are considered as conservative treatments. The fourth document provided the following points:

- i. The conservative treatment of indMI.
- ii. The conservative treatment of dirMI.
- iii. The physical therapy into the conservative treatment of MI.
- iv. The pharmacological treatment of MI.

### The treatment of DOMS, FIMD and grade 0 lesion (indMI 0°)

While there is no evidence in the literature concerning the conservative treatment of DOMS, FIMD and indMI 0°, the CC merely proposes treatment guidelines based on expert advice (level of evidence IV).

It is possible to summarise the main points of the rehabilitation programme as follows:

- i. Suspension or reduction of the functional load until total or partial resolution of symptoms.<sup>31 63</sup>
- ii. Contrast therapy (hot/cold).<sup>64 65</sup>
- iii. Hydrokinesitherapy.<sup>64 65</sup>
- iv. Endogenous thermotherapy.<sup>66</sup>
- v. Massage.<sup>67 68</sup>

It is important to note that, despite the controversy in literature<sup>69-71</sup> of the above-mentioned treatment, many athletes are seeking them because they feel their benefits.<sup>67 68</sup>

### Treatment guidelines according to the biological tissue repair steps for grade I indirect lesions (indMI I°) and onwards

As already discussed, muscle tissue repair/regeneration process is completed in a longer or shorter period depending on the severity of the lesion. During this period, there are well-defined biological phases (first phase of destruction, the second phase of repair/regeneration and third phase of remodelling).<sup>31 63</sup> The CC, therefore, recommends a three-phase break-up rehabilitation protocol. Each of these phases must be characterised by a well-defined type of muscular contraction that is consistent with the biological condition observed within the injured area.<sup>31 63</sup> Therefore, the rehabilitation programme should be set as follows:

#### The first phase (approximately between the second and the fifth to seventh postlesion days)

The biological situation within the injured area

At the beginning of the first phase (second postlesion day), the necrotised parts of the muscle fibres are removed by the macrophages. At the same time, the formation of the scarring connective tissue within the central lesion zone (CZ; ie, the gap of the lesion) by fibroblasts starts. At the end of the first phase (approximately seventh postlesion day), the repairing processes of the muscle cells extend beyond the old basal laminae cylinders in the CZ and begin to penetrate through the scar zone.<sup>10 27 31 32 63 72 73</sup>

#### Type of contraction in the first phase

Considering that the first 5–7 postlesion days are characterised by the fact that the CZ has not yet developed a sufficiently dense and compact scarring connective tissue, the major risk in this period is that an excessive muscle contraction, especially with eccentric modality, increases the already existing lesion gap. Therefore, the type of contraction recommended in this first phase is an isometric modality. In fact, during the isometric contraction there is no myofilaments slippage and, therefore, there is no macrochange of the muscle length. For this reason, the CZ lesion gap is not structurally stressed.<sup>74</sup> The intensity of the isometric contraction required must, however, remain below the threshold of pain.<sup>63</sup>

In this first phase, the CC also recommends:

- i. In the immediate postinjury period (24–72 hours) it is advisable to apply the PRICE (Protection, Rest, Ice, Compression, Elevation) principle.<sup>75</sup>
- ii. It is possible to consider having a short rest period and/or relative immobilisation immediately after the injury. This rest period optimises the formation of connective tissue by fibroblasts within the CZ, thereby reducing the risk of recurrences.<sup>31 63 76</sup> However, rest and immobilisation should be reduced to only the first postlesion days (3–5 days).<sup>31 63 76</sup>
- iii. In the first 72 hours postlesion, physical therapies that induce endothermia should be avoided in order to avoid the possible increase in blood extravasation.
- iv. All forms of massage on the affected area should be avoided. The practice of massage is allowed only after the completion of tissue healing processes.<sup>77</sup>
- v. If there is an excessive haematoma formation within the injured area, it is advisable to proceed to an echo-guided aspiration before the haematoma organisation.<sup>76 78</sup>

#### Second rehabilitation phase (approximately between 8th and 14th postlesion days)

Clinical and functional data and imaging techniques are the criteria for proceeding from the first to the third phase of rehabilitation.

##### Clinic criteria

- i. Resolution of swelling, if initially present.<sup>77 79</sup>
- ii. Absence of pain in response to maximal isometric contraction.<sup>77 79</sup>
- iii. Absence of pain in response to end-range stretching tests carried out in the active and passive modes.<sup>49 77 79</sup>
- iv. Complete ROM of the joints involved in the movement.<sup>77 79</sup>

##### Imaging criteria

- i. Reduction of the lesion gap as observed with US or MRI imaging.<sup>80 81</sup>
- ii. The presence of granulation repair tissue within the CZ as revealed by the US.<sup>80 81</sup>



### The biological situation within the injured area

At this stage, the scar zone in the CZ is further condensed and reduced in size, and myofibres fill the residual gap of the CZ.<sup>10 27 31 32 63 72 73</sup> During this phase, the granulation tissue gains compactness and elasticity.<sup>82</sup> However, the possible weak points of the lesion repair in this and the next phase<sup>44 45</sup> could be:

- i. Immature scar tissue within the CZ.<sup>80</sup>
- ii. Healthy muscle tissue adjacent to the CZ which can be overtensioned.<sup>80</sup>

### Type of contraction in the second phase

The CC recommends that the second phase of treatment respects the following points:

- i. The introduction of progressively intense exercises based on concentric contractions. During a concentric contraction, the bulk of the muscle shortens due to the sliding motion of the myofilaments with a relatively constant force proportional to the external load. Subsequently, the CZ is not subjected to traction and the jagged muscle edges, undergoing reorganisation/repair, avoiding diastasis.<sup>83</sup>
- ii. The concentric contraction can be manual at the beginning and subsequently with isotonic equipment (ie, Olympic weightlifting devices).<sup>84</sup>
- iii. The eccentric (ie, negative) phase of the movement must, in all cases, be reduced to the minimum possible intensity.<sup>77</sup>
- iv. Since there is evidence<sup>85</sup> that a rehabilitation protocol, following an indMI which includes exercises aimed to stabilise and strengthen the 'core' muscles (in particular abdominal, quadratus lumborum and paravertebral muscles) yields better results (in terms of reduced relapses and in an earlier return to sport), a 'core stability program' should be systematically introduced in the rehabilitation plan.<sup>86</sup>
- v. Stationary bike and deloaded run can be introduced during this phase.<sup>79</sup>

### Third rehabilitation phase (~14th–21st day, postinjury)

Clinical data and imaging techniques are the criteria for proceeding from the second to the third phase of rehabilitation.

#### Clinical criteria

- i. The absence of pain in response to concentric contraction performed at increasing intensity against resistance performed by the physiotherapist.<sup>77 79</sup>
- ii. The absence of pain in response to submaximal eccentric contraction.<sup>77 79</sup>

#### Imaging criteria

- i. The substantial disappearance of the lesion gap on US or MR examination.<sup>80 81</sup>
- ii. The presence of compact granulation repair tissue within the CZ as revealed by US or MR.<sup>80 81</sup>

### The biological situation within the injured area

In this phase, the myofibres intertwining is effectively completed by the interposition of a small amount of scar tissue. The remodelling phase may last more than 60 days, depending on the anatomical extent of the injury.

Treatment during the third week of the postinjury should, therefore, respect the following points:

- i. The inclusion of isokinetic exercises<sup>76</sup> followed by:
- ii. The inclusion of elastic resistance exercises where the intensity of the eccentric phase is progressively increased, followed by<sup>77 79</sup>:
- iii. Exercises predominantly based on eccentric contractions of progressively increasing intensity.<sup>77 79</sup>
- iv. The introduction of stretching. Stretching must be introduced gradually and exercises must not cause the onset of pain. The time of elongation initially is 10–15 s and subsequently up to 1 min, in order to induce a durable, and not just a transient, plastic deformation within the area of structural reorganisation.<sup>77 79 87</sup>
- v. Running may be introduced during this phase, on the condition that dynamometric values of the injured muscle have been reinstated to at least 70% of the preinjury level or that of the opposite limb.<sup>77</sup>
- vi. Sport-specific exercises can be introduced with caution at the end of the third phase.<sup>77</sup>

### Phase duration

The duration of each phase is consistent with the dynamics of the healing processes occurring in the muscle tissue affected by the injury and therefore, the duration of each of the three phases is directly related to the severity of the injury. In other words, for every grade 3 lesion, the duration of each of the three phases will vary. The duration of each phase has to be determined *ad personam*, in accordance with the clinical and imaging criteria required for proceeding from one phase to the next. Therefore, although rehabilitation indMI I°, indMI II° and indMI III° will be subdivided into three phases, the duration of phases will be different, and progression is not time based, but clinical, functional and imaging criteria based.<sup>77 79</sup>

### The conservative treatment of haematoma

Since the blood loss causes the formation of a haematoma, it is necessary to distinguish between intermuscular haematoma (interH) and intramuscular haematoma (intraH).

*interH*: In this case, the fascia appears to be injured so that the blood can be released from the muscle belly. Pain generally persists for a period ranging from 24 to 48 hours.<sup>88 89</sup>

*intraH*: In this case, the muscle fascia remains intact and the blood extravasation remains confined within the injured muscle. Since the blood collection within the muscle produces an osmotic gradient, the swelling can persist, or increase, beyond 48 hours postlesions.<sup>90</sup>

The CC recommends that the treatment of the haematoma follows the following points:

- i. Into the case of intraH, the PRICE principle needs to be changed. Indeed, into the intraH compression therapy should be avoided in order to avoid the onset of a compartmental syndrome.<sup>22</sup> Furthermore, there is no need to apply the principle of the ‘protection’ of the injured limb. On the contrary, in order to facilitate the haematoma reabsorption in intraH, early mobilisation is preferable since from the second-day postlesion.<sup>79 91</sup>
- ii. In the presence of excessive haematoma formation, it is advisable to proceed to an ultrasound-guided aspiration before the solid haematoma organisation.<sup>76 78</sup>
- iii. The so-called ‘contrast therapies’ (ie, the alternate administration of hot and cold in order to speed up the absorption of haematoma) can be initiated only at the end of the haemorrhagic phase, so usually not before 72 hours.<sup>92</sup>
- iv. Massage must be avoided in the first postlesion days, in order to avoid a possible exacerbation of the haemorrhagic process.<sup>79</sup> Massage can be started when the haematoma has completely disappeared.<sup>79</sup>

#### Instrumental therapy in the conservative treatment of MI

In the first postlesion days, it is of paramount importance to allow the implantation of muscle resident stem cells (MRSC) inside the injured area.<sup>93–95</sup> The MRSC implant process is strongly dependent on the injured muscle angiogenesis process. This process is stimulated by both voluntary exercise and neuromuscular electrostimulation (NMES).<sup>93–95</sup> For this reason, the use of NMES by promoting an early angiogenesis in the post-traumatic regeneration phase could increase both the presence of MRSC and postnatal muscle-derived stem cells (MDSC) resulting from the vascular endothelium. In fact, some authors have advanced the hypothesis that MDSCs originate from blood vessels.<sup>96–98</sup> The use of NMES for vascularisation should be encouraged until the end of the regeneration phase (ie, up to about the third postlesion week).<sup>99 100</sup>

#### Ultrasound therapy

There is limited evidence that ultrasound therapy (UST) is able to increase the levels of basic fibroblastic growth factor and vascular endothelial growth factor (VEGF).<sup>101</sup> The use of UST in MI is justified by the fact that tissue micromassage induced by the UST frequencies can generate an antalgic effect.<sup>102</sup> However, it is important to note that UST can inhibit the expression of the RNA messenger (mechano growth factor (MGF) mRNA).<sup>102</sup> The MGF mRNA plays an important role in the insulin-like growth-1 (IGF)-1 upregulation mechanism. Therefore, it is advisable not to use UST in the first 24 hours postlesion.<sup>102</sup> In summary, UST may be recommended in the conservative treatment of MI after the first 24 hours postinjury.<sup>101 102</sup>

#### Laser therapy

Many studies have shown that laser therapy (LT) can reduce the inflammatory process of the damaged muscle tissue,<sup>103</sup> speed up the tissue regeneration/repair processes by stimulating myogenic processes,<sup>104</sup> optimise the oxidative metabolism by increasing ATP synthesis<sup>105–107</sup> and stimulate the synthesis of RNA and regulatory protein cycles in cell proliferation.<sup>108</sup> Finally, LT could increase the expression of VEGF.<sup>109 110</sup> Therefore, the use of LT in the treatment of MIs appears to be justified by sufficient evidence.<sup>111</sup>

#### Hyperthermia (endogenous thermotherapy)

Hyperthermia therapy (HT) (ie, microwave diathermy) increases the temperature of the deep tissue up to 41°C–45°C, through electromagnetic energy. HT has proven to be able to stimulate the tissue repair processes, diminish pain symptoms, increase tissue flexibility and reduce muscular and joint stiffness.<sup>112 113</sup> Some studies point out its effectiveness even in the specific field of skeletal muscle repair/regeneration processes.<sup>112–117</sup> HT may also facilitate the resolution of haematoma following MI.<sup>118</sup> Furthermore, HT increase increases pain threshold through a direct action of heat on free nerve endings<sup>119</sup> and trunks<sup>120</sup> sufficiently to block the transmission of pain.<sup>119 120</sup> Finally, HT reduces the muscle spasm resulting from MI contributing to the pain decreasing.<sup>117 121 122</sup> Therefore, for CC experts’ opinion, the use of HT in the treatment of MI is justified by a sufficient evidence.

#### Hyperbaric oxygen therapy

Currently, in the literature, there is a total lack of evidence on the effectiveness of hyperbaric oxygen therapy (HOT) in the MI conservative treatment, both indirect and direct. Therefore, the HOT needs further evidence to prove its effectiveness in MI treatment.

#### Extracorporeal shock wave therapy

Extracorporeal shock wave therapy (ESWT) is a ‘mechanotherapy’, whose biological effects have been now widely described: modulation of inflammation and macrophages activity, angiogenesis and tissue-specific growth factor (GF) induction, SC activity stimulation, besides antioedema and antinociceptive effect.<sup>123–125</sup> Based on its ‘trophic’ effects and in accordance with the Consensus Statement of the International Society for Medical Shockwave Treatment<sup>126</sup> regarding clinical indications, the CC suggests to apply ESWT in DOMS, reserving to ‘ESWT skilled hands’ its application after muscle lesions as possible adjuvant therapy, in order to reduce oedema and pain, improve healing and accelerate remodelling of tissue fibrosis regardless of the degree of the injury.<sup>123–127</sup>

#### Pharmacological treatment of MI

The most commonly used pharmacological therapies have been taken into consideration by the CC. The CC’s recommendations in this specific field can be summarised as follows:

### Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drug (NSAID) prescription in the early postinjury period, especially in the case of a medium to severe MI (II°–III°), can be considered as a justified medical treatment.<sup>128</sup> It should be remembered, however, that there is still no evidence of the benefits and the adverse effects that the intake of non-selective NSAIDs may provide.<sup>129</sup>

### The use of analgesic drugs

The most commonly used analgesic drug is paracetamol.<sup>129</sup> Its analgesic effect is mainly related to the action on the systems involved in pain modulation, such as serotonin system. Paracetamol does not act at peripheral level and therefore does not have anti-inflammatory activity. Some studies recommend the use of analgesics for low-intensity pain in neuromuscular disorders in the first postlesion days.<sup>130</sup> In conclusion, the CC suggests that analgesics can be used in case of pain in the first postlesion days.

### The use of calcium chelants

Chelation therapy is a drug therapy utilising chelation to treat some forms of intoxication due to heavy metals. In the case of MI, chelators may limit the calcium overload phase (calcium is an alkaline earth metal). The most widely used and well known of chelants is EDTA. EDTA would seem to be able to limit the histopathological changes present in the context of muscular lesions.<sup>131</sup> However, the use of calcium chelants needs further evidence to be justified for the treatment of MIs.

### The use of corticosteroids

The use of corticosteroid drugs should be avoided. Indeed, among different adverse effects,<sup>67</sup> they involve delayed absorption of haematoma, increased necrosis in the injured myofibrils, delay in muscle tissue regeneration processes and loss of muscle strength.<sup>132</sup>

### The use of muscle relaxant drugs

The use of muscle relaxant drugs for a limited period could, in theory, reduce, or at least contain, the self-aggravation stage of the lesion. In any case, CC recommends that the use of muscle relaxants requires further evidence-based studies regarding their efficacy in MI treatment.

### Actovegin

Actovegin is a deproteinised derivative—ultrafiltrate of calf serum from animals under 8 months of age. It is important to remember that the use of Actovegin may, although in rare cases, have serious adverse effects (anaphylactic shock with multiorgan failure in a cyclist after intravenous administration of Actovegin),<sup>133</sup> also if in effect this effect is most likely not due to Actovegin administration but due to a bacterial/infection contamination. In the literature, it is still yet to define the Actovegin's active compounds,<sup>134</sup> in any case current literature suggests that Actovegin shows antioxidant and antiapoptotic properties, and may also have an

upregulating action on macrophage responses following muscle repair.<sup>134</sup> However, the Actovegin's clinical efficacy is supported by only one new original research article.<sup>135</sup> Finally, the CC, after the examination of the current literature, believes that Actovegin needs further evidence to demonstrate its efficacy in the MI treatment.<sup>133–139</sup>

### Traumeel

Traumeel is a homeopathic medicine marketed in Italy under the name of Arnica compositum (most recently under the name of Hell Traumeels), in the form of a gel or solution for injection. In literature, there are studies (randomised controlled trials) that show its efficacy in the reduction of pain and swelling following MIs,<sup>140</sup> in rotator cuff syndrome<sup>141</sup> and in ankle and knee sprains.<sup>142,143</sup> Finally, Traumeel has proven to be a well-tolerated product with little adverse effects.<sup>144–146</sup> However, since Traumeel is a homeopathic product, this CC still expresses a certain perplexity about its effectiveness and hopes that further evidence in the future will confirm its therapeutic validity.

### Losartan

Losartan is an angiotensin II antagonist drug used to treat essential hypertension. Some studies show that losartan, if used in a time period ranging from 3 to 7 days on mouse model,<sup>147</sup> in addition to platelet rich plasma (PRP) therapy (PRPt),<sup>148</sup> is able to reduce fibrotic processes in MI, promote tissue repair/regeneration processes and stimulate angiogenesis. Further and more thorough studies will have to demonstrate the effectiveness and safety in humans.

### The use of mesenchymal stem cells

Mesenchymal stem cells (MSC) are adult, immature, undifferentiated and multipotent SCs that originate from mesoderm, and which can be extracted from the adipose and synovial tissues, blood, skeletal muscle, umbilical cord, placenta and bone marrow.<sup>28</sup> The Australasian College of Sport and Exercise Physicians, formulating a change<sup>29</sup> to the previously stated position statement on the use of MSCs,<sup>28</sup> strongly advised to restrict the use of MSCs only into well-controlled clinical research trials. This recommendation is the result of serious complications (glioproliferative lesion of the spinal cord arising from the use of MSCs).<sup>149</sup> Therefore, the CC does not advocate the use of MSCs as part of MI care, as long as scientific evidence does not confirm its effectiveness and safety.

### The use of platelet GFs

The methodology using PRP is based on the rationality that GFs contained in platelets stimulate the proliferation of skeletal muscle cell progenitors, guide cell differentiation and modify the local inflammatory response.<sup>150–154</sup> On this rationale of application, research investigating the efficacy of PRP in cartilage, bone and muscular-tendon diseases was carried out.<sup>150–154</sup> However, there are many problems actually still unresolved as well as many doubts about the actual efficacy of PRPt.

Synthetically, the various fields of investigation still in progress can be summarised as follows:

- i. Nomenclature and classification.<sup>155–158</sup>
- ii. Standardisation and preparation of the product.<sup>153 159 160</sup>
- iii. The specific indications of PRPt.<sup>161 162</sup>
- iv. The release kinetics of the various GFs.<sup>163–165</sup>
- v. The timing of administration.<sup>163–165</sup>

After discussing the above points, CC formulates the following recommendations:

- i. As there is currently no consensus concerning the PRP classification,<sup>155–158 166</sup> a universally shared classification of all different autologous blood and plasma preparations of PRPt has to be urgently developed.
- ii. Since the effects of various PRP preparations in function of their different formulations are not yet well understood,<sup>153 159 160 166</sup> there is a need for a consensus on standardised product preparation.
- iii. Since a key point in PRPt is the full understanding of the different roles of the various GFs and different cytokines within the different biological contexts considered,<sup>161 162 167 168</sup> the CC underlines the strong need for further major studies to clarify the specific indications of different types of GF and cytokines present in different types of PRPt currently proposed.
- iv. Since any pathological conditions may have a therapeutic window within which PRPt would be able to make the greatest benefit,<sup>163–165</sup> the CC hopes that further studies will be implemented in the future to elucidate the kinetics of release and activation of cytokines and GFs, and the subsequent activation methods according to different tissues and different pathological conditions.
- v. As the optimum timing of PRP administration remains an essentially unknown aspect,<sup>163–165</sup> the CC underlines the strong need for further high level of evidence studies to clarify the timing of administration, according to the specific indications of the different types of GF and cytokines present in different types of PRPs currently proposed.

## CC CONCLUSIONS

The main strength of the Italian CC on guidelines for conservative treatment of lower limb injuries in athlete was the presence of recognised leading experts in this field with different backgrounds. This multidisciplinary expert attendance guaranteed a deep and comprehensive approach to the topic.

During the CC some important points of discussion and reflection emerged. They can be summarised as follows:

- i. The CC underlined the importance of a full understanding of biological and biomechanical mechanisms of MI aetiology. This is a key point in applying rational conservative treatment protocols for MI.

- ii. The presented MI classification is reproducible, clearly distinct, easy to memorise, concise, easy to understand and linked to prognostic factors.
- iii. The CC referred clear references concerning the presented clinical evaluation of MI.
- iv. The CC presented a rehabilitation programme plan conceived in accordance with the biological repair phases of muscle tissue.
- v. The CC presented a clear overview of the state of the art of pharmacological and instrumental therapy concerning MI.

## FUTURE DIRECTIONS

The CC hopes in the future to develop and study the following points:

- i. A greater control of the actual effectiveness and scientific rationality of the application of physical therapy regarding MI.
- ii. The implementation of research projects searching for more evidence regarding pharmacological therapies in general and especially regarding the use of PRPt and MSCs.

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