# Fibrosis and Sports Injuries: Concept and Implications

# The **GESMUTE-SETRADE** Consensus Statement

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**Background:** Musculoskeletal fibrosis can be frequently observed in the scope of sports medicine; however, there is no consensus regarding its definition, nor do we have substantial knowledge regarding its epidemiology or best therapeutic alternatives.

**Purpose:** The GESMUTE (Group for the Study of the Muscle Tendon System) Epidemiology Group, integrated into SETRADE (The Spanish Society for Sports Traumatology) propose a definition for musculoskeletal fibrosis within the field of physical exercise.

Study Design: Consensus statement.

**Methods:** A bibliographic review of the existing scientific evidence and consensus was developed by the authors on the definition of fibrosis in the field of sport.

**Results:** Our working group proposed the definition of fibrosis as an abnormal accumulation of extracellular matrix, usually with regards to an injury complication, showing various clinical findings affecting muscles, tendons, ligaments, articular capsules and nerves which, in turn, mars the recovery process, causing symptoms and finally leading to relapses.

**Conclusion:** Fibrosis in sport may be considered as an abnormal accumulation of extracellular matrix, usually related to complications of an injury, showing a wide range of clinical symptomatology, affecting muscles, tendons, ligaments, articular capsules, and nerves.

Keywords: consensus; fibrosis; sport; sport injury

Not only is there no current consensus in the sports medicine community with regards to the onset of fibrosis or its definition, but we are neither aware of its incidence nor prevalence, and no validated strategies have been elaborated in order to treat musculoskeletal fibrosis despite its common presence in the world of sports.

The GESMUTE (Group for the Study of the Muscle Tendon System) Epidemiology Group, integrated into SETRADE (The Spanish Society for Sports Traumatology), in its second Annual Meeting held in Madrid in September 2011, thus decided to elaborate on the current consensus document with the aim of contextualizing the presence of fibrosis in the world of sport. Fibrosis may be considered as a disorder affecting the cell matrix,<sup>5,7,11-13</sup> showing a chronic, abnormal, and unrepairable increase of the extracellular connective tissue, a process which interferes with the affected organ's own function<sup>16,20</sup>; it may also appear as a result of an abnormal accumulation of extracellular matrix, due to excessive production and/or degeneration variations.<sup>9,15,18</sup> This latter circumstance may manifest itself diffusely such as in myopathies or in cerebral vascular accidents, as well as in a localized manner such as in Dupuytren contracture, plantar fibromatosis, or retractile capsulitis.

In the case of muscle tissue, fibrosis is considered a defect in the muscle regeneration process causing an incomplete functional recovery<sup>25</sup> and a progressive substitution of muscle myofibril by collagen and proteins from the extracellular matrix (chronic myopathies).<sup>6</sup> This transformation of the extracellular matrix, related to a sports

The Orthopaedic Journal of Sports Medicine, 12(9), 23259671241266604 DOI: 10.1177/23259671241266604 © The Author(s) 2024

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Epidemiological Aspects of Fibrosis in Sports				
	Epidemi	ology		
Descriptive		Analy	<i>r</i> tic	
What Who Where	× ×, + +	How Why	× ×	
When	×, +			

 TABLE 1

 Epidemiological Aspects of Fibrosis in Sports

x, absence or low-quality scientific evidence; +, quality scientific evidence available.

injury, may affect muscles, tendons, or ligaments, either in an isolated manner or as a group; it may appear as granulomatous scarring, and it could also affect muscular aponeurosis thus compromising injury evolution. In addition, it may be found as a fibrous encapsulated hematoma or could well be a surgical sequelae whereas on other occasions it will be the way in which the injury fully recovers, meaning we would need to ask ourselves in such situations whether we are talking about adaptation to exercise or a pathology since on numerous occasions, functionality is compromised and regeneration curtailed, leading to the appearance of recurring injuries in those affected tissues.

# DEFINITION OF FIBROSIS

Fibrosis may be considered, within the scope of sports, as an abnormal build-up of extracellular matrix, usually related to injuries leading to complications, with signs of various clinical findings affecting muscles, tendons, ligaments, articular capsules, and nerves, all of which mar the recovery process, causing symptomatology and enabling recurrent injuries.

# Epidemiology

Few papers have been published to date discussing epidemiological data on the incidence of muscle or tendon injuries leading to fibrosis in sport.<sup>3,8,21-24,26</sup>

From a descriptive point of view, and to a certain extent, we know where fibrosis may be located, the type of patient who develops it, together with its onset; however, there is

Muscle		
Suture granulomas		
Injured intramuscular septum of rectus femoris		
of quadriceps		
Semitendinosus septum injury		
Bone lengthening		
Laceration		
Encapsulated hematoma		
Sarcopenia/Aging		
Adhesions/Fibrous bands		
Periostitis		
Tendon		
Rotator cuff pathology		
Tendinous fibrosis		
Tendon scar		
Ligament		
Ligament scar		
Sprain (ligament thickening)		
Articular capsule		
Retractile capsulitis		
Postimmobilization		
Other		
Nerve entrapment		

Figure 1. Entities considered to show the presence of fibrosis in sports.

no generally agreed definition and there is also limited knowledge of when or how it appears (Table 1).

The scarce number of currently available studies, just 1 on tendon<sup>8</sup> and 4 on muscle,<sup>3,23,24,26</sup> generally include a series or cases including data discussing the incidence of this disorder in post-muscle-injury scar tissue magnetic resonance (MR) or ultrasound images, with values which vary widely from 29.5% to 78%, showing the need for further studies with a more robust methodology in order to more thoroughly understand the appearance and presence of fibrosis.

#### Entities That May be Considered Fibrosis in Sport

Within the scope of sport activities and without the need to be extensive and thorough, the appearance and existence of fibrosis may be accepted in the following entities (Figure 1).

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Final revision submitted January 7, 2024; accepted February 16, 2024.

The authors declared that they have no conflicts of interest in the authorship and publication of this contribution. AOSSM checks author disclosures against the Open Payments Database (OPD). AOSSM has not conducted an independent investigation on the OPD and disclaims any liability or responsibility relating thereto.

#### **Diagnosis and Coding**

Fibrosis diagnosis, in the context of a sport injury, should always be associated with a methodical diagnosis by imaging, generally ultrasound or MR, to objectively confirm its presence, characteristics, and extension. This diagnosis process should also enable us to tell whether it is chronic or acute and localized or diffused and to determine the presence of other associated pathologies that may have led to the fibrosis itself (diabetes mellitus, thyroid disorders, myopathies, ischemia, denervation, kidney disease, hyperhomocysteinemia, etc).<sup>1,28</sup> Additional studies may well be needed to properly relate findings from those images with fibrosis pathological anatomy results. During echograph explorations of fibrosis, the disorder shows increased localized or diffused echogenicity, with changes of elasticity in the tissue and, thus, abnormal range of mobility as shown by dynamic maneuvers, as well as adherences to nearby structures, compressing or aggravating them.<sup>17</sup>

Musculoskeletal fibrosis MRs may commonly show hyperintensity in T2 pondered sequences, whereas, in T1 pondered sequences, hypointensity is shown. Other possible findings associated to musculoskeletal fibrosis when using this technique are fasciae thickening and, in the case of advanced fibrosis, loss of definition of the muscle contour associated to muscle atrophy.<sup>29</sup>

As for epidemiological coding of fibrosis in sports injuries, there is no current classification that includes fibrosis as a disorder or as a consequence of other associated pathologies.

An adequate definition of fibrosis and its consequent epidemiological classification as an sports injury, will allow us to not only perform a quick search for other cases involved but also select several specific cases worth studying, with the aim of establishing effective preventive measures as well as assessing treatment procedures and their results, amongst other variables.

To carry out this ambitious goal of coding fibrotic injuries, we cannot forget that fibrosis is an evolutive process, that is, it undergoes changes over time such that the result of these changes defines the extent of an affected tissue's capacity or incapacity and the presence or absence of limitations.

Following a proposal carried out by this group during GESMUTE First Congress in 2020,<sup>4</sup> the inclusion of a numerical factor which refers to the degree of functionality shown by the affected tissue in sports activities can be considered as a first approach to fibrosis-associated injuries. However, the evolution of the fibrosis process itself means injury classification must be recoded in parallel, from its origin (acute or subacute) to its chronic state, based on treatments received, possible functional improvements observed (whether changes in echographs or MR images are or are not observed), and irrespective of whether such observations show a functional correlation or not.

#### Treatment

Once the presence of fibrosis has been agreed, its reverse is highly unlikely and even the use of certain drugs (indomethacin, losartan, curcuma, chitosan) has shown very poor outcomes.<sup>10,14,19</sup> Physical exercise seems to play an essential role in preventing the onset of fibrosis in sports injuries. However, the effects played by the nature of the exercise and how loads are programmed are still unclear.

Predisposing pathologies should be duly assessed as controlling them may well enhance fibrosis prevention. Aerobic exercise has thus proven to be effective in preventing diabetic myopathies, a condition in which muscle fibrosis progressively develops.<sup>2,28</sup>

Prevention of sports injuries and a premature application of an adequate treatment to such conditions therefore seem to be the most effective preventive measures with regards to the onset of fibrosis. In this sense, the use of nutraceuticals, orthobiologics, or cell therapies for postworkout, postcompetition, and/or postinjury recovery could well turn out to be effective future lines of treatment and prevention for fibrosis in the world of sport.<sup>27</sup>

Another common finding among athletes is an asymptomatic version of fibrosis, very often considered a functional adaptation to exercise after an injury. Further evolutive studies are necessary to discern which of these fibroses should receive treatment and which preventive strategies may be used in each situation.

#### DISCUSSION

As per our understanding, the main contribution of the present document is the proposal of a first-ever and extremely useful definition in the scope of sports medicine of fibrosis: an abnormal accumulation of extracellular matrix, usually associated with an injury complication, with various clinical manifestations, involving muscle, tendon, ligament, joint capsule, and nerve, hindering recovery, causing symptoms, and finally leading to injury relapses. In addition, we propose a list of the main sports pathologies that involve fibrosis (Figure 1).

Despite fibrosis being frequently observed at the clinical practice in sports medicine, this phenomenon has remained surprisingly unstudied. No consensus documents have been published to date on what could be considered fibrosis in the sports context and there are few published studies discussing epidemiological, diagnostic, and treatment aspects of this disorder.

In the study of sports fibrosis, there is everything to research: (1) epidemiology; (2) main associated or predisposing pathologies; (3) injury mechanisms, injuries, or sports situations favoring its appearance; (4) prevention and treatment by means of nutrition, medicines, nutraceuticals, orthobiologics, and cell therapies; (5) genetic aspects; and (6) correlation of diagnosis methods and fibrosis histology.

#### CONCLUSION

Fibrosis in sport may be considered as an abnormal accumulation of extracellular matrix, usually related to complications of an injury, showing a wide range of clinical symptomatology, affecting muscles, tendons, ligaments, articular capsules, and nerves. It hinders recovery, causes symptomatology, and finally leads to injury relapses.

A greater research effort is needed to improve our knowledge in this area, hence our proposal to carry out further studies which have a robust and adequate methodological quality, to deepen our understanding of fibrosis in sport.

### ACKNOWLEDGMENTS

We thank SETRADE for the support provided to be able to produce and publish this consensus statement and to Dr Tomás F. Fernández Jaén for his permanent encouragement and support.

#### REFERENCES

- Abramowitz MK, Paredes W, Zhang K, et al. Skeletal muscle fibrosis is associated with decreased muscle inflammation and weakness in patients with chronic kidney disease. *Am J Physiol Renal Physiol.* 2018;315(6):F1658-F1669. doi:10.1152/ajprenal.00314.2018
- Amani M, Rahmati M, Fathi M, Ahmadvand H. Reduce muscle fibrosis through exercise via NRG1/ErbB2 modification in diabetic rats. *J Diabetes Res*. 2020;2020:6053161. doi:10.1155/2020/6053161
- Balius R, Pedret C, Galilea P, Idoate F, Ruiz-Cotorro A. Ultrasound assessment of asymmetric hypertrophy of the rectus abdominis muscle and prevalence of associated injury in professional tennis players. *Skeletal Radiol*. 2012;41:1575-1581. doi:10.1007/s00256-012-1429-y
- Beas Jiménez JD, León Garrigosa A, Doñoro Cuevas P, et al. Translation into Spanish and proposal to modify the Orchard Sports Injury Classification System (OSICS) Version 12. Orthop J Sports Med. 2021;9(4):2325967121993814. doi:10.1177/2325967121993814
- Bersini S, Gilardi M, Mora M, Kiol S. Tackling muscle fibrosis: from molecular mechanisms to next generations engineered models to predict drug delivery. *Adv Drug Deliv Rev.* 2018;129:64-77. doi:10 .1016/j.addr.2018.02.009
- Bo Li Z, Kollias HD, Wagner KR. Myostatin directly regulates skeletal muscle fibrosis. J Biol Chem. 2008;283(28):19371-19378. doi:10 .1074/jbc.m802585200
- Chapman MA, Meza R, Lieber RL. Skeletal muscle fibroblasts in health and disease. *Differentiation*. 2016;92(3):108-115. doi:10.1016/ j.diff.2016.05.007
- Chillemi C, Petrozza V, Garro L, et al. Rotator cuff re-tear or non-healing: histopathological aspects and predictive factors. *Knee Surg Sports Traumatol Arthrosc.* 2011;19:1588-1596. doi:10.1007/ s00167-011-1521-1
- Forcina L, Miano C, Scicchitano BM, Musaro A. Signals from the niche: insights into the role of IGF-1 and IL-6 in modulating skeletal muscle fibrosis. *Cells*. 2019;8:232. doi:10.3390/cells8030232
- Garg K, Corona BT, Walters TJ. Therapeutic strategies for preventing skeletal muscle fibrosis after injury. *Front Pharmacol.* 2015;6:87. doi:10.3389/fphar.2015.00087
- Gillies AR, Bushong EA, Deerinck TJ, Ellisman MH, Lieber RL. Threedimensional reconstruction of skeletal muscle extracellular matrix ultrastructure. *Microsc Microanal*. 2014;20(6):1835-1840. doi:10.1017/ s1431927614013300

- Gillies AR, Chapman Ma, Bushong EA, et al. High resolution threedimensional reconstruction of fibrotic skeletal muscle extracellular matrix. J Physiol. 2017;595(4):1159-1171. doi:10.1113/jp273376
- Gillies AR, Lieber RL. Structure and function of the skeletal muscle extracellular matrix. *Muscle Nerve*. 2011;44(3):318-331. doi:10.1002/ mus.22094
- Hara M, Yokota K, Saito T, et al. Periostin promotes fibroblast migration and inhibits muscle repair after skeletal muscle injury. *J Bone Joint Surg Am*. 2018;100:e108. doi:10.2106/jbjs.17.01230
- Ismaeel A, Kim JS, Kirk JS, et al. Role of transforming growth factorβ in skeletal muscle fibrosis: a review. *Int J Mol Sci.* 2019; 20(10):2446. doi:10.3390/ijms20102446
- Lieber RL, Ward SR. Cellular mechanisms of tissue fibrosis. 4. Structural and functional consequences of skeletal muscle fibrosis. *Am J Physiol Cell Physiol*. 2013;305(3):C241-C252. doi:10.1152/ajpcell .00173.2013
- Maeda A, Yamagishi M, Otsuka Y, et al. Characteristics of the passive muscle stiffness of the vastus lateralis: a feasibility study to assess muscle fibrosis. *Int J Environ Res Public Health*. 2021; 18:8947. doi:10.3390/ijerph18178947
- Mahdy MAA. Skeletal muscle fibrosis: an overview. *Cell Tissue Res.* 2019;375(3)575-588. doi:10.1007/s00441-018-2955-2
- Mahdy MAA, Akl MA, Madkour A. Effect of chitosan and curcumin nanoparticles against skeletal muscle fibrosis at early regenerative stage of glycerol-injured rat muscles. *BMC Musculoskelet Disord*. 2022;23: 670. doi:10.1186/s12891-022-05633-x
- Meyer GA, Lieber RL. Skeletal muscle fibrosis develops in response to desmin deletion. *Am J Physiol Cell Physiol*. 2012;302(11):C1609-C1620. doi:10.1152/ajpcell.00441.2011
- Pedret C, Balius R. Lesiones musculares en el deporte. Actualización de un artículo del Dr. Cabot publicado en Apuntes de Medicina Deportiva en 1965. Apunts Med Esport. 2015;50(187):111-120. https://www.apunts.org/es-lesiones-musculares-el-deporte-actualiz acion-articulo-X0213371715389042
- Pérez del Pozo D. Epidemiología de la lesión deportiva. TFG. Facultad Ciencias Actividad Física y Deporte. Universidad Politécnica. *Madrid*. 2015. https://oa.upm.es/36508/
- Reurink G, Almusa E, Goudswaard GJ, et al. No association between fibrosis on magnetic resonance imaging at return to play and hamstring reinjury risk. *Am J Sports Med.* 2015;43(5):1228-1234. doi:10 .1177/0363546515572603
- Reurink G, Goudswaard GJ, Tol JL, et al. MRI observations at return to play of clinically recovered hamstring injuries. *Br J Sports Med*. 2014;48(18):1370-1376. doi:10.1136/bjsports-2013-092450
- Sass FA, Fuchs M, Pumberger M, et al. Immunology guides skeletal muscle regeneration. *Int J Mol Sci.* 2018;19:835. doi:10.3390/ ijms19030835
- Silder A, Heiderscheit BC, Thelen DF, Enright T, Tuite MJ. MR observations of long-term musculotendon remodeling following a hamstring strain injury. *Skeletal Radiol.* 2008;37:1101-1109. doi:10.1007/s00256-008-0546-0
- Tonogai I, Hayashi F, Iwame T, et al. Platelet-rich plasma does not reduce skeletal muscle fibrosis after distraction osteogenesis. J Exp Orthop. 2018;5:26. doi:10.1186/s40634-018-0143-7
- Winchester LJ, Veeranki S, Pushpakumar S, Tyagi SC. Exercise mitigates the effects of hyperhomocysteinemia on adverse muscle remodeling. *Physiol Rep.* 2018;6(6):e13637. doi:10.14814/phy2 .13637
- Winkler T, von Roth P, Matziolis G, et al. Time course of skeletal muscle regeneration after severe trauma. *Acta Orthop.* 2011;82(1):102-111. doi:10.3109/17453674.2010.539498