Role of Hypoxia in the Genesis of Anterior Knee Pain
Anterior Knee Pain

ORIGIN

LATERAL RETINACULUM

Infrapatellar Fat Pad

Syxovium

Subchondral Bone

INFLUENCING FACTORS

Gender

Psychological

Instability

Overload

INFLUENCING FACTORS
NOT ALL PFM ARE SYMPTOMATIC

Symptomatic

Asymptomatic

Why?

Sanchis-Alfonso et al, 2006
What have we learned from realignment surgery?

No relation between the result (satisfactory vs non-satisfactory) and the presence or absence of PFM ($\chi^2 = 0.025, p=0.875$)

<table>
<thead>
<tr>
<th>Presence of PFM</th>
<th>Satisfactory</th>
<th>Poor/Fair</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFM</td>
<td>18 / 21</td>
<td>3 / 21</td>
</tr>
<tr>
<td>NO PFM</td>
<td>14 / 16</td>
<td>2 / 16</td>
</tr>
</tbody>
</table>

Satisfactory centralization at long-term follow-up in 16 cases (43.24%)

Sanchis-Alfonso et al, 2006
A RADIOGRAPHICAL PMF MAY NOT BE REAL

It could induce us to indicate a realignment surgery that could provoke an iatrogenic PFM leading to a worsening of preoperative symptoms.
25 yo F / Medial Patellar Instability After Insall’s Proximal Realignment

Preop stress CT in extension

Postop stress CT in extension

Preop Gait Analysis

Postop Gait Analysis
We look PFM as representing internal load shifting within the patellofemoral joint that may lower the threshold (i.e., decrease of the Envelope of Function) for the initiation and persistence of loss of tissue homeostasis leading to the perception of patellofemoral pain. Pain always denotes loss of tissue homeostasis.
Hypothesis

Anterior knee pain in the young patient—what causes the pain?

"Neural model"

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Articular damage is the “provoking aggravating factor” (Sanchis-Alfonso et al., 1998). Pain is a subjective experience of the patient, which may have a multifactorial origin. In our surgical experience, we have observed that patients with symptoms in both knees usually report more symptoms on the less symptomatic knee, while in the contralateral knee, the symptoms are less severe. Although it is possible that patients with bilateral pain may have more severe pain in one knee than in the other, the symptoms in the contralateral less symptomatic knee disappear or decrease in many cases, perhaps because we have reduced the load on this knee. However, some of the patients who have PFM may be asymptomatic because they have adequate dynamic control of patellar tracking during activities.

The great number of surgical techniques used to treat patients with AKP suggests a lack of understanding of the pathophysiology, which is another reason against the universal acceptance of the PFM theory. Our studies have centered on pathophysiology (Sanchis-Alfonso et al., 1998, 2001, Sanchis-Alfonso and Roselló-Sastre, 1998, 2000). It is well-known that pain in patients with PFM cannot be ascribed to a single factor, but to several. The infrapatellar fat pad, subchondral bone, the quadriceps tendon, patellar ligament, synovium, the medial and lateral retinaculum all have a rich nerve supply and these structures, individually or in combination, may cause pain (Fuller et al., 1983, Fuller et al. 1985, Wajszczuk et al. 1990, Dye et al. 1998, 1999, Witoniski and Wugowska-Danilewicz, 1999, Sanchis-Alfonso et al. 1999, Biedert and Sanchis-Alfonso 2002).

A criticism of the patellofemoral malalignment theory

In the 1970's, anterior knee pain (AKP) was ascribed to the presence of patellofemoral malalignment (PFM) (Hughston 1968, Merchant et al. 1974, Merchant and Marxer 1974, Picat et al. 1975, Insall 1979). We define PFM as an abnormality of patellar tracking consisting of lateral displacement or lateral tilt of the patella, or both, in extension, that reduces in flexion (Figure 1) (Insall 1979). For many years, the PFM theory was widely accepted as an explanation for the genesis of AKP. Currently, however, it is questioned by many and one reason is the poor relationship between symptoms and malalignment (Figures 2 and 3). We believe that PFM is a necessary but not the sole cause of pain—i.e., it produces a "favorable"
Hyperinnervation in the lateral retinaculum is a factor implicated in the pathogenesis of anterior knee pain

Severe pain vs moderate-light pain (p = 0.03; F = 4.93)

Sanchis-Alfonso et al, 1998
Free nerve endings

Sanchis-Alfonso et al, 2000
Substance P immunoreactive nerves

Innervation adopting mainly a perivascular location

Severe pain (94%) vs moderate-light pain (30%) (p = 0.005)

We hypothesize that periodic short episodes of ischemia due to vascular bending could be implicated in pain in most of the cases of young patients with anterior knee pain syndrome.

We believe that homeostasis in the knee region of anterior knee pain syndrome patients could be disturbed by vascular problems.
Ischemia

NGF

PAIN (1-4) - INSTABILITY (5-7)

Hyperinnervation

Lesions that produce ischemia

Sanchis-Alfonso et al, 1998, 2005
Lesions that are a consequence of ischemia (I)

- Myxoid stromal degeneration
- Infarcted foci of the connective tissue

*Sanchis-Alfonso et al, 2005*
Lesions that are a consequence of ischemia (II)

Sanchis-Alfonso et al, 1998, 2005
We have found higher values in the number of vessels in the lateral retinaculum of patients with severe pain than in those with moderate or light pain ($p = 0.03; F = 4.58$)

*Factor VIII*

*Sanchis-Alfonso et al, 2005*
VESSELS IN 5 HOT SPOTS

Vascular innervation

Yes

No

PAIN SCORE

n = 31

Sanchis-Alfonso et al, 2005
Immunohistochemistry (VEGF)

Sanchis-Alfonso et al, 2005
Western Blot

Sanchis-Alfonso et al, 2005
Ischemia

Hypoxia  →  Neurons

VEGF  →  Hypervascularization

NGF  →  Neural sprouting  →  Hyperinnervation
                 →  Neural proliferation in vessel walls
Role of hypoxia in the genesis of anterior knee pain

Clinical findings


Pathogenesis of Anterior Knee Pain

- Hypoxia
- NGF
- Free nerve endings
- Substance P
- Prostaglandin E2
- Bone resorption
- Mast cells
- Histamine
- PAIN
- Hyperinnervation
Thank You