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Comparative study of intra-articular pressure dynamics in joints with acute traumatic and chronic inflammatory effusions: potential implications for hypoxic-reperfusion injury

P Merry, R Williams, N Cox, J B King, D R Blake

Abstract

It has been proposed that the process of hypoxic-reperfusion injury contributes to the persistence of synovitis in the inflamed human joint. The generation of pathological, exercise induced, intra-articular pressure leading to occlusion of the synovial microcirculation is central to this mechanism. However, acute traumatic inflammatory joint effusions rarely result in chronic synovitis, suggesting that either the basic hypothesis is incorrect, or that joints with acute traumatic effusions show different intra-articular pressure dynamics.

In this study the intra-articular pressure was measured at rest and during isometric exercise in five patients with acute traumatic joint effusions and in nine patients with chronic inflammatory joint effusions. The generation of intra-articular pressure in the patients with acute traumatic effusions was significantly lower at rest (mean 2·0 *v* 19·6 mm Hg) and during exercise (mean 13·7 *v* 222·5 mm Hg) than in the patients with chronic effusions. This was due to reflex muscular inhibition around the joint, which inhibited the pathological generation of intra-articular pressure. This difference in the ability to generate intra-articular pressure might mitigate against hypoxic-reperfusion injury in joints with acute traumatic effusions, thereby explaining the paradoxical clinical observation that patients with acute traumatic inflammatory joint effusions rarely develop chronic synovitis.

The Inflammation Research Group, London Hospital Medical College, London E1 2AD, UK
P Merry
D R Blake

Department of Rheumatology, Royal Hampshire County Hospital, Romsey Road, Winchester SO22 5DG, UK
R Williams
N Cox

Department of Orthopaedics, The Royal London Hospital, London E1 2AD, UK
J B King

Correspondence to:
Professor Blake.

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Hypoxic-reperfusion injury is an established mechanism for the generation of reactive oxygen species, which leads to tissue damage in many organs.[1] It has recently been shown, ex vivo, that human synovium exposed to hypoxic-reoxygenation cycles generates reactive oxygen species,[2] whereas hypoxic-reperfusion injury has been shown to occur in vivo in the chronically inflamed human knee joint.[3–5] Exercise of the joint causes the intra-articular pressure to rise above the capillary perfusion pressure, resulting in occlusion of the synovial capillary bed and hypoxia.[6 7] When exercise stops, the intra-articular pressure falls and reperfusion occurs. As a result, reactive oxygen species are generated by the uncoupling of a variety of intracellular redox systems, and oxidative damage occurs which affects lipids, IgG, hyaluronate, and albumin within the joint.[3 8 9] Oxidative damage to many of these biomolecules may initiate a chain of proinflammatory events, and we therefore conclude that hypoxic-reperfusion injury may contribute to the peculiar persistence of chronic inflammatory synovitis.

Intra-articular pressure is central to the mechanism of hypoxic-reperfusion injury to the joint. The dynamics of intra-articular pressure in acute traumatic effusions have never previously been investigated in humans. However, they are of interest because of the intriguing, and to us paradoxical, clinical observation that patients with acute traumatic inflammatory effusions rarely develop chronic synovitis.

In this study, we compared the pathophysiology of the generation of intra-articular pressure in patients with acute traumatic and chronic inflammatory joint effusions to assess whether a difference exists that might mitigate against hypoxic-reperfusion injury in joints with acute traumatic effusions, thereby explaining the paradox.

Patients and methods

PATIENTS

After approval by an ethical committee, two different groups of patients were studied: (*a*) patients with chronic inflammatory knee effusions and (*b*) patients with acute traumatic knee effusions.

Eight patients with chronic knee effusions and one patient with a chronic shoulder effusion were studied. The age range was 30–86 years (mean 62 years) and the group consisted of three men and six women. There were four patients with rheumatoid arthritis, two with psoriatic arthritis, two with inflammatory osteoarthritis, and one with ankylosing spondylitis. All effusions had occurred for longer than two months (table 1).

Five patients (four men, one woman) with acute traumatic knee effusions were studied. The age range was 21–38 years (mean 28 years). Three patients had lateral ligament strains, one a dislocated patella, and one an anterior cruciate ligament tear. All the effusions were detectable clinically and had been present for at least 24 hours but less than three days (table 2).

METHODS

A miniature pressure transducer with a silicon diaphragm housed at the end of a 10 cm long stainless steel 14·5 gauge probe was used (Entran UK). The response of the transducer

Table 1 Intra-articular pressure in patients with chronic inflammatory synovitis

Patient no	Age	Sex*	Diagnosis*	Duration of effusion (months)	Intra-articular pressure at rest (mm Hg)	Mean (SD) intra-articular pressure during exercise (mm Hg)
1	30	F	RA	6	15	354 (8·5)
2	67	M	OA	12	6	142·5 (4·2)
3	67	M	PsA	3	23	252·6 (124·8)
4	52	M	AS	2	10	228·5 (63·8)
5	62	F	RA	3	12	102·5 (28·5)
6	76	M	RA	4	76	532·5 (39·3)
7	68	M	PsA	12	5	50 (1·6)
8	49	F	RA	12	10	117·5 (17·1)
9†	86	F	OA	12	15	105·25 (26·2)

*Abbreviations: RA=rheumatoid arthritis; OA=osteoarthritis; PsA=psoriatic arthritis; AS=ankylosing spondylitis. F=female; M=male.
†Patient 9 had a shoulder effusion; all other patients had knee effusions.

Table 2 Intra-articular pressure in patients with acute traumatic knee effusions

Patient no	Age	Sex*	Diagnosis*	Duration of effusion (months)	Intra-articular pressure at rest (mm Hg)	Mean (SD) intra-articular pressure during exercise (mm Hg)
10	38	M	Ligament strain	3	0	17·5 (3)
11	21	M	Dislocated patella	1	0	18·(4·3)
12	28	M	Anterior cruciate tear	3	6	21·4 (0·9)
13	28	M	Ligament strain	3	0	−0·6 (3·3)
14	25	M	Ligament strain	2	4	12·2 (3·9)

*Abbreviations: RA=rheumatoid arthritis; OA=osteoarthritis; PsA=psoriatic arthritis; AS=ankylosing spondylitis. F=female; M=male.

was linear from −50 to 1500 mm Hg between 0 and 60°C. The probe was sterilised by immersion in 2% activated glutaraldehyde solution for two hours.

The subjects were rested in a recumbent position for 30 minutes before the measurements were taken. A 14 gauge PTFE cannula was introduced into the suprapatellar recess of the knee, from the medial approach, after subcutaneous infiltration of 2% lignocaine. Care was taken not to inject any anaesthetic into the joint cavity for two reasons: (*a*) to avoid increasing the intra-articular effusion volume, hence raising the intra-articular pressure and (*b*) to avoid any influence of the anaesthetic on the muscle tone of the quadriceps. On removal of the trochar, the pressure transducer was immediately introduced into the knee cavity via the cannula to measure the intra-articular pressure directly. The pressure probe was connected to a chart recorder (BBC Austria) to allow continuous measurement of the intra-articular pressure (fig 1). The intra-articular pressure was recorded at rest and during cycles of isometric quadriceps contraction and subsequent relaxation. A minimum of four cycles was performed per patient and a mean value for the intra-articular pressure during exercise was obtained. The subjects held their heads in a neutral position during testing to avoid the effect of tonic neck reflexes on the Hoffman reflex.[10] The pressure probe was calibrated against a mercury manometer before and after all pressure measurements.

The intra-articular pressure was measured in one patient with a chronic inflammatory shoulder effusion. The joint cavity was cannulated from the anterior approach and exercise was by isometric shoulder abduction.

Statistical analysis was performed using the Wilcoxon pairs test, as the data did not satisfy the required assumptions for analysis using parametric procedures.

Results

None of the patients experienced pain during quadriceps contraction. In all the patients with acute effusions a high degree of quadriceps

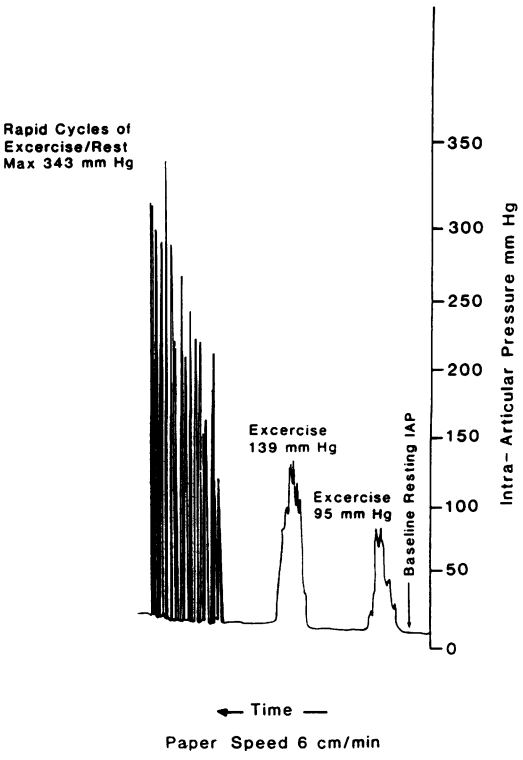

Figure 1 Typical example of recording of the intra-articular pressure from patient 4.

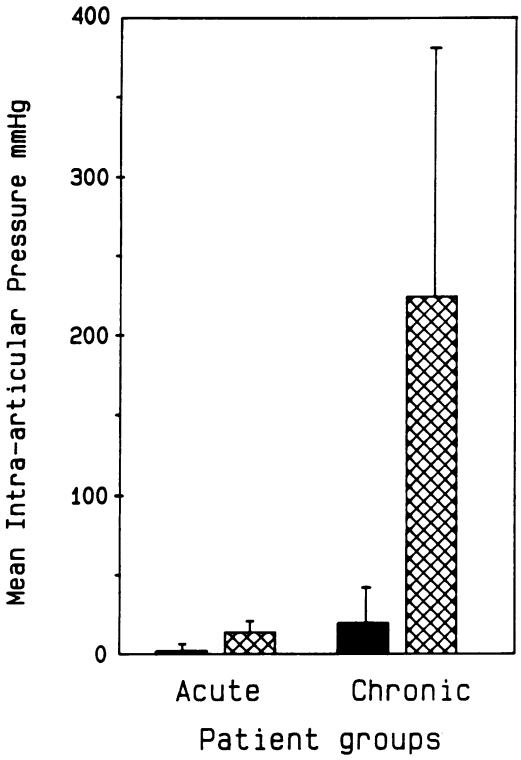

Figure 2 Bar chart illustrating the mean intra-articular pressure at rest and during isometric joint exercise, in patients with acute traumatic joint effusions and chronic inflammatory joint effusions. Solid blocks, rest; hatched blocks, exercise; bars, standard deviation.

inhibition was noted on contraction of the quadriceps. Quadriceps inhibition was not obvious in the patients with chronic effusions.

In the patients with chronic effusions, the mean (SD) intra-articular pressure at rest was 19·6 (23·5) mm Hg and the mean intra-articular pressure during exercise was 222·5 (158·6) mm Hg. In the patients with acute traumatic effusions, the mean (SD) intra-articular pressure at rest was 2·0 (2·8) mm Hg and the mean intra-articular pressure during exercise was 13·7 (8·6) mm Hg. There is a clear difference in the generation of intra-articular pressure between the two groups. This is significant both at rest ($p<0·01$) and during exercise ($p<0·001$).

Discussion

INTRA-ARTICULAR PRESSURE AT REST

In the patients with chronically inflamed joints the mean intra-articular pressure at rest was 19·6 mm Hg. This is consistent with the findings of other research groups.[11–13] Patient 6 had a reproducible pressure of 76 mm Hg. Palmer and Myers[12] recorded a similarly high resting intra-articular pressure of 80 mm Hg in one patient with an inflammatory effusion.

Guyton *et al*[14] have reported that the capillary perfusion pressure in healthy tissues ranges between 10 and 20 mm Hg, thus an intra-articular pressure of 76 mm Hg would be expected to compromise synovial perfusion and produce infarction of the synovium leading to gangrene. This did not occur in patient 6, suggesting the presence of a protective mechanism to prevent total ischaemia of the synovium. Levick[15] suggests that the synovial vasculature is partially protected by the dense intervening bands of fibrils and collagen. A further explanation may be related to the fact that there is considerable variation in the capillary perfusion pressure between different types of tissue—for example, the mesentery in cats has a capillary perfusion pressure ranging between 30 and 40 mm Hg.[16] The capillary perfusion pressure within normal human synovium is not yet known, but possibly it may be higher than that in the mesentery of cats, and in addition, it would be reasonable to expect a further increase in pressure in inflamed synovium (J R Levick, personal communication). Intra-articular pressure of 76 mm Hg may therefore not necessarily compromise synovial perfusion.

In the group of patients with acute traumatic effusions the mean intra-articular pressure at rest was 2·0 mm Hg, significantly less than in patients with chronic joint effusions. This difference may be explained by lower quadriceps muscle tone in the group with traumatic effusions; these patients showed clinically greater quadriceps inhibition, an observation supported by other workers.[17 18] In addition, the chronically inflamed joint capsule shows greater elasticity,[13] suggesting an increased ability for the generation of intra-articular pressure.

INTRA-ARTICULAR PRESSURE DURING ISOMETRIC EXERCISE OF THE JOINT

During isometric quadriceps contraction of the joints in the patients with chronic effusions there was a large increase in the intra-articular pressure in all instances (mean 222·5 mm Hg). Several types of synovitis were studied and the increase in intra-articular pressure is clearly not specific to a particular disease. These findings are consistent with the findings of other workers.[11 19 20] The increase in the intra-articular pressure in most instances, was larger than the expected capillary perfusion pressure of the synovium and sometimes greater than the systolic blood pressure. The increase in the intra-articular pressure on contraction of the quadriceps was immediate and lasted throughout the contraction, whether this was five seconds or two minutes. On relaxation of the quadriceps contraction, the intra-articular pressure immediately fell to the value of the intra-articular pressure at rest.

One patient studied had a chronic inflammatory effusion affecting the shoulder joint. Isometric abduction of the shoulder joint produced a similar increase in the intra-articular pressure to that seen in the chronically inflamed knees, suggesting that the increase in the intra-articular pressure during exercise is not necessarily specific to one joint.

It is known that exercise of the normal human knee does not produce significant positive fluxes in the intra-articular pressure,[19 21] emphasising the critical role of effusions in the generation of intra-articular pressure. However, during the isometric quadriceps contraction of knees with acute traumatic effusions, only a moderate rise in the intra-articular pressure was

seen (mean 13·7 mm Hg) despite the presence of a significant clinically detectable effusion.

EXERCISE INDUCED CHANGES IN THE INTRA-ARTICULAR PRESSURE

The reason for the observed difference in the generation of intra-articular pressure between the patients with acute and chronic joint effusions may be explained by the large quadriceps inhibition seen in the patients with acute traumatic knee effusions. The patients with acute traumatic effusions had all had trauma to the knee within the previous three days and it is known that post-traumatic quadriceps inhibition is at a maximum during this time.[17] No pain was experienced during attempted isometric quadriceps contraction in either group, which excluded the well described component of quadriceps inhibition secondary to pain.[22–24]

The production of quadriceps inhibition by knee joint effusions is well described[19 25] and it is likely that the quadriceps inhibition seen in this study was a result of the joint effusion exerting its inhibitory effect via capsular mechanoreceptors,[26 27] resulting in inhibition of the Hoffman reflex.[28] Jones *et al*[18] concluded that in chronic synovitis the effusion within the knee joint does not provoke significant quadriceps inhibition, in contrast with the marked inhibition seen in joints with acute traumatic effusions.[17] This study supports this observation and also exposes the pathophysiological consequence by showing that patients with acute traumatic knee effusions do not generate high intra-articular pressures during exercise of the joint.

There are several other possible explanations for the difference between the two groups. Acute effusion into a previously normal joint is known to generate a lower intra-articular pressure, volume for volume, than effusion into a chronically inflamed joint, owing to the higher capsular elasticity in the chronically inflamed joint.[13] However, this observation is complicated by the fact that the volume of a joint effusion does not correlate with its hydrostatic pressure[11 13] as the complex mechanical behaviour of the articular structures has to be considered—for example, capsular elasticity and viscoelasticity. In this study the mean age of patients with acute traumatic effusions was 28 years compared with 62 years for the group with chronic effusions, and it is known that joint elasticity increases with increasing age,[29] suggesting a greater ability to generate high intra-articular pressures. Conversely, the size and strength of quadricep muscles decline with increasing age,[30] suggesting a decreased ability for the generation of intra-articular pressure. Thus there are several factors that may influence the ability to generate high intra-articular pressures. In this study the effect of quadriceps inhibition in the patients with acute traumatic effusions appears to be the most fundamental and influential factor on their failure to generate high intra-articular pressures.

As the generation of increased intra-articular pressure is central to the mechanism of hypoxic-reperfusion injury, the failure to generate pathologically high intra-articular pressures in patients with acute traumatic effusions suggests that quadriceps inhibition, in this instance, may be a protective mechanism.

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