# Spontaneous rupture of the Achilles tendon is preceded by widespread and bilateral tendon damage and ipsilateral inflammation

## A clinical and histopathologic study of 60 patients

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**ABSTRACT – 60 consecutive patients with spontaneous rupture of the Achilles tendon (AT) underwent surgery. Biopsies were taken at the operations from the site of the rupture, the proximal part, the calcaneal insertion, and the peritendium of the injured tendon. A percutaneous needle biopsy was taken from the contralateral (uninjured) AT.**

**On histological examination, collagen degeneration, tenocyte necrosis, and acute inflammation were found at the rupture site in all cases. In the proximal part and at the insertion, degeneration was present in 56/56 and 51/55 of the cases, necrosis in 55/56 and 50/55, and acute inflammation in 49/56 and 35/55, respectively. The severity of the histological changes decreased from the rupture site to the proximal part to the site of insertion, and showed no relation to the age of the patients or the time from the rupture to the operation. Peritendineal vascular changes were minor. In the contralateral AT, degeneration and necrosis were present in 47/50 and 42/50 of the cases, respectively, but the severity of the changes was less than in the injured tendon. Acute inflammation was present in only 1 case.**

**Spontaneous rupture of AT seems to be preceded by widespread, bilateral damage of the tendon and widespread ipsilateral acute inflammation.**

In patients who have no history of steroid treatment or systemic disease, the etiology of spontaneous rupture of the Achilles tendon (AT) is uncertain. Hypoxia due to a vascular lesion, ageing and repeated microtraumas from overuse are the factors most commonly considered (Williams 1986, Kannus and Józsa 1991, Kannus 1997, Leppilahti and Orava 1998).

In large studies, pathological changes—mainly described as collagen degeneration—at the rupture site have been found in a few (Picaud et al. 1966), most (Burchhardt et al. 1992) or all cases of AT (Orell 1958, Arner et al. 1958/59, Kannus and Józsa 1991). When present, degenerative changes are seen even when the rupture is only a few hours old, indicating that they precede the rupture (Arner et al. 1958/59). On the other hand, Williams (1986) stated that AT is not usually the consequence of previous degeneration.

None of the previous studies have focused on histological examination of the changes in the tendon outside the rupture site. We evaluated the histopathology of AT in various parts of the ruptured tendon as well as in the contralateral AT.

## Patients and methods

The criteria for inclusion were: 1) a total rupture diagnosed by a palpable gap in the tendon, a reduction in plantar flexion of the injured foot, and a positive Thompson's test (Thompson and Doherty 1962); 2) age between 18 and 60 years; 3) operation on the rupture within 7 days; 4) no previous disease or medication which could interfere with the structure of the tendon; 5) informed consent

for biopsies taken from both the ruptured and the contralateral AT.

60 consecutive patients (mean age 37 (20–60) years, 50 men) admitted to the Department of Orthopaedic Surgery, Bispebjerg University Hospital, and fulfilling the above criteria, were included. Their mean weight was 76 (55–97) kg, and mean height 177 (150–196) cm. 32 patients had the rupture on the left side. 25 of them were athletes, while 32 had taken part in recreational sports and 3 had not.

53 patients had sustained the rupture during sports when pushing off with the weight-bearing forefoot while extending the knee joint as at the start of a sprint. In the others, the rupture had followed a sudden unexpected (4) or violent (3) dorsiflexion of the ankle.

The mean time from rupture to operation was 38 (7–112) hours. The preoperative evaluation also included measurement of the thickness of the AT. All patients were operated on by the same surgeon (RC). A tourniquet was not applied. The distance from the insertion of the tendon to the site of rupture was recorded. During the operation, 3 surgical biopsies were taken: at the site of the rupture, the proximal part of the tendon (10 cm above the calcaneus), and at the insertion of the calcaneus. A surgical biopsy was also obtained from the peritendium at the level of the rupture, and a percutaneous needle biopsy was taken from the contralateral, unruptured AT at the same level as the rupture.

All biopsy specimens were fixed in 4% phosphate buffered formalin at pH 7.4 and embedded in paraffin. 5 $\mu$m sections were stained with hematoxylin-eosin and Picro-Sirius. In selected cases, immunohistochemical studies were done using antibodies to calgranulin (CG; clone mac387, Dako) and neutrophilic elastase (NE; clone NP57, Dako, Glostrup, Denmark). Demasking for both antibodies was carried out using Pronase E (0.05% for 5 min. at 37 °C). The EnVision+ technique (Vyberg and Nielsen 1998) was used for visualization.

A morphologic analysis was done by the two pathologists (JJ and MV) together, but they were blinded as to the clinical data or the biopsy site. Of the 300 biopsy specimens, 19 were excluded because of insufficient material. Tendon degeneration, tenocyte necrosis and acute inflammation were assessed in each specimen and graded as follows: 0 (absent), 1 (slight), 2 (moderate) and 3 (severe). Degeneration was defined as collagen fiber fragmentation and fraying. Necrosis was defined as occurrence of tenocytes with pyknotic, fragmented or dissolved nuclei. Acute inflammation was defined as infiltration of neutrophils in the tendon (a few perivascular neutrophils being discarded). In cases where it could not be unequivocally decided whether pyknotic nuclei or nuclear fragments represented neutrophils or tenocytes, a positive staining reaction for CG and/or NE was interpreted as the presence of neutrophils. All other histological changes were also recorded.

As control material, AT sections obtained at 3 autopsies (patients aged 30–50 years with no history of AT lesions) were included in the study. No histological changes were seen in the control sections (Figure 1).

In the statistical analyses, we used the sign test for paired data and the Wilcoxon test for unpaired data. Spearman's rank-order correlation coefficient was calculated for measures of association. $P = 0.05$ was used as the level of significance.

The study was accepted by the Scientific Ethics Committee in Copenhagen and performed in accordence with the Helsinki Declaration.

## Results

On the clinical examination, all ruptured AT were diffusely thickened as compared to the contralateral AT (mean outer thickness 4 cm above the insertion 2.9 (2.2–3.8) cm versus 1.9 (1.3–2.6) cm). At operation, the mean distance from the insertion in the calcaneus to the site of rupture was 4.7 (2.2–8.4) cm.

### *Histological findings (Tables 1 and 2)*

In the ruptured AT, degeneration, tenocyte necrosis and acute inflammation were found at the site of rupture in all cases. In the proximal part and at the insertion site, the same changes were seen in most cases, although slightly less than at the rupture site. However, the difference between this and the proximal part regarding degeneration was not statistically significant. As compared to the normal control tendons (Figure 1), we found

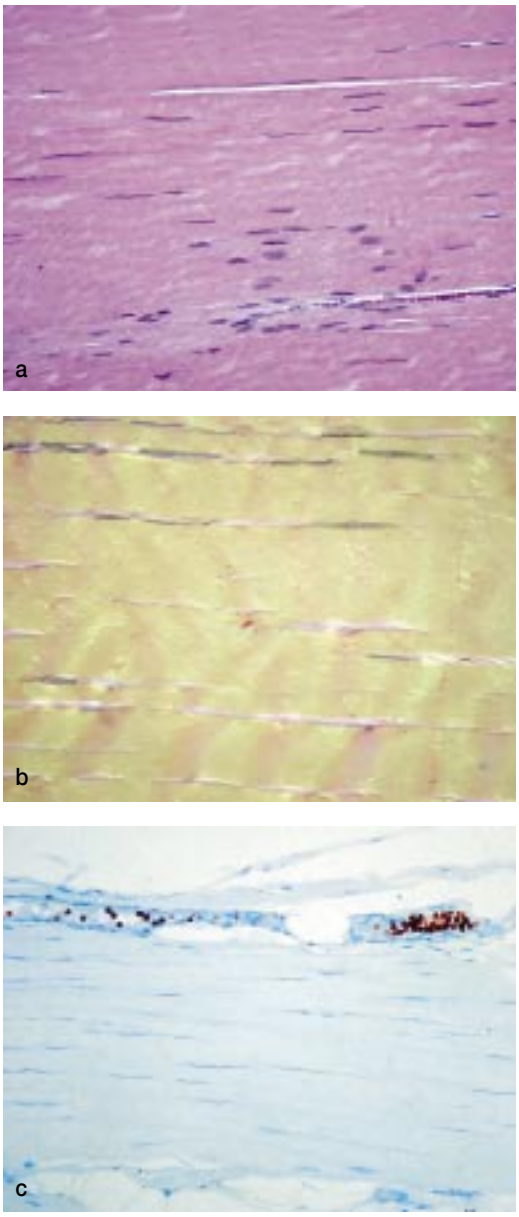


Figure 1. Sections from a normal tendon (control) (×200).
a. The elongated tenocyte nuclei are seen in parallel rows between uniform hyaline collagen bands. They are more rounded along the edge of an intratendinous vessel, HE.
b. With Picro-Sirius staining, the normal collagen structure can be seen better with polarized light.
c. Immunohistochemical staining for calgranulin markedly increases the cytoplasmatic reaction of intravascular neutrophils, but no staining is seen in the tendon.

marked changes in the damaged ATs (Figure 2). Degenerated and well-preserved areas were seen as alternating streaks. The degenerated collagen had irregular, often thin, wavy or angulated fibers which stained poorly, and sometimes formed almost structureless, slightly basophilic (mucoid) areas. Collagen degeneration and tenocyte necrosis were closely associated. The changes were often accompanied by rounding of tenocyte nuclei and regional variations in cellularity. Scattered neutrophils were usully found in the damaged tissue and between preserved collagen fibers, where they became markedly elongated, at times lying together with tenocytes, apparently replacing them. Stainings for CG and NE gave almost identical results, accentuating the neutrophils, which were often seen as disintegrated cells. The severity of neutrophilic infiltration (0–3) was strongly correlated to the severity of the degeneration and necrosis.

Small vessels in the tendon sometimes showed swelling of the endothelium, and neutrophils were frequently seen migrating through venular walls and infiltrating the perivascular connective tissue sheath. The presence of neutrophils perivascularly and between the collagen fibers was closely associated. In a single case, the histological examination revealed chondroid metaplasia in the AT at the site of rupture. We found no signs of previous disease in the tendons.

All biopsies from the peritendium showed varying degrees of edema, fibrinoid, and neutrophilic

**Table 1. Histological changes in biopsies of ruptured and contralateral AT**

| Grade [a] | 0 | 1 | 2 | 3 | 1–3 |
|---|---|---|---|---|---|
| *Rupture site (n = 60)* | | | | | |
| Degeneration | 0 | 8 | 40 | 12 | 60 |
| Tenocyte necrosis | 0 | 7 | 35 | 18 | 60 |
| Acute inflammation | 0 | 27 | 26 | 7 | 60 |
| *Proximal part (n = 56)* | | | | | |
| Degeneration | 0 | 14 | 30 | 12 | 56 |
| Tenocyte necrosis | 1 | 16 | 24 | 15 | 55 |
| Acute inflammation | 7 | 31 | 15 | 3 | 49 |
| *Insertion site (n = 55)* | | | | | |
| Degeneration | 4 | 32 | 17 | 2 | 51 |
| Tenocyte necrosis | 5 | 28 | 19 | 3 | 50 |
| Acute inflammation | 20 | 30 | 5 | 0 | 35 |
| *Contralateral AT (n = 50)* | | | | | |
| Degeneration | 3 | 38 | 8 | 1 | 47 |
| Tenocyte necrosis | 8 | 31 | 11 | 0 | 42 |
| Acute inflammation | 48 | 0 | 1 | 0 | 1 |

[a] Grading of pathological changes: 0 none, 1 slight, 2 moderate, 3 severe.

**Table 2. Mean grade (on a scale of 0–3) of histopathological changes in AT areas in relation to the time from rupture to biopsy (≤ 36 h, >36 h; mean and range) and in relation to the age of the patients (≤ 37 years, > 37 years; mean and range)**

| | N | CD [a] | | | | TN | | | | AI | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | RS [b] | PP | IS | CAT | RS | PP | IS | CAT | RS | PP | IS |
| Total | 60 | 2.1 [c] | 2.0 | 1.3 | 1.1 | 2.2 [d] | 2.0 | 1.3 | 1.1 | 1.7 [e] | 1.3 | 0.7 |
| Time (h) | | | | | | | | | | | | |
| 25.9 (7–35) | 36 | 2.2 | 2.0 | 1.4 | 1.2 | 2.2 | 2.1 | 1.4 | 1.1 | 1.8 | 1.4 | 0.8 |
| 57.0 (37–112) | 24 | 1.9 | 1.8 | 1.3 | 1.0 | 2.1 | 1.8 | 1.3 | 0.9 | 1.5 | 1.0 | 0.7 |
| Age (years) | | | | | | | | | | | | |
| 29 (20–36) | 26 | 2.1 | 2.0 | 1.4 | 1.0 | 2.2 | 2.0 | 1.4 | 1.0 | 1.7 | 1.2 | 0.8 |
| 44 (37–60) | 34 | 2.1 | 1.9 | 1.1 | 1.1 | 2.2 | 1.9 | 1.1 | 1.1 | 1.6 | 1.3 | 0.6 |

[a] CD collagen degeneration, TN tenocyte necrosis, AI acute inflammation.
[b] RS rupture site, PP proximal part (i.e., 10 cm above the insertion), IS insertion site, CAT contralateral AT.
[c] The severity of collagen degeneration at the rupture site and in the proximal part are significantly greater than at the insertion site and in the contralateral AT ($p < 0.0009$). No difference was found between the two former sites ($p = 0.08$), but that at the insertion site was greater than in the contralateral AT ($p = 0.004$).
[d] The severity of tenocyte necrosis at the rupture site is significantly greater than at the other three sites ($p < 0.0009$ versus the insertion site and contralateral AT, $p = 0.0007$ versus the proximal part). The severity of tenocyte necrosis in the proximal part is also greater than at the other sites ($p < 0.0009$), and that of the insertion site is greater than that in the contralateral AT ($p < 0.001$).
[e] The severity of acute inflammation is significantly greater at the rupture site than at the other two sites, and the severity of acute inflammation at the proximal site is greater than that at the insertion site ($p < 0.0009$ in all cases). The severity of acute inflammation shows a significant correlation with the severity of collagen degeneration and tenocyte necrosis ($p < 0.0009$).

infiltration. A few mononuclear inflammatory cells were seen. Some cases had swelling of venular endothelial cells, but fibrinoid and necrosis of vessel walls were rare. No thrombosis or other vascular changes were observed. There was no obvious fibroblast proliferation or scar formation.

In the contralateral tendon, most cases had degeneration and tenocyte necrosis (Figure 3), albeit less than in the ruptured tendon. Acute inflammation was seen in a single case (apart from a few perivascular neutrophils in several biopsies).

When the histological results were correlated with the time from rupture to biopsy, it seemed that the degree of degeneration, necrosis, and acute inflammation tended to decrease, but none of the differences were significant. We found no correlation between the histologic results and the age of the patients.

## Discussion

Numerous studies of the histopathology at the site of AT rupture have been done (Lawrence et al. 1955, Orell 1958, Arner et al. 1958/59, Hooker 1963, Picaud et al. 1966, Kannus and Józsa 1991, Burchhardt et al. 1992), but the results have varied greatly.

In accordance with our observations, Arner et al. (1958/59) described degeneration and necrosis in all 74 cases of AT. Since they found hardly any neutrophilic infiltration of the tendons on the first day after the rupture, they concluded the inflammation had been caused by the rupture. In a study of 397 cases of AT rupture with light microscopy and transmission and scanning electron microscopy, Kannus and Józsa (1991) found degenerative changes in all cases as well as pathological changes in 31% of the controls. No inflammation of the tendons was present.

As a new observation, we found the same degenerative and necrotic changes—albeit to a lesser

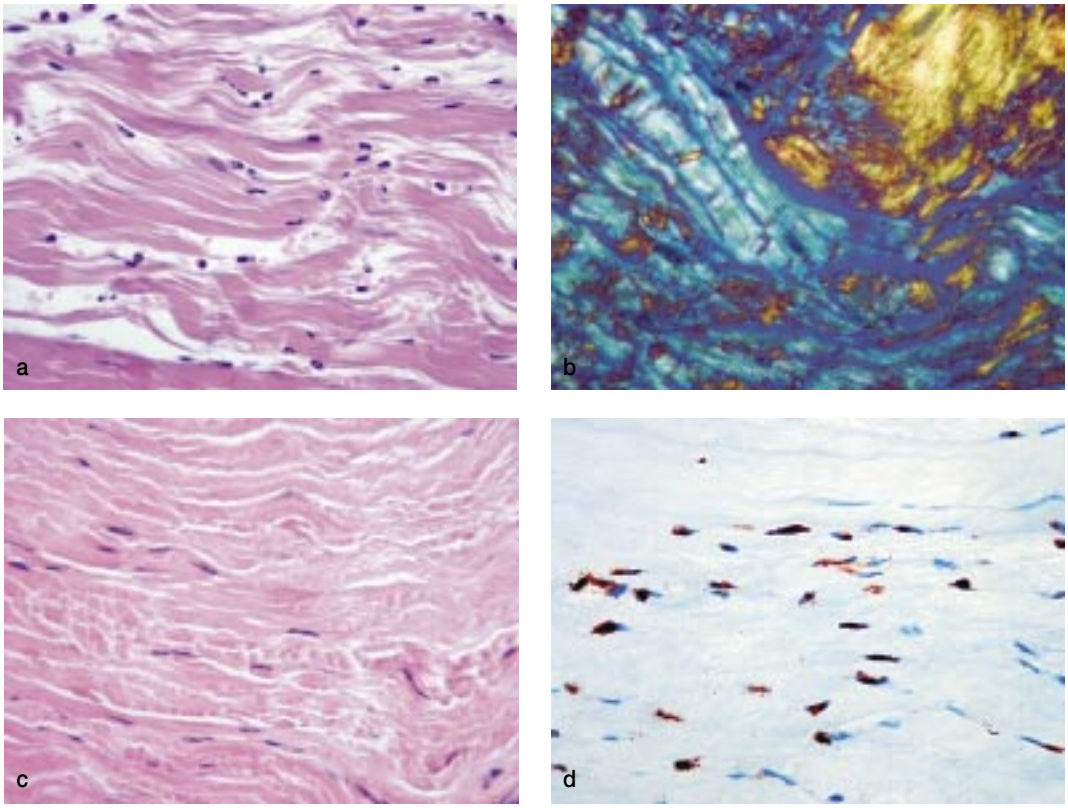


Figure 2. Sections from a ruptured tendon (×200).
a. Degenerated collagen is seen as irregular, often thin, wavy, angulated or fragmented fibers. Only a few angulated or pyknotic nuclei are present. Scattered neutrophils are found between collagen fibers, HE.
b. With Picro-Sirius staining, the abnormal collagen structure is seen better with polarized light.
c. Note the inconspicuous degenerative changes, pyknotic nuclei and no apparent infiltration by neutrophils, HE.
d. Same area as in c. Immunohistochemical staining for calgranulin greatly increases visualization of the neutrophils lying together with or replacing the tenocytes.

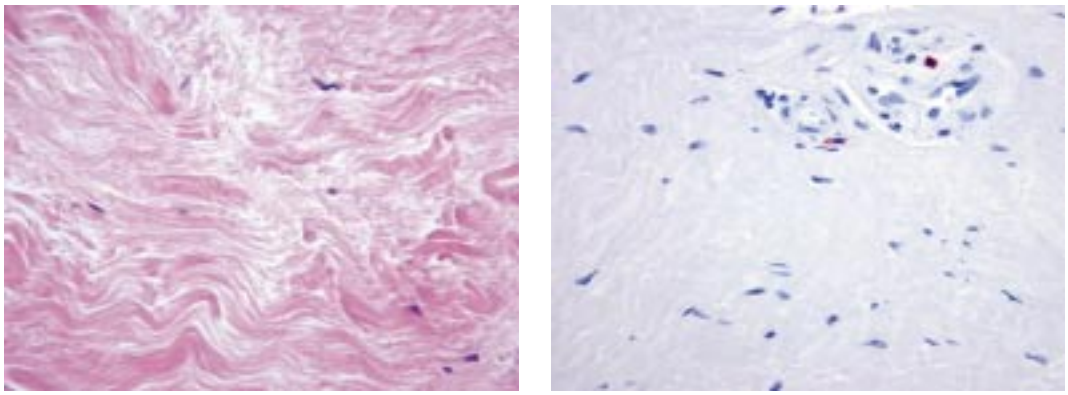

Figure 3. Biopsy from a contralateral (unruptured) tendon (×200).
a. Collagen degeneration and tenocyte necrosis are present, HE.
b. Immunohistochemical staining for calgranulin shows a few perivascular neutrophils, but no neutrophilic infiltration in the tendon per se is visible.

degree—in most biopsies from the proximal part and the insertion of the AT, as well as in the contralateral AT. Unlike in previous studies, we also detected acute inflammation at the site of rupture in all cases. The neutrophils were frequently barely identifiable, having a morphology reminiscent of necrotic tenocytes, but their presence was confirmed with immunohistochemical stainings.

The blood flow in tendons is lower in middle-aged than in young people (Håstad et al. 1958/59, Rothman and Parke 1965), matching the age distribution of AT rupture. The degenerative changes in rupture of tendons, as seen with light and electron microscopy, resemble those in hypoxic lesions (Kannus and Józsa 1991). AT has a relatively sparse blood supply throughout its length (Ahmed et al. 1998), but tenocytes have a low metabolic rate and are therefore relatively insensitive to hypoxia (Webster and Burry 1982). It has also been argued that the most frequent site of AT rupture is the area with the poorest blood supply (Lagergren and Lindholm1958/59, Carr and Norris 1989, Graf et al. 1990, Stein et al. 2000). However, a recent quantitative angiographic study indicates that the number of blood vessels per unit of cross-sectional area is in fact the same in all parts of the AT (Ahmed et al. 1998). In some studies, marked vascular lesions associated with paratenonitis have been described, comprising narrowing and obliteration of the lumen of the arteries and arterioles (Arner et al. 1958/59, Kannus and Józsa 1991, Kvist et al. 1992). Unlike in these observations, we and others (Orell 1958) have found only slight vascular changes that could hardly be regarded as a cause of tendon hypoxia. Our demonstration of collagen degeneration, tenocyte necrosis and neutrophilic infiltration, not only at the rupture site but also, in most cases, in the proximal part of the AT and at the calcaneal insertion, speaks against a hypoxic lesion due to diseased paratenon vessels as a major cause of SRAT. A hypoxic state induced by repetitive stretching of the tendon impairing the blood flow has been suggested, but is not supported by experimental studies (Backman et al. 1991). Theories concerning relative hypoxia due to exercise-induced hyperthermia (Wilson and Goodship 1994) remain to be elucidated.

Many studies deal with ageing of AT as a factor in the rupture mechanism (Arner et al. 1958/59, Håstad et al. 1958/59, Ippolito et al. 1980). In rabbit ATs, ageing is associated with a reduction in the density of tenocytes and the content of tenocyte organelles responsible for protein synthesis (Ippolito et al. 1980). Ageing per se, however, is not accompanied by the morphological features of AT degeneration (Maffulli et al. 2000).

In chronic tendon disorders, 'overuse' implies injuries due to repeated tendon strains exceeding the limit where the tendon can endure further tension (Kannus 1997). The consequent overuse may denature the collagen fibers through breakages in the cross-linked structure. Insufficient cellular maintenance of the tendon matrix, including the collagen fibers, must occur before degeneration develops (Lehto et al. 1990). In rabbits exposed to AT overuse, Backman et al. (1990) showed degenerative tendon changes and nuclear changes in the tenocytes (probably necrosis). A disparity between the breakdown of collagen fibers and the cellular maintenance of the matrix must be aggravated in case of tenocyte necrosis. Our findings of widespread bilateral collagen degeneration and tenocyte necrosis support the overuse theory. The severity of the degeneration and necrosis were greater in the ruptured AT than the contralateral tendon. This probably explains why the rupture occurred on that side. In comparing the two sides, however, it should be emphasized that only a needle biopsy was available from the unruptured tendon. Apart from the mean degree of degeneration in the proximal part of the ruptured tendon being only insignificantly less than that of the rupture site, the severity of the changes was greatest at the site of rupture corresponding to the segment with the lowest cross-sectional area and, consequently, the largest tensile stress. This may not only support the overuse theory, but also explain the particular site of the rupture.

We found inflammation even in biopsies from patients operated on 7 hours after the rupture, and a tendency for the severity of inflammation to decline from the rupture to operation. It therefore seems unlikely that inflammation can be secondary to the rupture. Instead, we suggest that the inflammation is triggered by the tissue damage. The severity of the inflammation in our study paralleled the severity of degeneration and necrosis. Infiltration by neutrophils exposes the tendon to

numerous enzymes including collagenase and elastase, which may aggravate the breakdown of the collagen tissue.

In conclusion, we found that: 1) in SRAT, degeneration and necrosis of the ruptured AT not only constantly occur at the site of rupture, but also in most cases in the proximal part of the tendon and at the site of insertion, indicating that the entire tendon is involved in the pathological process; 2) the contralateral AT suffers from the same degenerative changes as the ruptured tendon, albeit to a lesser degree; and 3) acute inflammation involves the whole ruptured AT, but not the contralateral tendon. We suggest that diffuse damage of the AT occurs because of repeated microtraumas associated with overuse, leading to collagen degeneration and tenocyte necrosis. If this continues, these changes may trigger an acute inflammatory response that can further weaken the tendon until it can not resist the mechanical force during exercise.

None competing interests declared.

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