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Cricoarytenoid Articulation in Elderly Japanese With Special Reference to Morphology of the Synovial Tissue

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Abstract

Objective: To clarify composite fibers and cells in the synovial tissues of the cricoarytenoid joint (CA joint).

Methods: Routine histology and immunohistrochemistry using sagittal or nearly sagittal sections obtained from 18 elderly cadaveric specimens.

Results: The CA joint capsule was thin and contained few elastic fibers. A limited supportive ligament, namely, a thickened fascia of the posterior cricoarytenoid muscles, was sometimes evident on the lateral aspect of the CA joint. However, even in the weaker medial aspect of the joint, no marked destruction of the synovial tissues was found. The CA joint always contained synovial folds—a short medial fold and long lateral folds—but these contained no or few macrophages, lymphocytes, and blood capillaries. In 2 exceptional specimens showing inflammatory cell infiltration in the submucosal tissue of the larynx, the macrophage-rich area extended toward the capsule and medial synovial fold.

Conclusions: The lateral aspect of the CA joint was likely to be supported mechanically by the muscle-associated tissues. Strong support of the arytenoid by muscles might reduce the degree of CA joint injury with age. However, some patients with hoarseness due to mucosal inflammation of the larynx might have accompanying synovitis and subsequent cartilage injury in the CA joint.

Keywords

cricoarytenoid joint, elastic fibers, capsule, synovial fold, macrophages, human anatomy

Introduction

The cricoarytenoid (CA) joint has been 1 of the major focuses of anatomical studies of phonation, and a considerable body of information exists regarding loss of elastic cartilage and subsequent change to bone tissue in the arytenoid of elderly individuals.[1-5] Likewise, roughness and fibrillation of surface articular cartilages have been reported, especially in marginal areas.[6] In contrast, it has been considered that the synovial tissue, including the capsule, remains stable with increased age.[4] However, to our knowledge, no previous study has attempted to identify synovial macrophages lining the CA joint cavity, even though these cells are a recognized component of synovial tissues in the musculoskeletal system.[7-9] It is also recognized that degenerative changes in the articular cartilage, namely, osteoarthritis, are most likely secondary to inflammatory change in the synovial tissue.[10-12] Therefore, in the present study, we attempted to identify synovial macrophages and other morphologic features suggestive of inflammatory change in the CA joint of elderly individuals.

The congruity of a joint (adaptation between the 2 joint surfaces) is determined not only by the shape of the joint cartilage but also the associated soft tissues such as the joint disk or synovial fold. In the small saddle-like joints of the fingers, similarly to the CA joint, a thin synovial fold often plays a major role in compensating for loss of congruity due to degeneration.[13-15] Another requirement for the CA joint seems to be resistance to vibration. Kawase et al[16] considered that in the articulations between the ear ossicles, a very rich content of elastic fibers in the capsular ligaments (where the synovial capsule is fused with the external ligament) absorbs vibration, thus preventing loosening of the collagen fiber bundles. Therefore, in addition to investigating the

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composite cells, we studied the distribution of elastic fibers in the capsule and ligament as well as variations of the synovial fold in the CA joint of elderly individuals.

Materials and Methods

The study was performed in accordance with the provisions of the Declaration of Helsinki 1995 (as revised in Edinburgh 2000). We examined 18 donated cadavers (14 men and 4 women) ranging in age from 62 to 97 years, with a mean age of 85 years. The cause of death had been ischemic heart failure or intracranial bleeding. These cadavers had been donated to Tokyo Dental College for research and education on human anatomy, and their use for research did not require approval by the university ethics committee. The donated cadavers had been fixed by arterial perfusion of 10% v/v formalin solution and stored in 50% v/v ethanol solution for more than 3 months. From each cadaver, we prepared 1 tissue block that included the CA joint and the other small structures around the joint. Thus, any left/right difference was not examined. The sectional plane was sagittal or nearly sagittal (tilted sagittal toward frontal). The specimens were decalcified by incubating them at 4°C in 0.5 mol/L EDTA solution (pH 7.5; Decalcifying solution B; Wako, Tokyo) for 7 to 14 days.

After performing routine procedures for paraffin-embedded histology, semiserial sections, namely, 9 to 12 adjacent or near sections, were prepared at almost 0.5-mm intervals. Two of the sections were stained with hematoxylin and eosin (HE) and elastica-Masson (a variation of Masson-Goldner staining[17,18]), respectively. The other sections were used for immunohistochemistry. The primary antibodies used were (1) mouse monoclonal anti-bovine alpha-elastin (dilution 1:20; ab9519; Abcam, Cambridge, UK); (2) rabbit polyclonal anti-human; factor VIII-related antigen (von Willebrand factor) (dilution, 1:100; Dako IR527; Dako, Glostrup, Denmark); (3) mouse monoclonal anti-human CD68 KP1 (1:100, M0814, Dako); (4) rabbit polyclonal anti-human IgM (dilution, 1:100; Dako N1509; Dako); (5) mouse monoclonal anti-human CD79a (1:40; Dako M7050; Dako); (6) mouse monoclonal anti-human CD3 (1:100; Nichirei 413591, Tokyo, Japan); and (7) mouse monoclonal anti-human CD8 (1:100; Dako N1592; Dako). Antigen retrieval with microwave treatment (500 watt, 15 minutes, pH 6) was performed for antibodies Nos. 2 through 7, while trypsin treatment was used for antibody No. 1. The secondary antibody (incubation for 30 minutes; dilution 1:1000; Histofine Simple Stain Max-PO; Histofine, Nichirei, Tokyo) was labeled with horseradish peroxidase (HRP), and antigen-antibody reactions were detected by the HRP-catalyzed reaction with diaminobenzidine (incubation for 3-5 minutes; Histofine Simple Stain DAB; Histofine). Counterstaining with hematoxylin was performed on the same samples. A negative control without the first antibody was set up for each of the specimens.

Although elastica Masson staining may not be widely used, it colors elastic fibers clear black in contrast to the bright green color of collagen fibers. Among the aforementioned antibodies, that against CD68 was used for identification of macrophages, those against CD3 and CD8 for T-lymphocytes, those against IgM and CD79a for B-lymphocytes, and that against factor VIII for blood capillaries. Many antibodies can be used for detection of lymphocytes, such as anti-CD4 antibody for T-lymphocytes, but most of them are not applicable to long-preserved specimens from donated cadavers.[19] Observations and photography were usually performed with a Nikon Eclipse 80.

Results

Joint Cartilage

Both the arytenoid and cricoid cartilages were ossified in all specimens. The CA joint surface of the arytenoid cartilage was consistently concave, in contrast to the convex shape of the cricoid joint surface. The joint cartilage (hyaline cartilage) was usually larger in the arytenoid or upper side than the cricoid or lower side in the present sagittal or tilted sagittal sections (Figures 1-3). The upper surface of the CA joint tended to extend medially over the medial margin of the cricoid cartilage. In the arytenoid side, joint cartilage thinning was seen in 3 of the 18 specimens (Figure 4), and roughness was evident in the other 3 specimens. We did not find any cartilage defect in which the bone tissue was exposed to the joint cavity. In 2 of 18 specimens, elastin expression was seen in the medial area of the joint cartilage of the arytenoid, namely, a change of hyaline cartilage into fibrocartilage (Figure 3B). Those observations of the arytenoid cartilage are summarized in Table 1.

Capsule and Other Synovial Tissues

The CA joint capsule was thin and contained few elastic fibers. The lateral and posterior aspects of the CA joint were covered by the lateral and posterior cricoarytenoid muscles, respectively (Figure 1A). However, in association with increased fatty tissues in and around the muscle, thin loose tissue was usually (15/18) interposed between the muscle and capsule (Figures 2A, 2C, 3A, 3C, and 4A). The loose tissue contained a few nerves and vessels. The covering fascia of the posterior cricoarytenoid muscle was often (10/18) thick (0.1 mm at maximum) and contained abundant elastic fibers (Figures 1A, 1C, 2A, 2C, 3A, and 3C). When the elastic fiber-rich fascia was attached to the posterolateral aspect of the joint capsule (Figures 1A, 1C), the capsule itself was difficult to discriminate from the fascia. In contrast, the medial and anterior aspects of the CA joint faced a large area of loose tissue that was continuous with the submucosal tissue of the larynx. The submucosal tissue contained 2 to 3 thick bands of elastic fibers running parallel to

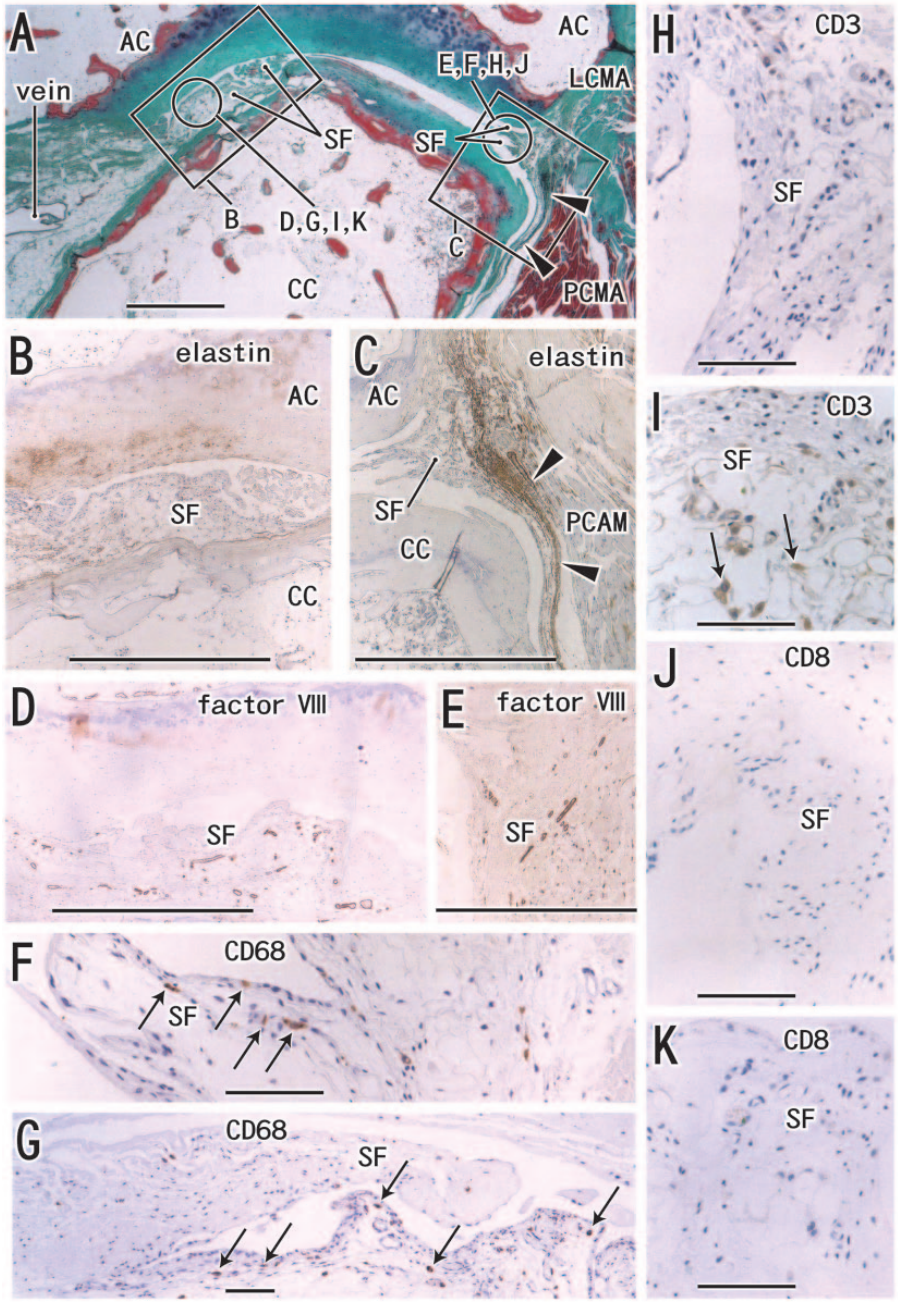

Figure 1. Elastic fiber-rich fascia attaching to the lateral aspect of the joint capsule.
A specimen from an 83-year-old man. All panels show near sections. In panel A (elastica Masson staining), the left-hand side of the panel corresponds to the medial side of the body. The joint cartilage is larger on the arytenoid side than on the cricoid side. The LCAM attaches to the joint, and a covering fascia (arrowheads) of the muscle contains abundant elastic fibers (black color). Panels B and C (immunohistochemistry for elastin) correspond to the squares marked B and C in panel A, respectively. Strong elastin expression is seen in the fascial structure (arrowheads) supporting the lateral aspect of the joint. Panels B and C (immunohistochemistry of elastin) show strong expression in the lateral fascial structure (arrowheads in panel C). A small triangular synovial fold in the lateral side of the joint (panel C) as well as a large belt-like fold on the medial side (panel B) are shown in panels D through K using immunohistochemistry: The medial fold is separated from the arytenoid in panel G but is attached to the arytenoid mostly or partly in panels A, B, and D. Panels D and E (immunohistochemistry of factor VIII) display multiple blood capillaries in the synovial folds. Panels F and G (immunohistochemistry for CD68) exhibit a few synovial macrophages (arrows) along the joint cavity. Panels H and I (immunohistochemistry for CD3) as well as panels J and K (immunohistochemistry of CD8) show no or few T-lymphocytes. Relatively large positive cells in panel I (arrows) appear not to be lymphocytes. Scale bars: 1 mm in panels A-E; 0.1 mm in panels F-K. AC, arytenoid cartilage; CC, cricoid cartilage; LCAM, lateral cricoarytenoid muscle; LX, laryngeal cavity; PCAM, posterior cricoarytenoid muscle; SF, synovial fold.

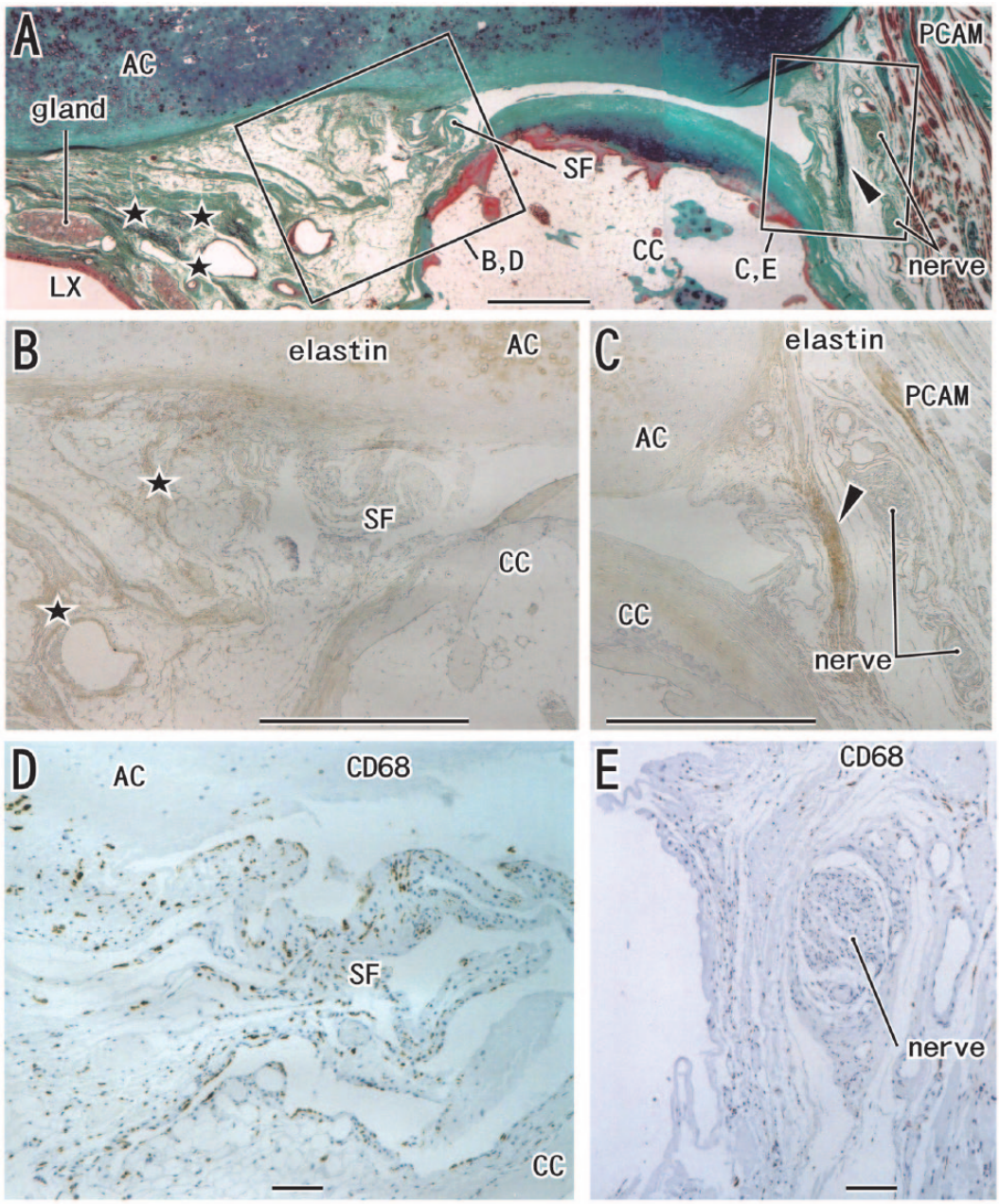

Figure 2. Elastic fiber-rich fascia is slightly distant from the posterior aspect of the joint capsule.
A specimen from a 97-year-old man. All panels show near sections. In panel A (elastica Masson staining), the left-hand side of the panel corresponds to the medial side of the body: an SF is evident on the medial side. The laryngeal submucosa contains a thick band of black-colored elastic fibers (stars). The PCAM is distant from the joint. Panels B and C (immunohistochemistry for elastin), corresponding to the squares in panel A, display elastin expression; the laryngeal submucosal tissue contains multiple elastic fiber bands (stars in panels A and B). A fascial structure of the posterior muscle contains abundant elastic fibers (arrowhead in panels A and C), but it is separated from the muscle by loose tissue containing a nerve (panel C). Panels D and E (immunohistochemistry for CD68) exhibit abundant synovial macrophages in the medial synovial fold (panel D), in contrast to few positive cells on the lateral side (panel E). Scale bars: 1 mm in panels A-C; 0.1 mm in panels D and E. AC, arytenoid cartilage; CC, cricoid cartilage; LCAM, lateral cricoarytenoid muscle; LX, laryngeal cavity; PCAM, posterior cricoarytenoid muscle; SF, synovial fold.

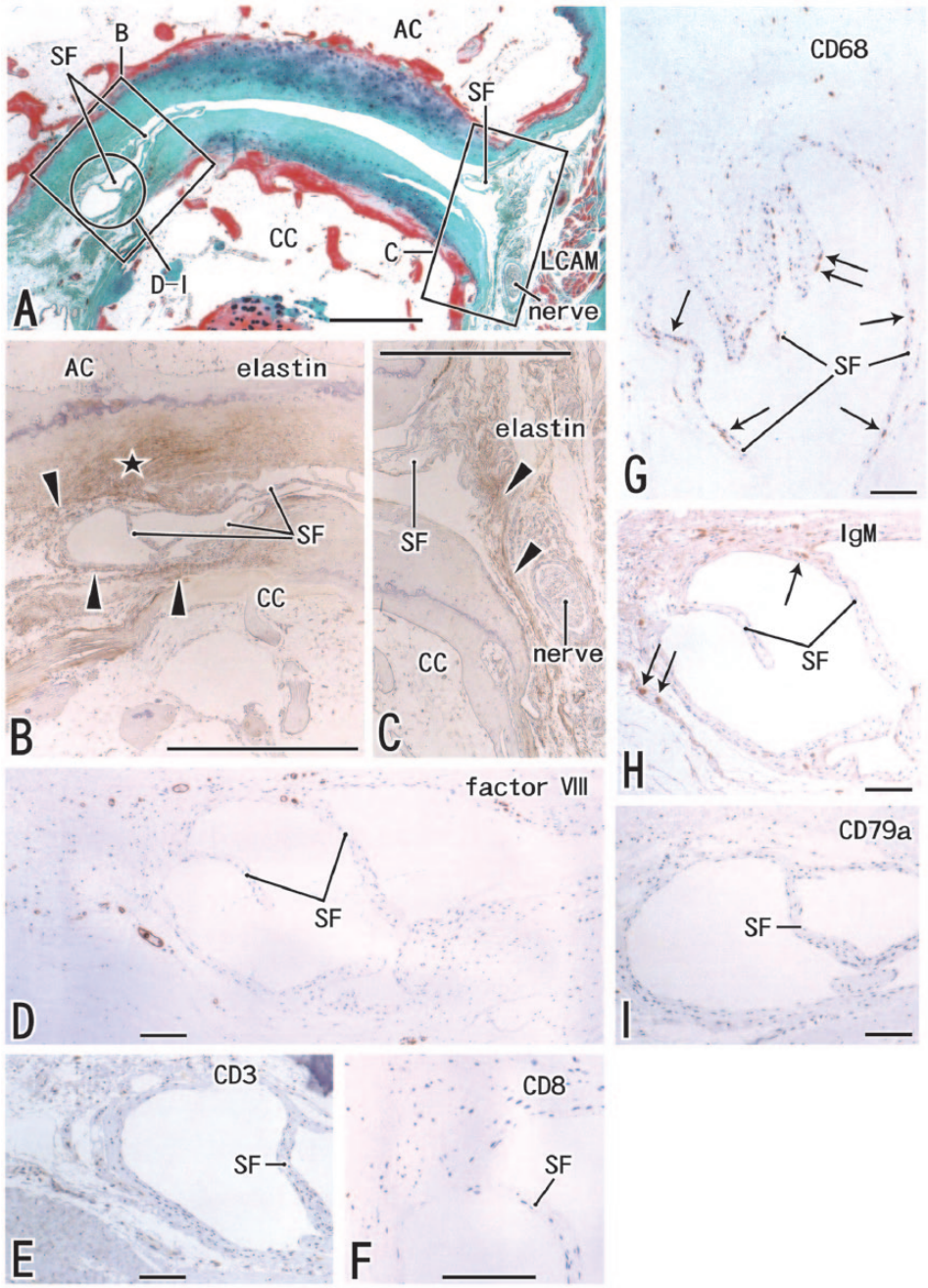

Figure 3. Few elastic fibers in and along the joint capsule.
A specimen from a 62-year-old man. All panels show near sections. In panel A (elastica Masson staining), the left-hand side of the panel corresponds to the lateral side of the body. The joint cartilage is larger on the arytenoid side than on the cricoid side. The LCAM is separated from the joint by loose tissue containing a nerve. Panels B and C (immunohistochemistry for elastin), corresponding to the squares in panel A, display weak elastin expression in and along the joint capsule (arrowheads). Part of the joint cartilage of the cricoid also expresses elastin (star in panel C). Synovial folds in panel C are shown in panels D through I using immunohistochemistry. Panel D (immunohistochemistry for factor VIII) displays few blood capillaries in the medial synovial folds. Panels E through (immunohistochemistry for CD8, CD3, CD68, IgM, and CD79a, respectively) show few lymphocytes and macrophages in the medial folds (arrows). Scale bars: 1 mm in panels A-C; 0.1 mm in panels D-I. AC, arytenoid cartilage; CC, cricoid cartilage; LCAM, lateral cricoarytenoid muscle; LX, laryngeal cavity; PCAM, posterior cricoarytenoid muscle; SF, synovial fold.

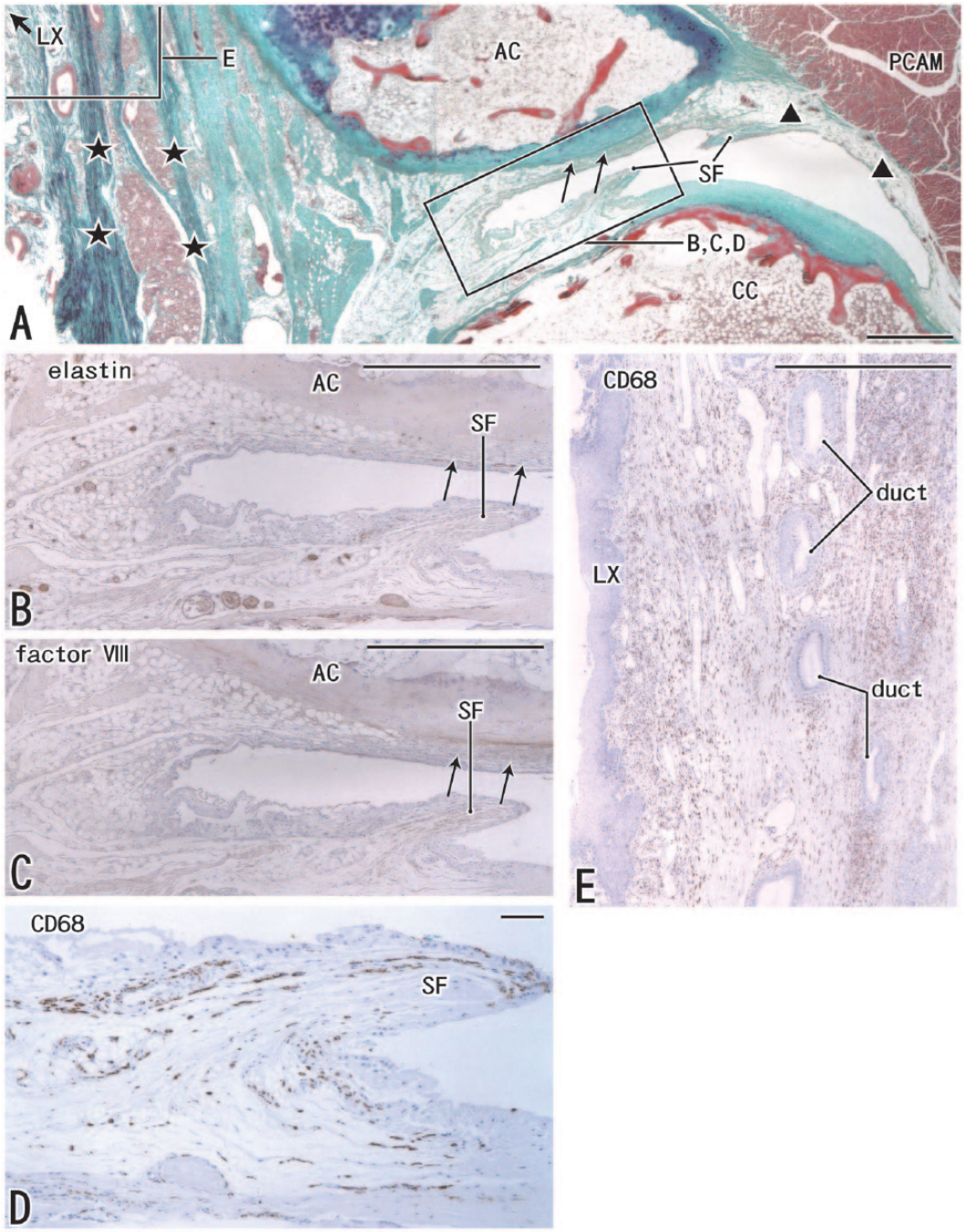

Figure 4. Inflammatory cell infiltration of the laryngeal submucosa.
A specimen from an 82-year-old man. All panels show near sections. In panel A (elastica Masson staining), the left-hand side of the panel corresponds to the medial side of the body. The joint cartilage is larger on the arytenoid side than on the cricoid side. The PCAM is separated from the joint by thin loose tissue (triangles in panel A). In the medial side of the joint, the submucosal tissue of the larynx contains thick bands of elastic fibers (stars). Panels B and C (immunohistochemistry for elastin and factor VII, respectively), corresponding to the square in panel A, display few blood capillaries and elastic fibers in and along the joint capsule. The joint cartilage of the AC is thin and does not face the joint cavity; it is covered by thin synovial tissue (arrows in panels A through C). Panel D (immunohistochemistry for CD68) shows abundant macrophages in an SF. Panel E (immunohistochemistry for CD68), the inferior part of which corresponds to the left upper angle of panel A, shows inflammatory cell infiltration of the laryngeal submucosa. Scale bars: 1 mm in panels A, B, C, and E; 0.1 mm in panel D. AC, arytenoid cartilage; CC, cricoid cartilage; LCAM, lateral cricoarytenoid muscle; LX, laryngeal cavity; PCAM, posterior cricoarytenoid muscle; SF, synovial fold.

Table 1. Morphologies of the Cricoarytenoid Joint in 18 Elderly Specimens.[a]

Age/Gender	Joint Cartilage Degeneration in the Arytenoid Side	Synovial Fold	Thick Posterior Fascia	Macrophage Density	Mucosal Inflammation
62M	Elastic fibers into joint cartilage	++ (Figure 3)	+	Low	—
74M	Roughness of the surface	+	+	Low	—
75F		++	+	Low	—
76M		++	—	Low	—
80F		+	+	Low	—
81M	Cartilage thinning	+	++	Low	—
82M	Cartilage thinning	++ (Figure 4)	—	High	+
83M		++ (Figure 5)	++	Low	—
83F		+	++	Low	—
85M	Elastic fibers into joint cartilage	+	—	Low	—
89M		++	+	Low	—
90M	Cartilage thinning	++	—	Low	—
90M		++	—	Low	—
91M	Roughness of the surface	+	—	Low	—
93M		++	—	High	+
94M		+	+	Low	—
97M		+ (Figure 2)	+	Low	—
97F	Roughness of the surface	++	—	Low	—

[a]Synovial fold: +, long medial fold(s) only; ++, long medial fold(s) and short lateral fold. Thick posterior fascia: +, a thickened fascia of the posterior cricoarytenoid muscle attaching to or extending near the lateral aspect of the joint capsule; ++, the fascia was developed well and fused with the joint capsule. Macrophage density: low or high, lesser or greater than 10 positive cells per 100 micron square along the joint cavity in immunohistochemistry of CD68. Mucosal inflammation of the larynx was associated with high density of synovial macrophages.

the mucosa (Figures 2A, 4A). Therefore, a definite supporting structure was always absent in the anterior and medial aspects of the CA joint. Marginal parts of the CA joint cavity usually enlarged to provide recesses: Most of their spaces were filled with synovial folds (see following).

Synovial folds were consistently present in the CA joint: The short lateral fold was a triangular mass, while the long medial fold was composed of multiple belt- or tongue-like thin folds (Figures 1B, 1C, 3B, 3C). The synovial fold covered an area of joint surface with or without cartilage roughness: The fold was likely to cover or attach to the rough area. The capsule and synovial folds usually contained multiple capillaries (Figures 1D, 1E, 3D, and 4C). CD68-positive synovial macrophages as well as lymphocytes were usually scant or absent: 0 to 10 cells per 100 μm^2 in section (Figures 1F, through 1K, 2D, 2E, and 3E through 3I). Some of the folds contained no macrophages, and this was confirmed by observation of serial sections. In 2 of 18 specimens, we observed round or oval large cells that were positive for CD3 (Figure 1I), but these did not appear to be usual T-lymphocytes on the basis of morphology. Overall, in most specimens, we did not find any evidence of synovitis despite the fact that joint cartilage degeneration was sometimes present.

In 2 of the 18 specimens (from an 82-year-old man and a 93-year-old man), inflammatory cell infiltration was evident in the submucosal tissue of the larynx (Figure 4E): Most of the cells expressed either CD68 or CD3. The ducts of the mucosal glands were dilated and appeared to be increased in number. Notably, the macrophage-rich area was continuous with the capsule and synovial fold in the medial aspect of the CA joint, in contrast to few macrophages in the lateral aspect. The density of medial synovial macrophages reached 10 to 20 cells per 100 μm^2 in these specimens (Figure 4D). Moreover, almost the entire joint surface of the arytenoid cartilage was covered by a long synovial fold (Figures 4A through 4C). Therefore, the arytenoid cartilage appeared not to face the joint cavity. Those observations of the synovium are summarized in Table 1. We did not find a clear gender difference in the synovium as well as joint cartilage.

Discussion

The CA joint was found to be characterized by weak supportive structures. Actually, according to Berry et al,[20] the CA joint looseness along the mediolateral axis was roughly 3 times larger than that along the anteroposterior axis. Lacking any ligament, the anterior and medial aspects faced loose tissue that was continuous with the laryngeal submucosal tissue. Surprisingly, this medial weakness of the supportive tissue also appears to be present in

specimens from young individuals, according to a photo presented by Casiano et al.[4] According to Reidenbach,[21] the cricoarytenoid ligament does not attach to the joint capsule but is located in the medial (or mucosal) side of the joint to limit abduction of the arytenoid. However, we did not find such a medial check ligament in the present specimens. Indeed, a thickened fascia of the posterior cricoarytenoid muscle seemed to correspond to the "posterior cricoarytenoid ligament" emphasized by Sellars and Keen.[22] However, this structure was not common in the specimens we examined from elderly individuals; even when the ligament was present, it was often separated from the joint capsule because of increased fatty tissue around the muscle. Being different from ligaments, synovial folds were always present in the CA joint: Multiple long folds were evident on the medial side, and a triangular mass occupied a recess on the lateral side. Synovial folds for maintenance of joint congruity are very common in the musculoskeletal system, even during fetal development (eg, Isogai et al[23]). However, emphasis on synovial folds in the CA joint appears to be limited to Paulsen et al,[24] who focused on damage to the folds resulting from endotracheal intubation. Using Indian ink pin-prick assessment, Kahn and Kahane[6] reported marginal roughness and fibrillation of the CA joint surface: This marginal lesion may correspond to sites covered by the synovial folds.

At the beginning of this study, we assumed vibration conducting through the CA joint, but the present observations demonstrated elastic fibers restricted in the aforementioned, unusual lateral ligament (ie, a thickened fascia of the posterior cricoarytenoid muscle). Vibration of the vocal cord seemed not to influence on the CA joint possibly because of tight fixation by laryngeal muscles during phonation. In spite of the good congruity, the saddle-like CA joint appeared to be sufficiently loose, as ligaments were lacking or weak and large marginal recesses were present. The synovial folds appeared to consistently increase and maintain high congruity. Notably, a typical saddle joint, for example, the carpometacarpal joint of the thumb, is characterized by loose ligaments and a capsule that allows a wide range of movement, including slight rotation at the neutral position.[25] Likewise, therefore, weak ligaments seem to be important for rotation and sliding of the saddle-like CA joint. The strong laryngeal muscles inserting to the arytenoid seem to absorb the vibration. When a greater vibration occurs in the vocal cord, the muscles are likely to make greater contraction to fix the arytenoid more tightly to the cricoid. This hypothetical mechanism seems to be just the same as a dynamic stabilization of the shoulder joint by the rotator cuff muscles.[25] Consequently, vibration does not seem to accelerate degeneration and destruction of the CA joint.

Gacek and Gacek[26] reported that after long-term paralysis (more than 6 months), none of 10 CA joints in elderly subjects showed histological evidence of ankylosis. However, they did not pay attention to the synovial folds, which are likely to disappear during long-term paralysis. We found that the CA joint cavity has a synovial macrophage lining, as is usually the case for joints of the musculoskeletal system.[7-9] In contrast, however, inflammatory change of the synovium was not considered to play an important role in the progression of CA joint degeneration.[10-12] In 2 exceptional specimens showing inflammatory cell infiltration in the laryngeal submucosa, the increased numbers of macrophages reached the medial aspect of the CA joint. Because of their region-specific distribution, inflammatory cells did not seem to be of synovial origin but rather appeared to have invaded from the laryngeal submucosa. Some patients with a rough voice due to mucosal inflammation of the larynx might have accompanying synovitis and subsequent cartilage injury in the CA joint. The most basic action of the CA joint seems to be switching from the respiratory to the phonatory position. According to Storck et al,[27] this movement has 3 components: (1) an inward rocking action of the CA joint, (2) a forward sliding movement along the longitudinal axis of the CA joint, and (3) an inward rotation around a virtual axis that runs perpendicular to the CA joint axis. We speculate that in synovitis induced by mucosal inflammation, sliding and rotation are likely to be the first actions that are impaired, producing a weak and breathy voice caused by glottal gap.

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Declaration of Conflicting Interests

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