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Muscle Pathology in Total Knee Replacement for Severe Osteoarthritis: A Histochemical and Morphometric Study

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We evaluated a series of 12 biopsies from 11 patients with total knee replacements for severe osteoarthritis. All 12 biopsies showed denervation atrophy, while five cases had significant myopathic changes. Morphometric studies indicated a positive atrophy factor (greater than 150) in the type I myofibers in seven cases, the IIA myofibers in nine cases, and the IIB myofibers in all 12 cases. Type I predominance occurred in six cases, IIA paucity in two cases, and IIB paucity in two cases. The results indicate that patients with severe osteoarthritis of the knee have both significant neuropathic and myopathic changes in quadriceps biopsies. The changes in osteoarthritis of the knee differ from previously reported muscle biopsy results in patients with rheumatoid arthritis, femoropatellar or femorotibial osteoarthrosis, dislocating patella, meniscus tear or chondromalacia. (Henry Ford Hosp Med J 1986;34:37-40)

Muscle aching and wasting have long been recognized as common symptoms in patients with rheumatoid arthritis. Pathological changes in muscle biopsies include: in mild disease, type II fiber atrophy accompanied by moth-eaten and whorled fibers and in severe disease, type I fiber atrophy, ring fibers and often degenerating fibers and inflammatory infiltrates (1). Osteoarthritis, by contrast, has previously been felt to produce no muscle pathology other than type II fiber atrophy, secondary to disuse. Since skeletal dysmorphism and anatomical and mechanical factors sustaining tendoskeletal interaction and normal muscle tension have long been postulated to cause significant alterations in muscle structure, we postulated that severe osteoarthritis would show similar changes. A systematic evaluation of the quadriceps muscle in severe osteoarthritis of the knee was performed showing an interesting spectrum of pathological changes, some of which are remarkable for their severity.

Materials and Methods

Sixteen men, ages 57 to 70 years of age, with total knee replacement for severe osteoarthritis, had concomitant vastus lateralis biopsies. Three patients had diabetes mellitus, one had psoriatic arthritis, and another seronegative rheumatoid arthritis; these five cases were eliminated from the study. The diagnosis of osteoarthritis was confirmed in all patients by radiologic studies. Severe changes were present in all patients and consisted of either tricompartmental disease or total destruction of the joint with osteoporosis. Other changes included severe osteophyte formation involving the entire knee and valgus or varus deformities. All the patients had severe knee pain for at least ten years which was unresponsive to nonsteroidal antiinflammatory agents. Three patients had prior traumatic knee injury. Nine patients had a New Jersey orthopedic knee evaluation, with a median score of 58 (maximum is 100, 85 to 100 excellent, 60 to 69 fair, and 0 to 59 poor). Five of the nine had a score in the poor range with a median score of 53, and four of the nine were in the fair range with a median score of 65.

Eleven men and 12 biopsies were studied. One man had both knees replaced, ten months apart. The knee problems had lasted from eight to 35 years. Four patients had prior meniscectomies. The man with both knees replaced had prior meniscectomies and osteotomies on both knees. One had a previous knee replacement. One had a patellectomy, and two had arthroscopies as the only surgical procedure. Two patients had no procedures, and one patient's history was not documented. None of the patients had any known neurological illness and were not seen by a neurologist during their hospitalization for the total knee replacements. None of the patients had any symptoms associated with peripheral neuropathies including distal numbness, burning, tingling, other paresthesias, or distal muscle weakness. The EMG performed on two patients was negative for either neuropathic or myopathic disease.

The biopsy material was immediately frozen in isopentane, cooled in liquid nitrogen. The following staining methods were employed: hematoxylin and eosin (H&E); modified Gomori trichrome; nicotinamide adenine dinucleotide, reduced-tetrazolium reductase (NADH-TR); succinic dehydrogenase (SDH); nonspecific esterase; ATPase; pH 9.4, 4.6, and 4.3; periodic acid-shiff reaction (PAS) with and without diastase; oil red 0; phosphorylase; crystal violet; and alizarin red. Morphometric studies were performed by measuring the maximum diameter across the lesser aspect of the muscle fiber (2). The mean fiber diameter together with the standard deviation, vari-

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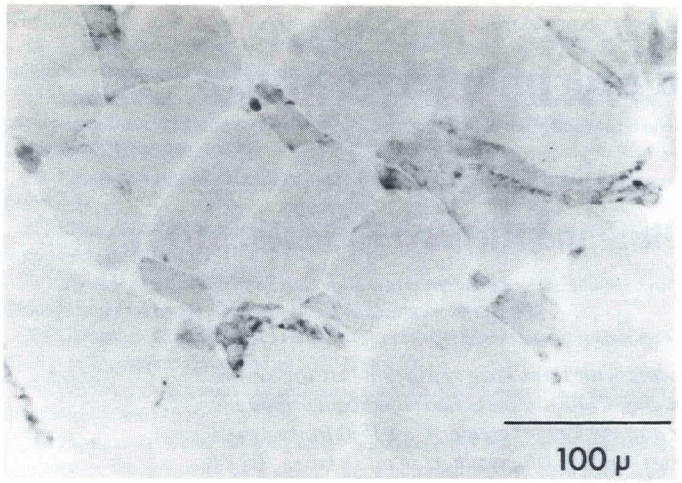

Fig 1—Nonspecific esterase. Dark staining angular atrophic fibers.

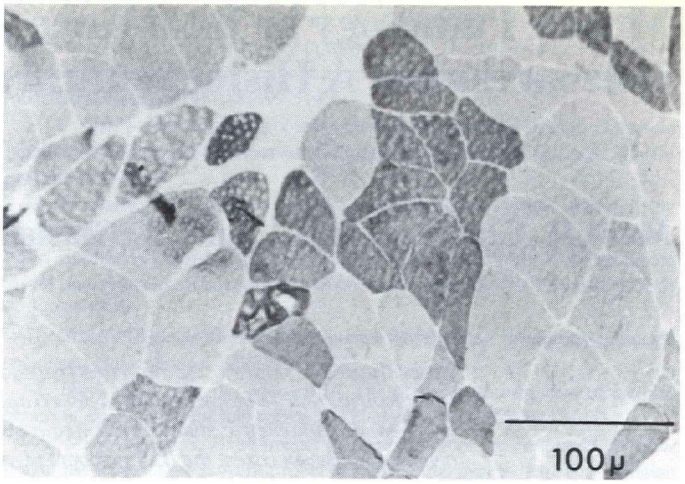

Fig 2—ATPase, pH 9.4. Fiber type grouping.

Table 1
Pathological Changes

Case Number	(1) Esterase Positive Fibers	(2) Fiber Type Grouping	(3) Pyknotic Nuclear Clumps	(4) Oxidative Enzyme Changes	(5) Rods	(6) Central Nuclei	(7) Degeneration Regeneration	(8) Inflammation
1	●	●		pale centers moth eaten				
2	●		●	ragged red fibers	●			
3	●	●		moth eaten			●	●
4*	●	●						
5	●	●	●					
6	●	●	●	central cores				
7*	●	●				●		
8	●	●						
9	●	●					●	
10	●		●	tubular aggregates	●		●	●
11	●		●				●	●
12	●	●	●			●		●
Cases/Total	12/12	9/12	6/12	5/12	2/12	2/12	4/12	4/12

*Same man, both knees done.

ability coefficient, atrophy and hypertrophy factors were obtained for each case.

Results

All 12 biopsies (Table 1) showed denervation atrophy by the criteria of angular atrophic fibers of both fiber types, a minimum of ten esterase positive, angular atrophic fibers per biopsy (Fig 1) and either fiber type grouping, which occurred in nine cases (Fig 2) or in two cases, fiber type predominance. The one case that had neither fiber type grouping nor fiber type predominance had high atrophy factors for all three fiber types. Fiber type grouping is defined as groups of both fiber types, consisting of a minimum of 12 fibers adjacent to each other and at least one fiber completely surrounded by fibers of the same type. In most instances, the size of the fiber type groups was significantly larger than 12 and, at times, involved several fascicles. Fiber type grouping is associated with chronic denervation and reflects reinnervation. Fiber type predominance had a similar appearance to fiber type grouping. However, groups of only one fiber type occur. Type I fiber predominance is defined by more than 55% of the fibers being type I, and type II predominance occurs when more than 80% of the fibers are type II.

Five cases had significant myopathic changes. In three of these, there were scattered degenerating fibers with reactive macrophages. One case had degenerating fibers without inflammation, and another case had perivascular round cell infiltrates without degenerating or regenerating muscle fibers (Fig 3). There was one case with central cores in about 80% of the type I fibers (Fig 4). Two other cases had moth-eaten fibers; one case, pale centers. Three cases had increased central nuclei. Two had several fibers with rods (Fig 5); one had five ragged red fibers (Fig 6); and another showed a few fibers with tubular aggregates.

Morphometric studies (Table 2) indicated a positive atrophy factor (greater than 150) in type I fibers in seven cases; type IIA in nine cases; and type IIB in all 12 cases. In only one case was there a positive hypertrophy factor. Atrophy and hypertrophy factors were devised in an effort to quantitate the degree of

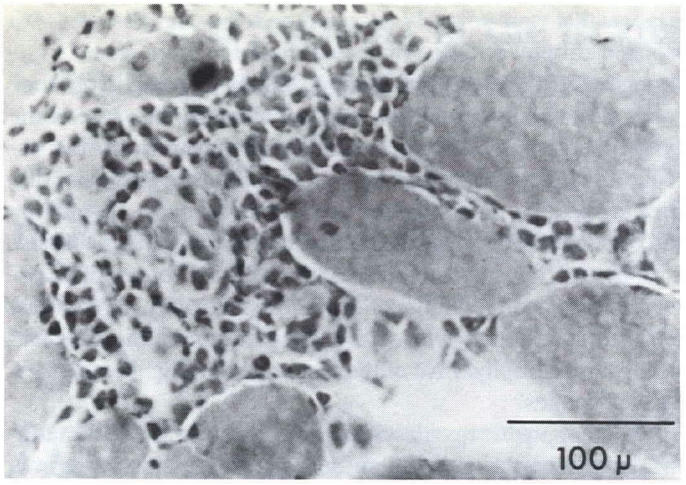

Fig 3—Modified Gomori trichrome. Perivascular mononuclear cell inflammatory infiltrates.

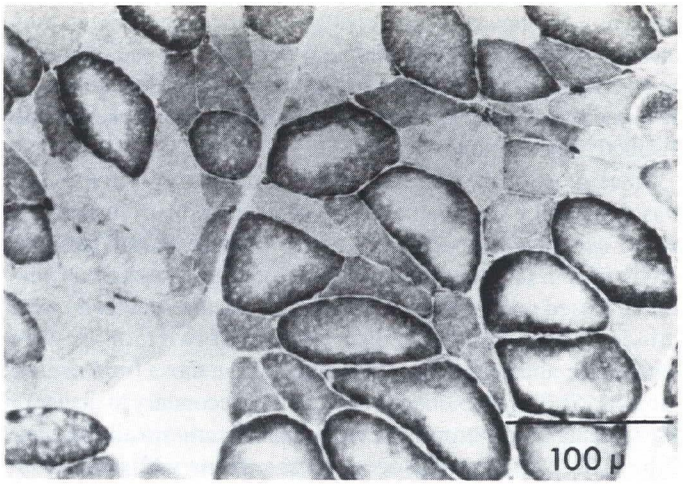

Fig 4—NADH-TR. Central cores in type I fibers.

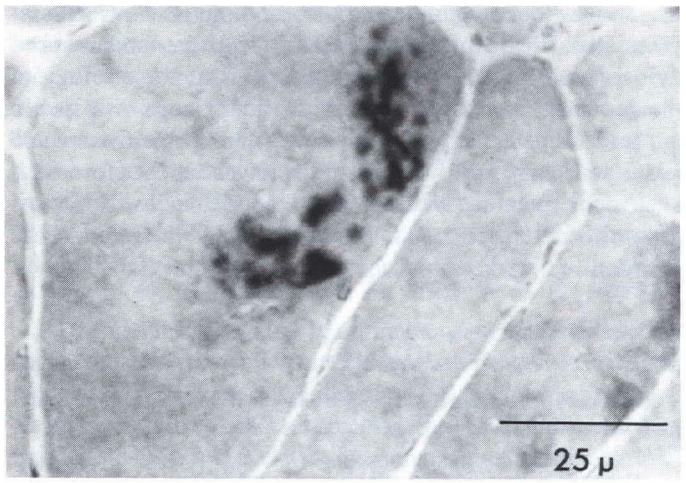

Fig 5—Modified Gomori trichrome. Rods in sarcoplasm.

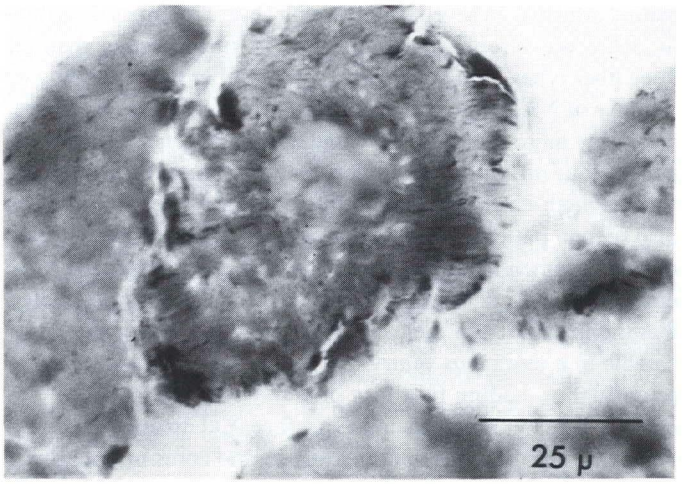

Fig 6—Modified Gomori trichrome. Ragged red fibers.

change of fiber size (2). These factors are calculated from the number of abnormal- and normal-sized fibers and the degree to which they are abnormal. The upper limit for the value of the atrophy factor in both type I and type II fibers in the normal male quadriceps is 150. The variability coefficient was positive (greater than 250) in eight type I, eight type IIA, and ten type IIB fibers. Type I predominance (greater than 55% of the fibers) occurred in six cases; IIA paucity (less than 10%) in two cases; and IIB paucity (less than 10%) in two cases.

Discussion

The results indicate that patients with severe osteoarthritis of the knee, requiring total knee replacement, have significant neuromuscular disease in the quadriceps muscle. This is primarily neuropathic and includes atrophy of type I, IIA, and IIB fibers. Frequent myopathic changes such as degenerating or regenerating fibers, inflammation, rods and ragged red fibers were also seen. Neither the neuropathic nor myopathic changes are due to

Table 2
Morphometry

Case Number	I Atrophy Factor Positive 150	IIA Atrophy Factor 150	IIB Atrophy Factor 150	% I 55P	% IIA 10p	% IIB 10p
1	118	53	**149**	**55**	**7**	29
2	32	**244**	**238**	**64**	19	17
3	**363**	**180**	**537**	**61**	18	21
4*	**150**	**336**	**500**	51	36	**3**
5	138	**192**	**372**	**70**	12	18
6	**266**	**357**	**168**	46	18	36
7*	**202**	**504**	**789**	41	39	20
8	69	0	**158**	**62**	29	**9**
9	**150**	**243**	**472**	47	32	21
10	**224**	**231**	**563**	39	19	42
11	29	77	**300**	**81**	**6**	13
12	**824**	**598**	**906**	49	30	21
Cases/Total	7/12	9/12	12/12	6/12	2/12	2/12

*Same man, both knees done.
Boldface type indicates abnormal values.
P = fiber type predominance.
p = fiber type paucity.

aging alone, since structural changes are inconspicuous in limb muscles of healthy elderly people before age 70, and then only an occasional fiber will show an alteration (3). Denervation atrophy of the quadriceps muscle in an autopsy control series was distinctly uncommon (4).

Since most of the patients were not physically active, there was an additional element of disuse atrophy. Muscle atrophy, which occurs with inactivity, may be considerable. The mean fiber sizes in the quadriceps muscle of patients who had sustained closed uncomplicated lower limb fractures and who were subsequently immobilized for periods of two months were found to be approximately 50% smaller than those from control subjects (5). Type IIB fiber atrophy, either secondary to disuse or due to denervation atrophy, occurred in our series in all 13 cases. Type II fiber atrophy also occurred in patients with either nonpainful or less severe rheumatoid arthritis (1) and osteoarthritis of the hip (6).

The changes in osteoarthritis at the knee differ from previously reported muscle biopsy results in patients with rheumatoid arthritis. In seven patients with severe rheumatoid arthritis, there was atrophy of type I and IIA fibers, rather than all three fiber types, and no reports of either fiber type grouping or esterase or NADH positive angular atrophic fibers. However, there were more frequent fibers undergoing degeneration and regeneration, inflammatory reactions, or architectural changes such as moth-eaten or whorled fibers. Type I fiber atrophy was also seen in patients with long-standing injury of the anterior cruciate ligament of the knee (7). These fibers were thought to be engaged in the maintenance of muscle tone. It was postulated that the instability in the knee joint was physiologically comparable to a tendinous injury and would interfere with spindle activity, thus leading to a loss of activity of type I fibers. Tenotomy is also known to cause preferential atrophy of type I fibers (8). The presence of numerous central cores in one biopsy may be secondary to mechanical factors and an abnormal tendoskeletal relationship (9). This may represent an acquired form of central core disease rather than the congenital disorder.

Dynamic studies of quadriceps' function following fractures of the femoral shaft demonstrated that in measurement of isometric strength and dynamic endurance, about ⅔ of the patients showed an abnormal reduced strength of the quadriceps (10). Osteoarthritis of the fractured leg was found to be severe in four patients, moderate in 14, and mild in 28 patients. Eighteen patients had osteoarthritis in both knees. Patients with slight shortening or mild to moderate osteoarthritis of the fractured leg did not have reduced strength. Similar dynamic changes in the quadriceps' functioning may well occur in severe osteoarthritis of the knee without an associated femoral fracture.

A study investigating changes in size and distribution of fiber types in the quadriceps muscle from a variety of different knee joint disorders showed type II fiber atrophy correlated with increasing age and moderate impairment; however, patients were still ambulatory (11). Both type I and II fibers showed atrophy in patients that were severely impaired or nearly immobilized. An isolated atrophy of type I fibers was found in three patients suffering from frequent, sudden, short, lancinating pain in the knee joint, although this condition may not alone be the cause of the type I fiber atrophy. Disorders included rheumatoid arthritis, osteoarthritis, femoropatellar or femorotibial osteoarthrosis, dislocating patella, meniscus tear and chondromalacia. Two of the three patients with osteoarthritis had both type I and type II fiber atrophy. All 11 patients with femoropatellar or femorotibial osteoarthrosis had predominant type II fiber atrophy. By contrast all 12 of our patients with severe osteoarthritis of the knee had denervation atrophy. Five of the cases also had significant myopathic changes.

Whether quadriceps muscle pathology antedates the development of osteoarthritis and therefore is a predisposing factor or is a phenomenon secondary to the development of arthritis is unknown. However, since skeletal dysmorphism, abnormal muscle tension, and other mechanical factors including tenotomy are all known to cause abnormal muscle structure, these factors may well be the cause of the muscle pathology. Patients with severe osteoarthritis of the knee could also have lumbar spondylosis with bilateral L4 radiculopathies as the etiology of the denervation atrophy seen in the quadriceps biopsies in our series. Further studies including a neurological exam and EMG and nerve conduction studies in patients before total knee replacement, as well as muscle biopsies in less severe osteoarthritis, are necessary to better understand the nature of the changes we observed.

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