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# No Relationship Between Fiber Type and Halothane Contracture Test Results in Malignant Hyperthermia

T. Heiman-Patterson, M.D.,\* J. E. Fletcher, Ph.D.,† H. Rosenberg, M.D.,‡ A. J. Tahmouh, M.D.\*

Previous studies in cat, rat, and swine have implicated fiber type as influencing the halothane and caffeine contracture test used to diagnose malignant hyperthermia (MH). The authors performed fiber type analysis using myosin ATPase stains on 31 fascicles of skeletal muscle from nine patients following contracture testing. There was no significant difference in fiber type composition between fascicles from MH negative ( $n = 5$ ) and MH positive ( $n = 4$ ) patients. Furthermore, examining each of the 31 fascicles, the authors found no correlation ( $P > .05$ ) of contracture magnitude with percentage of either Type I or Type II fibers using the Pearson Product-Moment correlation calculation. The authors conclude that fiber type composition does not influence contracture test results in human biopsies. (Key words: Malignant hyperthermia: contracture test; fiber type.)

MALIGNANT HYPERTHERMIA (MH) is a life-threatening disorder occurring upon exposure to halogenated anesthetic agents and succinylcholine. Manifestations include rhabdomyolysis, rigidity, hyperthermia, metabolic acidosis, and elevated CK levels. In the general population, 1 in 4200 exposures to the combination of halothane and succinylcholine results in episodes which resemble MH.<sup>1-2</sup>

MH susceptibility can be determined by use of the halothane and caffeine contracture tests. These tests have been shown to be the most reliable and specific indicator of MH susceptibility.<sup>3-6</sup> Contracture test results may be influenced by temperature.<sup>7-9</sup> Although weight, length, and diameter of the specimen might be expected to influence halothane and caffeine contracture testing, these factors do not significantly affect this relatively crude test of MH susceptibility.<sup>7</sup> Fiber type composition has been suggested to influence caffeine, halothane, and halothane-caffeine contractures in cat, rat, and swine muscle.<sup>10-12</sup> Rat muscles composed of predominantly Type I fibers developed contractures at

lower caffeine concentration than those comprised of Type II fibers. This was potentiated by halothane.<sup>10</sup> Similarly, Type I fibers of swine<sup>12</sup> and cat<sup>11</sup> appear more sensitive to caffeine, halothane, and halothane-caffeine contracture testing. To evaluate possible effects of fiber type on diagnostic testing for MH, we examined fiber type composition of those bundles used in the contracture test for MH evaluation.

### Methods

A muscle biopsy of the vastus lateralis was performed under femoral nerve block using 1.25% mepivacaine with supplemental sedation<sup>13</sup> in nine patients undergoing MH evaluation. The indications for biopsy were either a family history of MH or an anesthetic event suspicious for MH. The muscle removed was processed for contracture testing and subsequent histochemistry on the tested fibers, as described below.

Muscle samples were clamped *in situ* and processed as previously described.<sup>14</sup> Strips of muscle weighing 50-150 mg were dissected and placed in a 37° C bath of modified Krebs solution continuously bubbled with 95% O<sub>2</sub>-5% CO<sub>2</sub>. The muscle was directly stimulated at 0.2 Hz with supramaximal pulses of 2-10 msec duration. Subsequently, muscle was exposed to 3% halothane. Patients were considered MH susceptible if any preparation demonstrated equal to or greater than 0.7 g contracture when exposed to 3% halothane.<sup>14</sup> Thirty-one strips in nine patients were first evaluated with contracture testing and subsequently frozen in isopentane cooled in liquid nitrogen<sup>15</sup> for histochemical processing. Six- to ten-micron sections were cut on a freezing microtome and stained histochemically for myosin ATPase at pH 4.32, 4.6, and 9.4 in order to perform fiber type evaluations.<sup>15</sup> Polaroid photomicrographs were taken using a polaroid camera and Leitz Ortholux photomicroscope for counting fiber types. At least 200 fibers were evaluated for each strip. The per cent of Type I and Type II fibers were calculated for each of the 34 strips and correlated with contracture test results. Statistical analysis comparing fiber type composition and contracture test result was performed using *t* test analysis. Analysis of the magnitude of contracture

\* Associate Professor of Neurology.

† Assistant Professor of Anesthesiology.

‡ Professor and Chairman, Department of Anesthesiology.

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Address reprint requests to Dr. Heiman-Patterson: Department of Neurology, Hahnemann University Hospital, Broad and Vine Street, Philadelphia, Pennsylvania 19102.

and its correlation with fiber type was performed using Pearson Product Moment correlation calculations.

**Results**

Table 1 presents the results of fiber type analysis and corresponding halothane contracture tests on individual fascicles. The average distribution in bundles from five normal patients was ( $x \pm SEM$ )  $56 \pm 6\%$  Type I fibers and  $44 \pm 6\%$  Type II fibers, while, in bundles from 4 MH susceptible patients, it was  $46 \pm 3\%$  Type I fibers and  $54 \pm 3\%$  Type II fibers. There was no significant difference between MH- and MH+ strips of these values. For those patients in table 1 with at least three muscle strips, the correlation of fiber type to strength of contracture was tested. The Pearson Product-Moment correlation coefficient (mean 0.275; range 0-0.62) was not significant ( $P > .05$ ) for the data from any patient. The mean value for fiber type for each patient was compared to the mean contracture amplitude for the MH negative patients. The Pearson Product Moment correlation coefficient (0.259) was, again, not significant ( $P > .05$ ). The same test using the mean values for the MH positive patients yielded a Pearson Product Moment coefficient (0.223) that was not significant ( $P > .05$ ). Furthermore, pooling the responses from all fibers, there was no correlation ( $P > .05$ ) of contracture magnitude when compared to the percentage of either Type I or Type II fibers using the Pearson Product Moment correlation calculation. For negatively testing biopsies, the correlation coefficient was +0.15 for Type I fibers and -0.15 for Type II fibers. For positively testing biopsies, the correlation coefficient was -0.25 for Type I fibers and +0.25 for Type II fibers.

**Discussion**

This study examines the relationship of skeletal muscle fiber type composition to halothane contracture test results in patients undergoing diagnostic biopsies for MH susceptibility. The proportions of Type I and Type II fiber types within the vastus lateralis of our patients was comparable to those reported in the literature.<sup>16,17</sup> We found no correlation between fiber type composition and halothane contracture test results. This included comparisons between the overall averages from patients whose tests were positive and negative, as well as correlating fiber type with contracture response in all fiber bundles. The present study demonstrates the necessity that the actual fiber typing be done on the same fascicles which underwent contracture testing. Previous studies comparing the response of muscles of different fiber type predominance suggested that fiber type composition affects contractile response to halothane and/

TABLE 1. Percentage of Type I and Type II Fibers and Contracture (g) in Skeletal Muscle Fiber Strips Undergoing Halothane Contracture Testing

Patient	Strip	Type I (%)	Type II (%)	Halothane Contracture (g)
1	1	51	49	0
	2	56	44	.2
	3	57	43	.2
	4	61	39	.2
	5	62	38	0
	6	56	44	0
2	1	69	31	.1
	2	74	26	.1
	3	52	48	0
	4	70	30	0
3	1	36	64	.1
	2	31	69	.1
	3	32	68	.1
	4	35	65	.1
4	1	56	44	.3
	2	58	42	.1
	3	59	41	.4
5	1	66	34	.6
	2	63	37	0
6	1	37	63	2.7
	2	44	56	.5
	3	29	71	1.2
7	1	41	59	.3
	2	31	64	2.5
8	1	50	50	.6
	2	59	41	.1
	3	59	41	1.1
9	1	59	41	3
	2	54	46	1
	3	44	56	2.6
	4	42	58	2.8

or caffeine in normal cats,<sup>11</sup> rats,<sup>10</sup> and swine,<sup>12</sup> as well as MH susceptible swine.<sup>12</sup> Similar studies had not been evaluated in mixed fiber type muscles. It should be noted that one previous study of mixed fiber type muscles from MH susceptible swine noted no difference of fiber type composition and MH susceptibility<sup>18</sup> in agreement with the present study. There is generally a mixed proportion of fiber types within human skeletal muscle, and only few muscles show Type I predominance greater than 70%.<sup>19</sup> This work indicates that fiber type composition did not correlate with contracture test results in human biopsies. Fiber type is not a determinant of MH contracture test results in humans.

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