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Contraction versus contracture and centronuclear myopathy versus central part myopathy in malignant hyperthermia

Dear Editor,

We read with great interest the review article by Correia et al. "Malignant hyperthermia: clinical and molecular aspects"¹ (*Hipertermia maligna: aspectos moleculares e clínicos*) and would like to comment on some aspects.

In the section "Malignant hyperthermia", item "Contraction to exposure to halothane-caffeine (TCHC) Test", Correia et al. use the term "contraction" instead of the original term "contracture". The test for diagnosis of susceptibility to malignant hyperthermia (MH) is based on an abnormal contracture response after administration of caffeine/halothane, and not on the normal response of muscle contraction after electrical stimulation, which is applied throughout the test to prove viability of the muscle fragment tested. Fig. 1 shows the difference between contraction and contracture in the chart of a positive test in a patient susceptible to MH. Thus, the nomenclature should be "contracture test" in English and *teste de contratura* in Portuguese.²⁻⁴

Also in this subsection, we emphasize that the cutoff levels of TCHC cited correspond to values used in the U.S. group of HM (MHAUS - www.mhaus.org) protocol. Moreover, the protocol of the European MH Group (EMHG - www.emhg.org) differs from the U.S. one in additional aspects that were not mentioned, such as the number of fragments tested (six in the U.S. and four in the European protocol), halothane administration (single dose of 3% in the U.S. and an increasing dose from 0.5% to 3% in the European protocol) and finally the cutoff, which is 0.2 g to for halothane 2% and 0.2 g for caffeine 2 mm in the European protocol.^{5,6}

Unlike that noted by Correia et al., in Brazil the Cedhima (Center for the Study, Diagnosis and Research for Malignant Hyperthermia), Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP) uses the European MH group protocol for *in vitro* muscle contracture testing (IVCT).⁴

In the same section "Malignant hyperthermia", item "Treatment", Correia et al. include as an indicated measure the "Replacement of anesthesia circuit by other circuit uncontaminated by anesthetic agent". It is important to emphasize here that there is no indication for this measure during the treatment of a crisis, but only in the preparation of the anesthetic machine for anesthesia in a patient with a history of HM. At the time of a MH crisis we must "disconnect the vaporizer, but with no waste of time changing the circuit or the anesthetic machine".⁷ In "Dantrolene" item,

although Correia et al. state that the modern clinical use of dantrolene is restricted to malignant hyperthermia, this drug is still employed in the management of spasticity.⁸

Furthermore, the maintenance of dantrolene for 24–48 h after the initial treatment of HM crisis is important to avoid

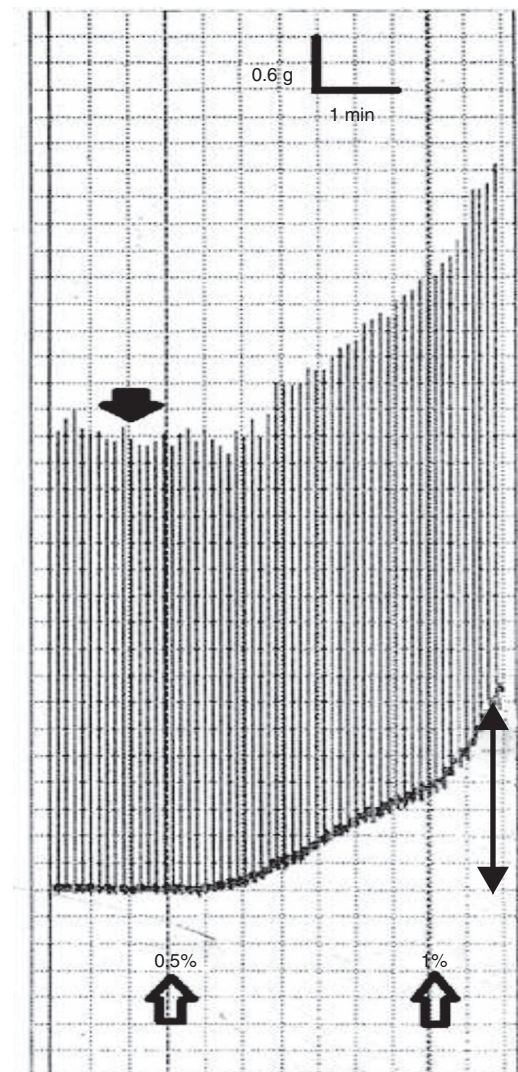


Figure 1 *In vitro* muscle contracture test (IVCT) in response to halothane. The two lower arrows indicate the time at which the drug was added. The upper arrow indicates the lines that correspond to muscle contractions triggered by electrical stimulation. The lateral double arrow indicates the ascension of the base line, which corresponds to an abnormal muscle contracture.

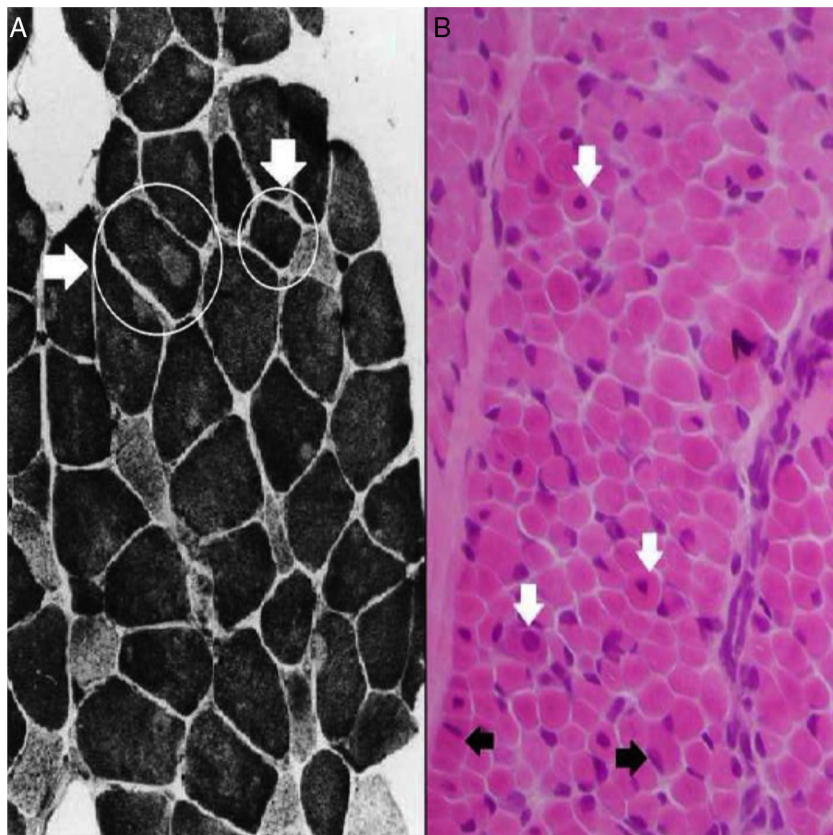


Figure 2 Cross-sectional histological sections of striated muscle (freezing). (A) *Miopatia da parte central*, or central core myopathy: the horizontal arrow indicates a muscle fiber with unmarked central circular area (*core*); the vertical arrow depicts a fiber with homogeneous normal marking; histochemical reaction with NADH. (B) Centronuclear myopathy: White arrows show fibers with central nucleus, and black arrows show fibers with normal position of the nucleus, just below the cytoplasmic membrane (subsarcolemmal); hematoxylin and eosin stain.

relapses; however, in a dosage of 1 mg/kg every 4–8 h, or continuously at 0.25 mg/kg/h (or 6 mg/kg/d).⁹

In the section “RYANODYNE RECEPTORS (RYRs)”, in “Correlated channelopathies” item, the term *doença do núcleo central* appears twice as a translation of “central core disease”. However, the suggested translation into Portuguese for *central core* myopathy would be *miopatia da parte central* (C05.651.575.300 C10.668.491.550.300), as recommended by the site Descriptors in Health Sciences (<http://decs.bvs.br/>), under the Unified Medical Language System (<http://www.nlm.nih.gov/research/umls/>). This distinction is important because, among other clinical and mutational associated differences, the histopathology is distinct, as can be seen in Fig. 2. Fig. 2A depicts the appearance of *miopatia* or *doença da parte central* (central core disease or CCD): There is a central marking flaw in oxidative histochemical reactions (such as SDH and NADH), thanks to the absence of mitochondria.¹⁰ On the other hand, Fig. 2B depicts the appearance of centronuclear myopathy (*i.e.*, *miopatia centronuclear*), in which the nucleus assumes a central place in the muscle fiber, while usually it would occupy a subsarcolemmal position, *i.e.*, just below the cytoplasmic membrane.¹¹

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