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THE EFFECTS OF PRESSURE AND SHEAR ON CAPILLARY CLOSURE IN THE MICROSTRUCTURE OF SKELETAL MUSCLES: COMPUTATIONAL STUDIES

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INTRODUCTION

Deep tissue injury (DTI) is a serious and potentially deadly type of pressure ulcers, which initiate in deep muscle tissue under bony prominences of immobilized patients, and progress outwards towards the skin with no clear visual indications of the injury at the surface of the body. It had been suggested that DTI appear in muscle tissue first, due to the dense capillary vasculature in skeletal muscles which is susceptible to obstruction and occlusion by mechanical forces [1-3]. Though mechanical forces may cause capillaries to collapse and thus induce ischemic conditions in adjacent muscle cells [2], some investigators stipulated that ischemia alone cannot explain the etiology of DTI, and so, other mechanisms, particularly excessive cellular deformations must be involved [1]. We hypothesize that physiological levels of stresses and strains in muscle tissue under bony prominences - even when muscles are highly loaded as during sitting - do not cause complete closure of muscle capillaries, and therefore, do not cause an acute ischemia in muscles. If this is indeed the case, then ischemia cannot be the only factor contributing to DTI onset. In order to test our hypothesis, we developed a finite element (FE) model of the microstructure of skeletal muscle, at the level of muscle fascicles, and employed the model to determine the stress and strain levels required for causing partial and complete closure of capillaries.

METHODS

To determine the mechanical conditions in the muscle microstructure we employed a hierarchical approach. Specifically, we first utilized a previously developed FE model of the whole rat hindlimb subjected to prolonged compression [1] for calculating the loading conditions that need to be applied on a second, muscle-fascicle-level FE model. The model of the rat hindlimb at the macro-scale and the relation of pressure on the muscle surface to

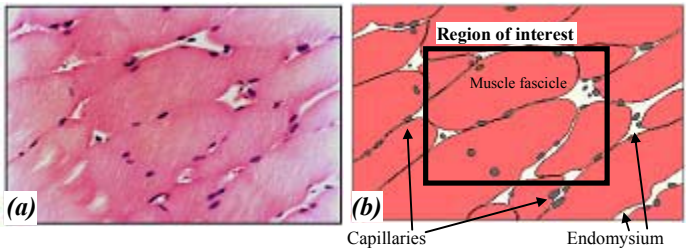

Figure 1. Representative histological slide of a rat skeletal muscle stained with hematoxylin and eosin (a), and geometry of the corresponding finite element model

intramuscular stress are described in detail in [2]. Here we focus on the development of the microstructural muscle model. This FE model was built based on geometry seen in a histological slide stained (with hematoxylin and eosin) to show muscle fascicles, endomysium and capillaries (Fig. 1, size 300 μm × 200 μm).

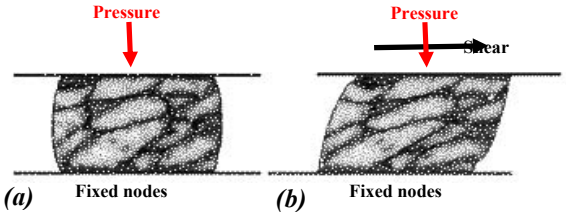

Figure 2. Finite element mesh and loading modes: pressure applied to a rigid plate fixed to the upper side of the model (a), and a combination of pressure and shear applied to the model (b).

The model was based on the large deformation theory. The non-linear pseudo-incompressible mechanical behaviors of muscle fascicles and endomysium were represented using Neo-Hookean constitutive laws, with material coefficients that were adopted from the literature [1]. The model was loaded between rigid plates, fixed to the "muscle" nodes, in two modes: (i) pressure only (Fig. 2a), and (ii) simultaneous pressure and shear (Fig. 2b). Pressure values of 12, 37, 78, 100 and 120 kPa [2] and shear strains of up to 8% were applied to the upper plate while the lower plate remained fixed. Frictionless contact conditions were set between the capillary walls in order to avoid self-intersections during compression at large deformations. We further took into account that in tissues subjected to external loading in vivo, there is a compensatory response of the capillary blood pressure (autoregulation) and this yielded capillary pressure of 80 mmHg for all simulation cases. The FE model was solved in the non-linear analysis mode of MARC (2005). For each simulation case, we determined the accumulative percentage of open capillary cross-sectional area (with respect to the unloaded case) in a region of interest (ROI, size 160 μm × 120 μm) that is not in the direct vicinity of the model fixed/displaced boundaries, consistent with Saint-Venant's principle (Fig. 1b).

RESULTS

In response to pressures of 12, 37, 78, 100 and 120 kPa, and no shear, the accumulative percentage of open capillary cross-sectional area decreased from the 100% baseline (i.e. open area for the unloaded geometry) by 2, 32, 58, 63 and 71%, respectively (Fig. 3). Interestingly, when shear strains were added to the simulations, the open cross-sectional area of capillaries decreased more rapidly; the higher the magnitude of shear strains, the more rapid the decrease in open capillary area (Fig. 3). For example, when shear strains of 4.1-4.6% were acting simultaneously with pressure, the accumulative open capillary area decreased by 21, 21, 26, 35 and 45% more than when only pressures (of 12, 37, 78, 100 and 120 kPa) were applied. A second important observation is that for the maximal loading in our simulations, where pressure of 120 kPa and shear strain of 8.8% were applied, only 46% of the capillaries contained in the ROI (i.e. 9 of 19 capillaries) completely collapsed.

Strain and stress tensors in the muscle microstructure were calculated for each simulation case (Fig. 4). For example, tissue-level maximal principal compression strain, shear strain, principal compression stress and shear stress for a pressure of 37 kPa and shear strain of 8.1% applied at the boundaries were 66%, 76%, 13.4 kPa and 12kPa, respectively. Again, the contribution of shear to the tissue-level strain and stress concentrations was found to be substantial, as peak principal compression strain, shear strain, principal compression stress and shear stress for the same pressure (37 kPa) but no shear were much lower, that is, 28%, 30%, 3.3 kPa and 1.6 kPa, respectively.

DISCUSSION

Using FE studies of the mechanical conditions in the microstructure of skeletal muscles, we showed that even low shear strains (>10%) have a substantial contribution to development of stress concentrations at the tissue-level. In particular, shear strains dramatically decrease the capillary cross-sectional area available for blood flow (Fig. 3), and therefore, the results support the hypothesis that shear strains cause ischemia. Nevertheless, we also showed that even for the maximal loading applied in our modeling, i.e. pressure of 120 kPa (which exceeds physiological passive intramuscular pressures in humans) coupled with shear strain of 8.8%, only 46% of the capillaries completely closed. This indicates that ischemia cannot be the only factor involved in muscle cell death leading to DTI. This finding is supported by our recent animal studies which showed that

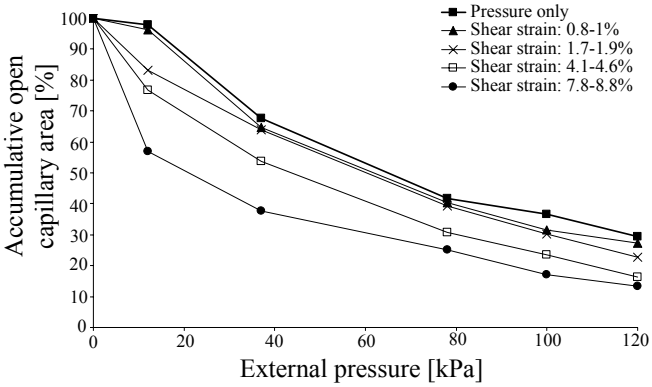

Figure 3. Accumulative percentage of open capillary cross-sectional area as function of the external pressure and shear.

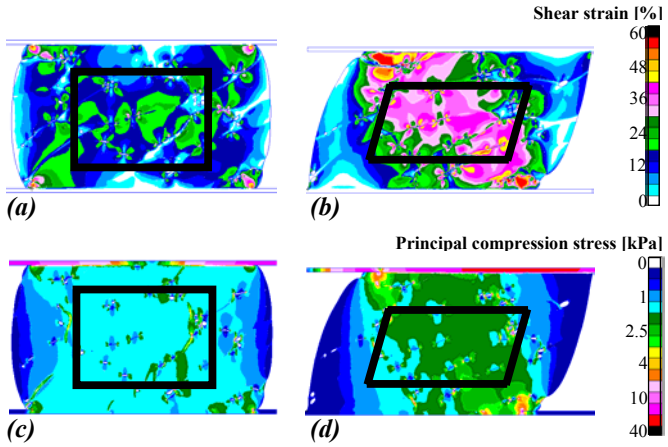

Figure 4. Tissue-level shear strain distributions for external pressure of 120 kPa (a), and when shear strain of 8.8% was applied simultaneously (b). Principal compression stress distributions for external pressure of 120 kPa (c), and when shear strain of 8.8% was applied simultaneously (d).

pressures as low as 37 kPa already result in muscle cell death [2,3]. Overall, we conclude that while shear strains are likely to promote ischemia and hypoxia, the ischemic conditions alone are insufficient to cause DTI. This supports the hypothesis that excessive cellular deformation must be involved in the onset of DTI [1]. Animal studies are now underway in our laboratory to validate the present model predictions.

ACKNOWLEDGEMENTS

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