Endothelial cells (ECs) form the innermost layer of all vasculature and constantly receive both biochemical and biomechanical signals, yielding a plethora of biomechanical responses. In response to various biochemical or biomechanical cues, ECs have been documented to generate biomechanical responses such as tractions and intercellular stresses between the cell and substrate and between adjacent cells in a confluent monolayer, respectively. Thus far, the ability of endothelial tight junctions and adherens junctions to transmit intercellular stresses has been actively investigated, but the role of gap junctions is currently unknown. In addition, there is no report of the independent influence of hyperglycemia on endothelial biomechanics present in the literature. To fill these gaps, we conducted a two-fold study where we investigated the influence of endothelial gap junction Cx43 and hyperglycemia in endothelial tractions and intercellular stress generation. In the first study, we selectively disrupted and enhanced EC gap junction Cx43 by using 2',5'-dihydroxychalcone and retinoic acid, respectively and in the second study, we cultured ECs in both normal glucose and hyperglycemic condition for 10 days. In both studies, tractions and intercellular stresses were calculated using traction force microscopy (TFM) and monolayer stress microscopy (MSM), respectively. Our results reveal that Cx43 downregulation increased as well as decreased endothelial avg. normal intercellular stresses in response to a low (0.83 µM) and a high dose (8.3 µM) chalcone treatment, respectively, while Cx43 upregulation decreases avg. normal intercellular stresses in both treatment conditions (2.5 µM and 25 µM) compared to control. In addition, we observed a decrease in intercellular stresses with the hyperglycemic condition compared to control. The results we present here represent, for the first time, a detailed and comprehensive biomechanical analysis of endothelial cells under the influence of glucose and the gap junction Cx43. We believe our results will provide valuable insights into endothelial permeability, barrier strength as well as leading to a greater understanding of overall endothelial mechanics.

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The public is welcome to attend.