

May 26, 2020

Editorial Office
World Journal of Cardiology

Title: Classic Ehlers-Danlos Syndrome and Cardiac Transplantation-Is There a Connection?

Dear Editor:

Please find the revised manuscript entitled, "Classic Ehlers-Danlos Syndrome and Cardiac Transplantation-Is There a Connection?" for consideration of publication in the *World Journal of Cardiology*. I have followed the editorial and reviewers' comments and recommendations prior to publication. I have added the PMID and DOI numbers for all references and added all authors in all references as requested. I have provided information earlier to the editorial office regarding evidence of the NIH grant acknowledged in the study as I am a local investigator at KUMC where I am employed where this grant supports the genomics core facility utilized by my research program for advanced genetic testing and the neuroscience institute.

Ehlers-Danlos syndrome (EDS) consists of a group of single gene connective tissue disorders often transmitted in an autosomal dominant pattern. To advance our understanding of connective tissue disorders, specifically classical EDS due to a COL5A1 gene variant seen in a father having a heart transplant, I sought to bring this apparent association to medical attention. Hence, others with classical Ehlers-Danlos syndrome may be at risk of unexplained heart failure and cardiac transplantation. Awareness of potential surgical complications or risks such as healing, blood pressure instability, aneurysms and anatomical vascular problems associated with connective tissue disorders should be noted by cardiologists, heart transplant specialists and surgeons prior to surgery.

The readership of your journal should find this report of interest and consider testing patients for hyperflexibility using the Beighton scale and with readily available next-generation DNA sequencing of connective tissue disorder gene panels in those patients with unexplained heart failure with or without evidence of a connective tissue disorder (e.g., stretchable skin, joint laxity, poor healing). I have also addressed the questions /comments raised by the reviewers as noted above.

There is no conflict of interest in the conduct and reporting of this research to declare. A signed consent form of the patient was included in the original submission. Hopefully, the manuscript will now be acceptable for publication.

Sincerely,

A handwritten signature in blue ink, appearing to read "Merlin G. Butler, MD, PhD". The signature is fluid and cursive, with the letters "M", "B", and "P" being particularly prominent.

Merlin G. Butler, MD, PhD
Director, Division of Research and Genetics
Director, KUMC Genetics Clinic
Professor of Psychiatry & Behavioral Sciences and Pediatrics