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Authors: João Santos-Antunes, Hélder Cardoso, Susana Lopes, Margarida Marques, Amadeu CR Nunes and Guilherme Macedo

Correspondence to: João Santos-Antunes, MD. Department of Gastroenterology, Faculty of Medicine, Centro Hospitalar S. João. Alameda Prof. Hernani Monteiro 4200-319 Porto, Portugal. E-mail address: joao.claudio.antunes@gmail.com

The first and the second authors of the manuscript have training in advanced biostatistics methodology, by concluding several courses and post-graduations in the Medical Faculty of Oporto, Portugal. Statistic analysis of this manuscript was conducted by these authors.