Journal Pre-proof

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PII: S0261-5614(20)30460-X

DOI: https://doi.org/10.1016/j.clnu.2020.09.004

Reference: YCLNU 4445

To appear in: *Clinical Nutrition*

Received Date: 6 September 2020

Accepted Date: 9 September 2020

Please cite this article as: Lukaski H, Selva LN, Cereda E, A tribute to Antonio Piccoli, a father and a pioneer in body composition assessment using bioelectrical impedance technology, *Clinical Nutrition*, https://doi.org/10.1016/j.clnu.2020.09.004.

A tribute to Antonio Piccoli, a father and a pioneer in body composition assessment using bioelectrical impedance technology

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Keywords: Body Composition; fat-free mass; phase angle; hydration; bioelectrical impedance vector analysis (BIVA)

Antonio Piccoli, MD, MSc, the pioneer and international leader in the development and application of bioelectrical impedance vector analysis (BIVA) for identification of fluid imbalance, sadly passed away on August 4, 2020.

Antonio was born into a farming family in the small town of Feltre (Pederobba) in the Province of Treviso in northeastern Italy on July 7,1949. As a youth, he enjoyed cycling in the natural setting of the Veneto region and developed an appreciation for the architecture of Andrea Palladio.

The University of Padua provided Antonio's formal education. He earned an undergraduate degree in General Medicine and Surgery *magna cum laude* (1975), was active in educational programs and social services, and contributed to two textbooks. He earned post-graduate specialization in Nephrology in 1978 with Professors Fiaschi and Borsatti and was nominated for an Academic Researcher award in the Faculty of Medicine in 1980. Antonio pursued his strong interests for mathematics and statistical science with advanced degrees in Statistics (1981) and Statistical and Demographic Sciences (*magna cum laude* 1983). He also earned a post-graduate specialization in Internal Medicine in 1988. Antonio served as associate professor and Chief of Nephrology since 1992.

Dr. Piccoli was active in research involving diverse aspects of health for chronic renal failure patients. His work included therapeutic strategies using erythropoietin to ameliorate anemia, identification of the risk factors for arterial hypertension, preservation of bone health, and the treatment of glomerulonephritis with nephrotic syndrome. Notably, his chapter on

glomerulonephritis therapy, prepared while an undergraduate, remains in use today at the school of medicine.

As a nephrologist, Antonio recognized the need for an objective point-of-care, non-invasive method to assess hydration status and malnutrition of patients with chronic renal disease. He was keenly aware of the emerging bioelectrical impedance (BI) method and its use to predict fluid volumes and soft tissue composition and thoughtfully identified its limitations for clinical use. Together with Antonio Talluri, an engineer, Dr. Piccoli advocated for the use of "direct BI measurements" to overcome the unreliability of BI predictions then conceptualized and applied bioelectrical impedance vector analysis (BIVA) for practical clinical application [1]. BIVA only uses 50 kHz phase-sensitive measurements of whole-body resistance (R) and reactance (Xc), standardized for height. He demonstrated the practical advantages of BIVA compared to BI-based multiple regression predictions of fluid volumes and soft tissue composition, which depend on faulty assumptions and multiple sources of error, and result in unreliable estimates that are too imprecise for clinical use in different disease models (e.g. kidney or heart failure). In contrast, BIVA classifies hydration (under-, normal and over-hydration) and tracks changes with treatment independent of body weight [2].

Another strength of the BIVA method is its objectivity. Dr. Piccoli used his robust mathematical and statistical knowledge to implement the bivariate normal distribution of BI measurements on the RXc graph to ascertain hydration status. The impedance vector, consisting of R and Xc values and plotted on the RXc graph, is evaluated relative to confidence intervals (50, 75 and 95%) depicting the distribution of BI data within a comparative sample

(e.g., age- and gender-matched healthy reference people) and illustrated in the form of ellipses. Piccoli hypothesized, and later validated, that length of the vector and position on the RXc graph, shown as phase angle, depicted hydration status. Vector length is a surrogate for total fluid volume and its position, shown as phase angle, relative to the reference intervals indicates fluid distribution (ECW/ICW). Studies with healthy adults, children and infants confirmed vector positions within the 50% tolerance range to indicate normal hydration whereas vectors positioned outside the 75% confidence interval signaled fluid overload. Observational and treatment comparisons between groups visually reveal the degree of the separation or over-lap of the reference and patient ellipses, and are objectively determined using rigorous statistical methods. Whereas Dr. Piccoli's initial research demonstrated striking differences in BI measurement values and vector positions on the RXc graph among patient groups and healthy controls, his critical contribution was the use of BIVA to monitor the effects of treatment on a fluid-overloaded patient [3,4]. This application of BIVA enabled an individualized assessment that was previously unavailable. This use of BIVA provides a practical bedside method that is easily interpreted by a care-giver and improves patient care

Dr. Piccoli concurrently established the importance of the measured phase angle as an index of nutritional status and a reliable indicator of morbidity and mortality in chronic renal failure patients. He cautioned against the indiscriminate use of phase angle to assess nutritional status without consideration of fluid status [5]. Other clinical investigators extended this use of phase angle as a prognostic biomarker into other chronic diseases as well as geriatrics with strong associations with various measures of quality of life and muscular function. Additionally,

sport assessments currently include phase angle as a categorical predictor of performance with discrimination among levels of performance.

Dr. Piccoli led research teams and collaborated with leading clinical investigators to enhance the utilization of BIVA in critically ill patients. His work included studies of fluid imbalance in patients with congestive heart failure and chronic kidney disease in conservative or substitutive therapy, and demonstration of supportive associations between BIVA and new biomarkers of kidney damage and heart failure.

Colleagues describe Dr. Piccoli as a quiet, albeit shy, person, a consummate scientist, dedicated physician, and fine arts aficionado. He was a meticulous researcher, who emphasized the importance of research methods as the foundation of a successful investigation, and flourished with rigorous discussions of statistical methods and interpretation of findings in publications with early career researchers. His professional publications and interactions with students displayed his exceptional ability to communicate the complex physical and physiological principles of BIVA and its appropriate interpretation in clinical medicine. His approach to patient care was holistic, treating not only the pathology but learning the circumstances of each patient to not only cure the patient but the person. Antonio had an ardent love of art and music, specifically chamber music, and was a proficient flute player. His sense of humor was guarded but generously shared with his trusted co-workers.

Dr. Piccoli was an exceptional clinical investigator and a thoughtful physician committed to the highest standard of patient care. His legacy to medical science is not only BIVA but a clear road map of its use to benefit patient care.

Contributed by:

Dr. Giuliano Brunori (President of the Italian Society of Nephrology), Prof. Dr. Lorenzo Calò, Dr. Marta Codognotto, Prof. Dr. Salvatore Di Somma, Prof. Dr. Piergiorgio Messa (incoming President of the Italian Society of Nephrology), Dr. Eng. Antonio Talluri and Dr. Eng. Jacopo Talluri.

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