

## VALIDATION OF MULTI-FREQUENCY BIOELECTRICAL IMPEDANCE ANALYSIS IN MONITORING FLUID BALANCE IN GERIATRIC PATIENTS

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**Background:** Multi-Frequency Bioelectrical Impedance Analysis (MFBLA) is a simple, rapid, and novel method to assess body composition. This study aimed at determining MFBLA's responsiveness to clinically relevant changes in geriatric patients' fluid balance.

**Methods:** In 16 months 218 patients were admitted to the geriatric department and 53 could be included in this prospective study. Fluid balance was assessed rigorously twice a week by physical examination and laboratory tests. Changes in fluid balance were quantified by measuring total body water and extracellular fluid applying deuterium- and bromide-dilution techniques. MFBLA and weighing was performed daily and their Responsiveness Indexes (RI) for de- and hyperhydration were determined (Guyatt G. 1987, J. Chron. Dis. 40,171-8).

**Results:** Totally, 1000 MFBLAs were performed, in which 14 transitions from dehydration to euvolemia and 13 from hyperhydration to euvolemia were monitored. Individual changes in MFBLA during these transitions were highly significant ( $P < 0.001$ ). RI of MFBLA for dehydration was 3.1 ( $\pm 2.0$ ) for all frequencies, weight loss was  $2.8 \pm 1.8$  kg ( $\text{RI}_{\text{weighing}} = 2.7 (\pm 1.8)$ ). RI of MFBLA for hyperhydration ranged from 2.0 ( $\pm 1.2$ ) at 1 kHz to 2.3 ( $\pm 1.6$ ) at 100 kHz, increase in weight during hyperhydration was  $3.7 \pm 4.2$  kg ( $\text{RI}_{\text{weighing}} = 3.6 (\pm 4.1)$ ).

**Conclusions:** Responsiveness of MFBLA to changes in fluid balance can be relied on ( $\text{RI} > 1$ ), but is similar to weighing. MFBLA might improve monitoring fluid balance in geriatric patients, especially if daily weights are hard to get.

## SUBJECT-SPECIFIC VERSUS POPULATION-BASED REFERENCE RANGES IN DIAGNOSING DEHYDRATION IN GERIATRIC PATIENTS

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**Background** This study aimed at comparing the accuracy of Subject-Specific Reference Ranges (SSRR) and Population-Based Reference Ranges (PBRR) in diagnosing dehydration in geriatric patients. Using PBRR this diagnosis is often jeopardized because age and comorbidity may affect individual patients' laboratory test results in stable fluid balance.

**Methods** In 16 months 218 patients were admitted to the geriatric department and 53 could be included in this prospective study. Fluid balance was assessed rigorously twice a week by physical examination, laboratory tests and weighing. Changes in fluid balance were quantified by measuring total

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body water and extracellular fluid applying deuterium- and bromide-dilution techniques. SSRR were calculated as: individual means  $\pm 2.3 \times$  mean within-subject variability (according to: Fraser GC 1993, Drugs & Aging, 3, 246-57).

**Results** Laboratory tests ( $n=271$ ) of 14 dehydrated and 27 euvoletic patients were analysed. Data from twelve hyperhydrated patients had to be excluded. PBRR of creatinine and urea had a sensitivity of 71% and 100% and a specificity of 79% and 41%, respectively. SSRR of creatinine and urea showed a sensitivity of 93% and 71%, and a specificity of 95% for both tests.

**Conclusion** Subject-specific reference ranges should be calculated more often to improve the accuracy of laboratory tests in detecting dehydration in geriatric patients and to benefit more from the relevant information enclosed in repeatedly performed tests.

## CLONAL EXPANSION OF MITOCHONDRIAL DNA MUTATIONS IN AGED HUMAN MUSCLE

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The accumulation of mitochondrial DNA (mtDNA) mutations during life has been proposed as a significant contributor to the ageing process. MtDNA codes for 13 polypeptides, 22tRNAs and 2rRNAs that are all concerned with the respiratory chain (RC), a series of enzymes that generates the majority of cellular ATP. Although MtDNA mutations do accumulate at low levels with age, there is not a corresponding decline in RC function<sup>(1)</sup>. MtDNA mutations are extremely recessive. Studies on patients with mitochondrial diseases have shown that the level of a mtDNA mutation needs to be over 80% before RC function is affected.

We hypothesised that for mitochondria to be involved in ageing then mtDNA mutations had to be focused to individual cells and that in skeletal muscle the likely site for this would be fibres deficient in cytochrome c oxidase (COX-ve); in mitochondrial diseases these are a pathological hallmark for mtDNA mutations. To test this hypothesis single muscle fibres were dissected out of 30um sections from 8 different normal elderly subjects. The fibre was lysed with KOH, neutralized with HCl/Tris-HCl then used directly for PCR<sup>(2)</sup>. A 3 primer PCR was used to screen and quantify mtDNA deletions between nt8273 and 13720. 89 COX-ve and 70 normal (COX+ve) fibres were examined. In all COX+ve and most COX-ve fibres 99.5-100% of the mtDNA was wild-type. However muscle from 4 individuals contained at least one COX-ve fibre that contained >85% mutated mtDNA. Sequencing of the PCR product confirmed that the majority were due to the 4977bp common deletion and one was a 5117bp deletion at the site of a 10bp repeat.

This suggests that the cause of the COX deficiency in these abnormal fibres is a single mitochondrial mutation that has clonally expanded with the causative mutation varying between fibres. Thus age related mitochondrial DNA mutations are not globally distributed in aged tissues but focused to individual cells within which they are causing significant dysfunction.

1. Brierley E.J. Q J Med 1996;89:251-258
2. Sciacco M Hum Mol Genet 1994;3:13-19

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