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Preclinical Cardiac Involvement In Progressive External Ophthalmoplegia

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Aim of this study was to evaluate in patients with progressive external ophthalmoplegia (PEO) the left ventricular function by standard echocardiography and tissue Doppler imaging (TDI) analysis. Twenty patients with PEO (55.4 ± 17.5 years) and 20 age- and sex-matched healthy subjects underwent standard echocardiography with TDI analysis to assess left ventricular function. TDI was performed by placing the sample volume in the center of the basal lateral segment and the basal interventricular septum in the apical 4-chamber view. Myocardial systolic wave (S_m) and early (E_m) and atrial (A_m) diastolic waves were measured.

On standard echocardiography examination, no significant changes in left ventricular systolic function parameters were observed. Instead, the indices of left ventricular diastolic function were significantly lower in PEO patients respect to controls (peak E, 75.4 ± 11.2 vs. 58.8 ± 12.5 cm/sec, $p < 0.01$; E/A ratio, 1.0 ± 0.3 vs. 0.8 ± 0.2, $p < 0.01$). Regarding TDI measures, the PEO patients exhibited as compared to control subjects a lower S_m peak (septum: 7.6 ± 1.1 vs. 9.9 ± 0.8 cm/sec; lateral wall: 9.7 ± 1.7 vs. 12.8 ± 1.2 cm/sec, $p < 0.001$), a lower E_m peak (septum: 9.3 ± 1.6 vs. 12.8 ± 1.7 cm/sec; lateral wall: 10.2 ± 2.4 vs. 14.1 ± 1.9 cm/sec, $p < 0.001$), and a reduced E_m/A_m ratio (septum: 1.0 ± 0.4 vs. 0.7 ± 0.2; lateral wall: 1.2 ± 0.5 vs. 0.7 ± 0.2, $p < 0.001$, respectively).

Our data indicate that although cardiac involvement in patients with PEO is generally considered to be limited to the cardiac conduction system, left ventricular dysfunction may be present and should receive more attention in the management of patients with PEO. Pulsed TDI offers an additional means to conventional echocardiography for assessing left ventricular diastolic function and to identify preclinical systolic myocardial involvement in PEO patients.

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Construction of a database for a nation-wide Italian collaborative network of mitochondrial diseases

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In recent years, a flurry of epidemiological studies has confirmed the notion that mitochondrial disorders (MD) are among the most common genetic disorders and a major burden for society. However, in contrast to the extraordinary progress in our understanding of the biochemical and molecular bases of MD, we are still extremely limited in our ability to treat these conditions. Small patient populations represent the major impediment to progress in research and care. The development, by a multicenter nationwide collaborative network, of a web-based register of patients with MD will be helpful to better understand the phenotypes and the natural history of these diseases.

The GUP09004 Telethon-Clinical Grant project started on January 2010. Eleven Centers with expertise on MD have been involved. The initial phases ("establishment of the steering committee and the oversee committee" and "development and validation of the register") are completed and, having discussed some ethical, procedural and statistical issues, a data matrix has been defined including the more relevant clinical and laboratory parameters, such as: patient code, family code, date of birth, gender, region of origin, ethnicity, family history, diagnosis, year of diagnosis, age at onset, form, first symptoms, clinical features, clinical course, date and cause of death, Newcastle Scale scores, date of the last contact, plasmatic/urinary/CSF biomarkers, neuro-ophtalmological features, neuroradiologic features, proton magnetic resonance spectroscopy, histological findings, respiratory chain complexes complexes, pyruvate dehydrogenase, molecular analysis (southern blotting, long PCR, real time PCR, nuclear DNA genotype, mtDNA genotype with haplogroups) and therapy. By using a digitalized version of this matrix 145 patients from the 11 participating Centers have been charged on the database.

The ongoing phase provides a validation step of the database build-up by reassessment of all the cases in each Center, preliminary to the web-database where the obtained data will be transferred for an estimated population of nearly 3000 patients.

Possible future applications, based on such nation-wide Italian collaborative network, will include: epidemiological studies, phenotype-genotype correlations, disease natural history definition, multicenter clinical trials.