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Cardiac evaluation of anthracycline therapy in adjuvant treatment of breast cancer: 8 years of follow-up in a single center

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Introduction: The role of anthracyclines in the adjuvant treatment of breast cancer is still considerable. Nowadays anthracyclines are associated to taxanes with a reduction in the cumulative dosage and collateral toxicity. Aim of this study was to evaluate cardiotoxicity in long-term survivors from breast cancer.

Methods: 50 consecutive patients (63±7 years old) were treated with anthracyclines between 2003 and 2004 for early breast cancer and were recognized free of disease at the last follow-up (2012). Among these, 30 underwent a complete cardiologic evaluation with physical examination, electrocardiogram and echocardiogram. 13 were lost in follow-up, 4 died and 3 did not accept the study.

Results: Median follow-up was 97,4 months. At baseline mean age was 55,1 years (range 30 to 68). Six patients (20%) had hypertension, one (3,3%) had diabetes, 11 (36,6%) had dyslipidemia and 10 (33,3%) had a body mass index > 25 kg/m². The cumulative dosage of anthracyclines depending on chemotherapy schemes ranged from 760 to 963 mg/mq. Before chemotherapy, all patients showed normal left ventricular ejection fraction (LVEF 64% - range 54% to 80%) at myocardial scintigraphy. At follow-up evaluation, hypertension was present in 15 patients (30%), diabetes in 4 (13,3%), dyslipidemia in 14 (46,6%). LVEF was 62,5% (range 49 to 73).

Ten (33,3%) patients had decrease in LVEF > 10%. Patients who developed HF and first or second degree of cardiotoxicity showed a higher number of risk factors (1,8±0,9 vs 1,3±0,9). Among this, 2 (6,6%) developed overt HF during follow-up. One 7 years after chemotherapy, at last follow-up she was 61 years old, NYHA II, LVEF 49%, BMI 27,4, hypertension, dyslipidemia and anthracycline dose was 640 mg/mq; the other had HF from 3 years after chemotherapy, at last follow-up: age 62, NYHA III, LVEF 25%, no cardiac risk factors, anthracycline dose was 960 mg/mq. Both of them showed a reduced S wave at TDI at basal septum (6 cm/sec versus 9,2 cm/sec of the patients without cardiotoxicity).

Conclusion: Long-term anthracyclines cardiotoxicity is relatively frequent and associated to higher dosage of anthracyclines and higher frequency of cardiac risk factors.

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Phenomenon of paradoxical improvement in renal function defined by a decreased concentration of serum creatinine despite heart failure worsening in patients with mild-to-moderate heart failure

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Purpose: There is little information regarding the phenomenon of "paradoxical" improvement in renal function defined by a decrease in the serum Creatinine (Cr) concentration despite Heart Failure (HF) worsening. Therefore, in the present study we examined the frequency of this phenomenon and its relation to body fluid retention, particularly intravascular volume status, from stability to worsening of HF.

Methods: Data from 47 patients (32% men; 78.2±9.7 years) with established mild-to-moderate HF that underwent monitoring for HF were analyzed. Worsening HF event (38±16 days from stability to worsening HF) was diagnosed based on the presence of two or more of the following HF-related signs/tests: classic physical signs (S3, rales, leg edema), fluid weight gain (≥1.5 kg), and/or pleural effusion on ultrasound. Blood tests included measurements of hemoglobin (Hb), hematocrit (Ht), total protein, albumin, blood urea nitrogen, Cr and b-type natriuretic peptide. The percent shift in the plasma volume (%PV) from stability to worsening HF was estimated from serial concomitant Hb and Ht concentrations using the following formula (before = at stability, after = under worsening HF): $100 \times \frac{[Hb \text{ (before)}] \times [1-Ht \text{ (after)}]}{[Hb \text{ (after)}] \times [1-Ht \text{ (before)}]} - 100$.

Results: The cumulative number of the appearance of HF-related signs/tests was 2.87±1.52 (range: 2-5). Serum Cr concentrations decreased from stability to worsening of HF in 33 (70%) of the 47 study patients. Of these, as many as 11 patients presented with a more than 0.3-mg/dl decrease in the serum Cr concentration. Compared with the 14 patients with increased serum Cr concentrations, the magnitudes of the reduction in Hb and Ht, and of the increase of %PV were larger in patients with decreased serum Cr (-0.93±0.59 vs. -0.1±0.75g/dl, p=0.0002; -2.32±1.84 vs. -0.436±2.34%, p=0.005; 12.8±8.89 vs. 1.85±10.6%, p=0.0007, respectively), although there was no difference in the body weight increase (2.67±1.44 vs. 2.14±1.33kg, p=0.244). In all 47 study patients, changes in the serum Cr concentration correlated positively with ΔHb (r=0.39, p=0.007) and negatively with %PV (r=-0.334, p=0.022).

Conclusions: "Paradoxical" improvement of renal function, defined by a decrease in the serum Cr concentration during HF worsening, is a common phenomenon in patients with mild-to-moderate HF and that is strongly associated with expansion of the intravascular volume. Besides the intrinsic renal functional changes, effects of intravascular volume status should be kept in mind while monitoring renal function based on changes in serum Cr concentrations.

CARDIAC EFFECTS OF ENDURANCE TRAINING

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Distribution of cardiovascular risk factors in athletes and no athletes in a population of 10.000 young Italian students

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Introduction: Regular physical exercise is recommended by medical community. It is associated with a decrease in all cause-mortality, particularly with cardiovascular causes. The aim of our prospective observational study is to detect the prevalence of cardiovascular risk factors (CvRFs) in a population of young Italian students, athletes (G-A) and no athletes (G-B). We considered both competitive and noncompetitive athletes.

Methods: From October 2010 to October 2012, we prospectively evaluated 10019 students (Age 18.2±0.8 years old; 56% female) 6812 (68%) no athletes (G-B) and 3207 (32%) athletes (G-A). Anamnestic risk factors were collected using a medical history questionnaire. All students underwent to blood pressure and body-mass index evaluation. For statistical analysis we used the t test and Fisher's test, when appropriate. The statistical difference was considered significant only for p-value ≤ 0.05.

Results: In young population there isn't a significant difference in the prevalence of high normal blood pressure value in two groups. In no athletes systolic (SBP) and diastolic blood pressure (DBP) average was significantly higher than athletes (SBP: G-A 110.00±3.54 vs G-B 117.00±21.21, p<0.0001; DBP: G-A 60.00±14.14; G-B 70.00±28.28; p< 0.0001). The body mass index (BMI) mean was significantly lower in G-A compared to G-B (20.11±0.13 vs 25.45±1.73; p<0.0001). Moreover we observed that 22% of no athletes with BMI >25 had a SBP >130 mmHg and only 12% with BMI <25 had a SBP >130 mmHg.

Conclusions: Our prospective observational study evidenced that the physical exercise decrease the blood pressure and BMI. Moreover the overweight is associated to an increase of systolic blood pressure also in young people.

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Galectin-3 increase in endurance athletes

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Background: Galectin-3 is a new and promising biomarker for heart failure and myocardial fibrosis. Although endurance exercise is a crucial element in cardiovascular disease prevention, the relationship between exercise and plasma levels of galectin-3 is still unknown. To date, the relationship between regular exercise and myocardial fibrosis is not fully understood. This study investigates the relationship between endurance exercise and plasma levels of galectin-3.

Methods: Twenty-one male, healthy non-elite marathon runners were examined before and within one hour after a strenuous run of 30 km after four-day training abstinence. Examination included blood samples for galectin-3, echocardiography, and cardiac magnetic resonance imaging (CMR). In addition, to distinguish between cardiac or skeletal muscular origin of galectin-3, C57Bl/6J mice performing voluntary wheel running and sedentary mice were analyzed.

Results: Plasma galectin-3 in endurance athletes increased from baseline to post-exercise (12.8±3.4 ng/mL to 19.9±3.9 ng/mL, p < 0.001) while the systolic left and right ventricular function remained unchanged. Interestingly, baseline plasma levels of galectin-3 were evidently elevated compared to previously published age-dependent normal values. However, in CMR there was no correlation between baseline galectin-3 levels and the detection of myocardial fibrosis. In animal studies, the relative level of mRNA for galectin-3 in active mice was significantly higher compared to sedentary mice. This increase was most pronounced in skeletal muscle (98.0% higher, with p < 0.001) and not in the myocardium of the left ventricle (19.9% higher, with p = 0.043).

Conclusions: Plasma galectin-3 is substantially elevated in endurance athletes after running but does not correlate with cardiac function, other biomarkers, or myocardial fibrosis. In mice, we demonstrate that galectin-3 increase during endurance exercise originates primarily from skeletal muscle.

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Optimized atrio-ventriculo-arterial coupling in endurance elite athletes

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Athlete's heart is associated with left ventricular hypertrophy and "supranormal"