Ottava Giornata della Ricerca della Svizzera Italiana
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Modulo per la sottomissione abstract ricerca di LABORATORIO

Titolo (massimo **15 parole**)

Electrical abnormalities and sarcolemmal T-tubular disarray of cardiomyocytes induced by doxorubicin vs. trastuzumab chemotherapy.

Autori (cognome e iniziali, es: Grassi L.)

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Testo (massimo **250 parole**, preferibilmente in italiano (accettato anche in inglese), suddiviso in Introduzione, ***Metodi***, ***Risultati***, ***Conclusioni*** e ***Finanziamento***

Introduction: Cardiotoxicity is a side effect of anti-cancer combination therapy of monoclonal antibody Trastuzumab (TRZ) and Doxorubicin (DOXO). The modulation of electrical and structural properties of cardiomyocytes (CMs) underlying these models of cardiotoxicity are still being uncovered.

Method: Rats were intraperitoneally injected with six equal doses over a period of 2 weeks with DOXO alone, TRZ alone, or DOXO followed by TRZ (DOXO+TRZ) to mimic clinical protocols. In-vivo echocardiographic analysis was performed. Ventricular CMs were isolated using Langendorff system. Action potential duration (APD) was evaluated by patch-clamp recordings. The periodic component of T-tubular (TT) disarray in CM was quantified by Fast Fourier Transform analysis.

Results: Left ventricular end-systolic volume (LVESV) significantly increased in DOXO or TRZ-treated rats. DOXO+TRZ treatment led to a synergic, irreversible worsening of LVESV and a reduction in LV Ejection Fraction at day 37. At single cell level APDs were strongly prolonged in DOXO-CMs compared to controls. TRZ treatment reversibly induced APD prolongation only in LV CMs. Delayed after depolarizations were significantly increased as well as the frequency of spontaneous elementary Ca2+-sparks in DOXO-CMs. The periodic component of transverse TT was decreased in the DOXO group. These results are consistent with a structural disarray of CM sarcomeres. In contrast, the periodic component of transverse TT was not affected by TRZ alone.

Conclusions: TRZ and DOXO treatments induce electrophysiological changes but only the latter is associated with perturbation of sarcomeric structure in CMs. These changes may contribute to doxorubicin-induced arrhythmogenicity.

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Visto superiore (prego indicare Nome e Cognome del superiore)

Giuseppe Vassalli

Criteri per sottomissione Abstract:
NO Case report
NO Abstract senza nessun risultato
VISTO da un superiore

Invio Abstract