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Early menarche and cardiovascular risk in young women

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Background: Previous studies of age at menarche and cardiometabolic risk had reported conflicting findings.
The aim of this study was to evaluate the association of early menarche with cardiovascular risk factors and target organ damage in young women.
Methods: 117 young women (18–40 y.o.) were included (45% with obesity). Median self-reported and rounded down to the nearest whole year menarcheal age was 12.2±1,4 yr (range, 8–16 y.o.). 46 women (33%) were classified as having early menarche (11 years or less). Serum levels of lipids, glucose, HbA1C, waist circumference (WC) were measured, body mass index, left ventricular mass index (LVMI) were calculated, 24-hour ABPM was performed. Intima-media thickness of common carotid artery (CCA-IMT), carotid-femoral pulse wave velocity (PWV), left ventricular mass (LVM) were measured by ultrasonography, echocardiography (Philips iU22, GE Healthcare Vivid E9).
Results: Women with early menarche (50% of them had obesity, mean menarche age 10,7±0,5 yrs) had higher levels of 24-hour SBP (123±9 vs 120±11 mm Hg, p=0,01) and day SBP (126±10 vs 122±11 mm Hg, p=0,04), CCA-IMT (0,56±0,1 vs 0,52±0,1mm, p=0,04), left ventricular mass index (48,56±4,6 vs 37,1±10,5 g/m$^{2.7}$, p=0,02), higher rates of hypertension (p=0,02) and LV hypertrophy (p=0,03), then women without early menarche (42% of them had obesity, mean menarche age 12,8±1,0 yrs). There were no difference in age (30,9±5,8 vs 30,4±7,7 y.o.), body mass index (27,9±5,7 vs 26,9±5,5 kg/m^2), WC, lipid, glucose levels and PWV (5,76±1,75 vs 5,25±1,57 m/s, p=0,3) between groups (p>0,05).
Conclusions: Young women with early menarche exhibited elevated blood pressure, higher left ventricular mass index and intima-media thickness of common carotid artery, they had higher rates of hypertension and LV hypertrophy compared with later maturing women, independent of body composition. We suggest that women who experience an early menarche are at greater risk of cardiovascular disease and therefore early menarche may represent an important marker for early preventive interventions in young women.
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CARDIO-ONCOLOGY

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3D-derived speckle tracking for the assessment of myocardial deformation in breast cancer patients submitted to anthracycline chemotherapy

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Introduction: Serial echocardiographic assessment of left ventricular ejection fraction (LVEF) and 2D left ventricular global longitudinal strain (GLS) is the gold standard in screening for cancer therapeutics-related cardiac dysfunction (CTRCD). Myocardial deformation assessed with 3D speckle tracking is not currently used in this setting, despite of a potential for a greater reliability, because of the lack of published data.
Methods: This was a prospective study of female breast cancer patients submitted to chemotherapy with anthracyclines with or without adjuvant immunotherapy and/or radiotherapy who underwent serial monitoring by 2D and 3D transthoracic echocardiography. Standard echocardiographic measures and 3D-derived volumetric measures were assessed. Speckle tracking was used to estimate 2D and 3D-derived GLS, and 3D-derived global circumferential strain (GCS), global area strain (GAS) and global radial strain (GRS). CTRCD was defined as an absolute decrease in 2D LVEF >10% to a value <54% or a relative decrease in 2D GLS >15%. Variables were compared using the t-student paired test and the Wilcoxon sign-rank test, when appropriate. Receiver operating curve analysis was used to assess the discrimination of 3D-derived deformation parameters for predicting CTRCD. An area under the curve (AUC) >0.65 was considered a good discrimination.
Results: 91 patients (mean age 54.6±12.9 years, 33.0% immunotherapy, 16.5% radiotherapy, baseline LVEF 63.4% ± 9.3%, baseline 2D GLS -20.7±3.0) were included. During a mean follow-up of 16.5±9.6 months, 13 patients (14.3%) developed CTRCD. When comparing variables before and during treatment, there was a significant difference in 2D-derived LVEF (63.4 vs. 56.6 p<0.001), 3D-derived LVEF (62.1 vs. 56.9 p 0.028), 2D-derived GLS (-20.7 vs. -18.5 p<0.001), 3D-derived GLS (-13.8 vs. -12.9 p 0.035), 3D-derived GRS (37.3 vs. 35.2 p 0.024), but not in GCS (-14.5 vs. -13.2 p 0.110) and GAS (-21.8 vs. -23.1 p 0.514). The AUC for 3D GLS was 0.656, -9.54 being the value with better discrimination for CTRCD (likelihood ratio 1.50). The AUC for GRS was 0.696, 36.5 being the value with better discrimination for CTRCD (likelihood ratio 1.49).
Conclusion: In this population, there was worsening of 3D GLS and GRS, besides conventional values, such as LVEF and 2D GLS, during anthracycline-based cancer treatment. 3D-derived myocardial deformation parameters show promise in the setting of CTRCD, since both 3D GLS and GRS have good discrimination for CTRCD.

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Oncology patients with atrial fibrillation: same or different story?

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Introduction: Cancer and cancer therapies pose a risk factor for developing AF, and an unpredictable response with vitamin K antagonist (VKA) is frequent. The balance between thromboembolic and bleeding risks in these patients is challenging. We aimed to describe baseline characteristics of a cohort of women diagnosed of breast cancer and atrial fibrillation, as compared with similar women without cancer, in order to clarify if there are differences among their ischemic and bleeding risk.
Methods: Observational prospective study of 9 tertiary hospitals. 465 patients were enrolled: 312 with AF & breast cancer (cases) and 153 with AF without cancer (controls). Clinical and therapeutic parameters were recorded, including ischemic and bleeding risk scores (CHA2DS2-VASc, HAS-BLED, ATRIA, SAMETT2R2 and HEMORR2HAGES). Antithrombotic drug usage with VKAs, direct oral anticoagulants (DOACs), low molecular weight heparin (LMWH) or antiaggregation was monitored during follow-up.
Results: Mean age was 73,86±14,16 yo, with no significant differences between groups. Mean follow-up was 3,51±3 years. Cases and controls showed no differences in the risk scores: CHA2DS2VASc (4.48 vs 4.46), HASBLED (2.29 vs 2.32), ATRIA (7.24 vs 7.48) or SAMETT2R2 (2.21 vs 2.27), although patients with cancer had higher bleeding risk as assessed by HEMORR2HAGES [since it includes malignancy as predictor] (2.7±1.3 vs 1.83±1.3, p=0.001) and had more frequently hepatic failure (11.9% Vs 2% in controls, p=0.001).
97.4% of the patients had indication for anticoagulation (CHA2DSVASc2≥2). Despite this, 15.5% of cancer & AF patients with indication of anticoagulation did not receive it, in contrast with 11.3% of controls (p 0.005). Prevalence of labile INR was as high as 43.4% within the cancer group, although direct oral anticoagulants were less frequently used (16.4 vs 24.9%, p 0.004).

Baseline antithrombotic therapy

	Breast Cancer (%)	Controls (%)
AVK	61.1	62.7
DOACS	16.4	24.9
LMWH	7	1.1
Antiaggregation	10.5	9
No Treatment	5	2.3

Conclusions: Patients with AF and breast cancer with indication of oral anticoagulation are deprived of a correct anticoagulant therapy more frequently than women without cancer. Although patients with breast cancer have frequently labile INR, DOACs are less used in this group.

P1575
Cardiac toxicity of capecitabine: a prospective study

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Background: Capecitabine (CAPE) is an oral anticancer drug widely used in gastrointestinal (GI), liver, breast and head/neck cancers; the courses of treatment last 2 to 5 weeks. It has the same kind of cardiotoxicity (TOX) of fluorouracil: angina, ventricular arrhythmias (VA), left ventricular dysfunction (LVD), bradycardia; cases of sudden death have been reported. The TOX rate is supposed to be 5–8%, but cases of silent cardiac ischemia (CI) and of effort-related toxicity have been described. It is not clear if the risk of TOX is related to the common cardiovascular risk factors (CVRF) for ischemic heart disease (IHD).
Purpose: To assess the incidence and clinical manifestation of TOX in patients undergoing CAPE chemotherapy. To identify the patients at risk of TOX.
Methods: We prospectively evaluated all consecutive patients (pts) undergoing CAPE therapy in our institutions, including: A) basal ECG, cardiologic evaluation and echocardiogram (ECHO); B) ECG and physical stress test (PST) after >10 days of treatment; C) further exams in case of suspected TOX. Patients unable to perform a PST or with basal ECG abnormalities as bundle branch blocks and repolarization abnormalities were excluded. To confirm the CAPE as the cause

of the cardiac events, all the patients with signs/symptoms of TOX during CAPE treatment were re-evaluated with a PST after CAPE wash-out for >7 days; TOX was confirmed only in those with disappearance of symptoms, normalization of ECG and a negative PST.
Results: We studied 192 patients (115 males, 77 females) age 37–85 (median 62): 137 pts had CVRF (36 smoke, 73 hypertension, 15 diabetes, 62 dyslipidemia; 74 pts had >2; 12 had also IHD, and 73 were taking cardiac drugs), 55 had no CVRF. Totally, we observed 32 cases of TOX (16.6%): 13 silent CI, 4 angina, 10 arrhythmias, 2 LVD, 3 pts had >1 abnormality. Six patients had rest TOX and did not underwent PST, 9 pts had suspect (non diagnostic) signs/symptoms at rest which worsened during PST; 17 pts had effort-related TOX only. ECG abnormalities at rest appeared in 11 pts (4 ST segment elevation, 3 ST depression, 5 negative T waves). During effort, 12 pts had ST elevation, 17 ST depression (14/29 without symptoms); 9 had complex VA, one complete a-v block. Age, sex, presence of CVRF or IHD did not differ between the pts who had TOX and those who had not. On the contrary, the complaint of even vague symptoms (chest pain, fatigue, shortness of breath, sore throat, dizziness) after starting CAPE therapy was highly predictive of TOX ($p<0.0001$).
Conclusions: In this prospective study CAPE TOX was more frequent than in previous retrospective studies; 50% of cases had silent ischemia and/or LVD, and >50% had CI and/or complex VA or complete a-v block elicited by physical effort. The pts under CAPE treatment should be advised avoiding efforts; ECG changes and/or the appearance of new symptoms after some days of treatment may identify the pts with TOX.

P1576
The influence of long-term hormone therapy for advanced prostate cancer on the ventricular repolarization and global longitudinal strain

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Aim: To evaluate the cardiac effects of luteinizing hormone-releasing hormone (LHRH) antagonists in advanced prostate cancer by assessing the parameters of electrical instability on the surface ECG and the global longitudinal strain on echocardiography.
Method: We evaluated 34 men (pts) with advanced prostate cancer treated by orchiectomy and LHRH antagonist degarelix. We noted clinical history and excluded pts with atrial fibrillation, NYHA III and IV class heart failure (HF), acute myocardial infarction (MI) within the last 6 months, chronic renal disease stages IV-V. We performed ECG, Holter ECG, echocardiography and evaluated QT interval dispersion (QTd), Tpeak-Tend interval (Tpe), J-T peak interval (JT) in V5 lead, Lown's grading ventricular premature beats (VPB) on Holter ECG, left ventricular ejection fraction (LVEF) by echocardiography, global longitudinal strain (GLS) by speckle tracking technique before the beginning of the treatment (V1), after 3 (V2) and 6 months (V3). Statistical analysis was performed using Epi Info 8 program: paired t-test for comparing the differences and correlation test.
Results: Pts were 69.8±10 years old. 26 (76.47%) pts had arterial hypertension, 18 (52.9%) pts stable angina, 8 (23.5%) pts old myocardial infarction, 7 (20.8%) pts diabetes mellitus, 7 (20.8%) pts chronic renal disease grade I-IIIb. They were stable throughout the study. 23 (67.64%) pts had a simultaneous increase of the QTd (+ Δ QTd) and JT (+Δ JT) between V1 and V3. Mean +ΔQTd was 83±10 ms, mean +ΔJT was 78±30 ms, both statistical significant ($p<0.05$). Tpe changes were not significant. 20 (58.82%) pts had a decrease of the GLS (- ΔGLS) between V1 and V3. Mean - ΔGLS was 1.5%.There was a significant correlation between + Δ QTd, +Δ JT and - GLS (r= -0.3). Mean LVEF was 60±5%, and did not vary between V1 and V3. We did not note an increase in the number or severity of VPB between V1, V2 and V3.
Conclusion: In pts with advanced prostate cancer receiving LHRH antagonist for 6 months there was a significant increase in electrical instability parameters estimated by the prolonging of the QTd and JT interval on ECG and a significant decrease in global longitudinal strain evaluated by speckle tracking technique. During this period there was no change in the number or severity of VPB.

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Cancer therapeutic related vaso- and cardio-toxicity in patients receiving chemotherapy for breast cancer

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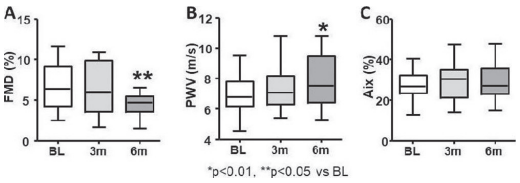
Background: Anthracyclines are the preferred agents for breast cancer chemotherapy, but their use is limited by their cardiotoxicity. Anthracyclines' effects on vascular function have been less well studied. We explored the effects of anthracycline chemotherapy on endothelial function and arterial stiffness in patients receiving chemotherapy for breast cancer.
Methods: 36 female patients (55.0±11.3 years old) with breast cancer scheduled for anthracycline chemotherapy were enrolled. At baseline and at 3 and 6 months after chemotherapy initiation patients underwent assessment of the brachial flow mediated dilatation (FMD), carotid-femoral pulse wave velocity (PWV) and arterial waves reflection by the augmentation index (Aix). Left ventricular ejection fraction (LVEF) was assessed by transthoracic echocardiography.
Results: LVEF was significantly reduced at 6 months compared to baseline [baseline: 60.3±5.5%, 3m: 58.0±5.2%, 6m: 57.2±6.1%, p=0.003]. A reduction in brachial FMD was observed at 6 months after chemotherapy [baseline: 7.12±3.08%, 3m: 6.80±3.24%, 6m: 4.73±1.83%, p=0.005] (A). Similarly, there was a significant increase in PWV at 6 months [baseline: 6.68±1.31m/sec, 3m: 7.28±1.98m/sec, 6m: 7.72±2.40m/sec, p=0.05] (B), whereas there was no significant change in Aix at either 3 or 6 months after treatment initiation (C).



Vasotoxic effects of anthracyclines

Conclusions: We report that anthracycline-induced cardiotoxicity is paralleled by vasotoxic effects, i.e., an increased in arterial stiffness and endothelial dysfunction. The reversibility of these effects on vascular function needs to be further explored in future studies.

P1578
Global longitudinal strain in the SAFE-HEaRT study (Cardiac SAFEty of HER2 targeted therapy in patients with HER2 positive breast cancer and reduced left ventricular function)

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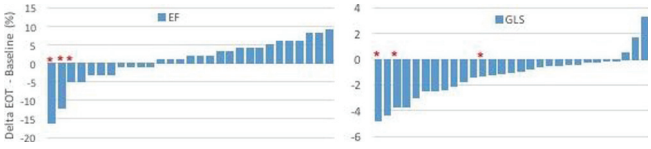
Background: Although HER2-targeted therapies (H2TT) have significantly improved prognosis of patients with HER2+ breast cancer (BC), cardiac toxicity limits their clinical use. Consequently, there is paucity of data on the effects of H2TT on LV global longitudinal strain (GLS) in patients with reduced cardiac function. SAFE-HEaRt is the first investigator-initiated study that prospectively tests the hypothesis that H2TT may be safely administered in BC patients with reduced LVEF in the setting of ongoing cardiac treatment and monitoring.
Purpose: We aimed to evaluate changes in GLS as a marker of progressive LV dysfunction during BC H2TT therapy and their association with adverse cardiac events (CE).
Methods: Patients were prospectively enrolled if they had HER2+ BC (stage I-IV), were candidates for H2TT (trastuzumab, pertuzumab or T-DM1) and had LVEF >40% and <50% without heart failure (HF) symptoms. All patients received carvedilol and ACEi/ARBs as tolerated. Cardiac visits and echocardiograms occurred at baseline, during treatment and at the end of H2TT. Maximum H2TT duration was 1 year. CE was defined as development of HF symptoms or asymptomatic LVEF decline by ≥10% from baseline and/or to LV EF ≤35%. LVEF was measured by the biplane method of disks and GLS was derived from 2-, 3- and 4-chamber views (TOMTEC). Wilcoxon-Mann-Whitney test was used to compare baseline and absolute changes in GLS and LVEF at different time intervals.
Results: Thirty-one patients were enrolled and 29 patients with evaluable baseline, 6-weeks and end of treatment (EOT) strain data were included in this analysis. All were women, mean age 54±13 years. Overall, GLS showed a small but statistically significant decline from baseline to EOT (-18.9±1.4% to -17.6±2.5%, $p<0.01$) while LVEF remained similar (45±3% to 46±6%, p=0.052). Baseline GLS was not different in patients with history of hypertension (N=17) compared to non-hypertensive patients (p=0.425). Three patients (10%) who met CE criteria (2 symptomatic HF and 1 LVEF decline to 35%) had lower baseline GLS compared to those without CE (-16.8±1 vs -19.1±1.2, p=0.01) while baseline LVEF was not statistically different (42±2% vs 45±3%, p=0.08). The Figure shows absolute changes (baseline to EOT) in LVEF and GLS on a per-patient basis with patients with CE marked with the stars.



Changes in EF & GLS from Baseline to EOT

Conclusions: In this prospective study of patients with BC and baseline reduced LV function, H2TT therapy proved to be safe with cardiac treatment and close monitoring. GLS at baseline was lower in those who subsequently developed CE.