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## EUROECHO Proves Value of Echocardiography



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One study presented at the meeting, which was held in Budapest, Hungary, 7 to 10 December, reports on an initiative using echocardiography to document early warning signs of adverse effects from trastuzumab (Herceptin®)<sup>1</sup>, while the other uses echocardiography to evaluate the protective role of ACE inhibitors and statins on the hearts of cancer patients<sup>2</sup>.

“These studies open the way for the early identification of myocardial damage at the subclinical level, thereby allowing clinicians to identify patients who might benefit from either changes in cancer therapy or the delivery of protective treatments,” says EAE president Dr Luigi Badano, from the University of Padua, Italy.

Already echocardiography is widely used to evaluating cardio toxicity, but the most commonly used parameter of left ventricular ejection fractions (LVEF), only identifies myocardial damage that has already occurred and fails to identify the early subtle alterations in left ventricular function that predict future functional decline.

Newer cancer therapies have improved the survival of patients with cancer and, in some cases, turned cancer into a chronic disease. The result is that patients are now surviving long enough for the adverse cardiovascular effects of some cancer therapies to become apparent. The anthracyclines and related compounds are the most frequently implicated agents, but other treatments such as 5-Fluorouracil, its prodrug capecitabine, and trastuzumab, a tumour-specific antibody, have also been associated with cardio toxicity. Currently it is estimated that 17% of patients have to stop cancer therapy due to adverse effects on their hearts.

The cardio toxic effects of cancer treatments encompass a heterogeneous group of disorders, says Dr Helder Does, from Santa Cruz Hospital/São Francisco Xavier Hospital, Lisbon, Portugal. “They range from relatively benign arrhythmias, and hypertension, to potentially lethal conditions such as thromboembolism, myocardial infarction and cardiomyopathy with symptomatic heart failure.”

Cardiotoxicity can be acute, appearing in the first 10 days of treatment, late, or experienced 15 to 20 years later, as sometimes found with the survivors of childhood cancers. While the damage is well documented, the mechanisms are incompletely understood. “They appear to be multifactorial, with the production of oxygen free radicals considered the main cause of morphological alterations,” explains Liliana Radulescu, from Municipal Hospital, Cluj-Napoca, Romania.

In October 2011 the European Association of Echocardiography (EAE) announced that it is working with the American Society of Echocardiography (ASE) and American Society of Clinical Oncology (ASCO) to issue joint recommendations on the usefulness of echocardiographic evaluations in cancer patients, expected to be published in 2012. “The document should lay down guidance for the frequency of assessment with different chemotherapy agents, and also identify when patients should stop treatment or be prescribed protective treatments,” says Badano.

### Study reveals early signs of myocardial damage

In the first study Helder Does and colleagues, set out to identify early warning signs of adverse cardiac effects in women treated with trastuzumab for breast cancer. In the study 51 consecutive women, enrolled for treatment between May and September 2010, were assessed at baseline with echocardiography and then again at three months.

The investigators found that within the first three months no patients presented with overt signs of heart failure or significant left ventricular systolic function deterioration, although almost one-fifth developed impaired ventricular relaxation. Impaired ventricular relaxation occurs when pressure reduction in the left ventricle does not happen as fast as normal leading to abnormalities in the heart’s ability to fill properly.

“Patients with impaired ventricular relaxation are known to be at higher risk for progression to advanced stages of cardiac dysfunction (both systolic and diastolic), making it important for these patients to be subject to more frequent evaluations both during and after therapy,” says Does.

Further studies are now needed, he says, to assess whether impaired ventricular relaxation occurs in larger populations of patients prescribed trastuzumab. “We need studies identifying the women who go on to develop overt cardiac dysfunction to see whether we can more accurately determine predictors of these adverse events at an earlier stage of treatment,” says Does.

### ACE inhibitors and statins deliver cardioprotection

In the second study Liliana Radulescu and colleagues used echo-Doppler echocardiography to investigate whether the ACE inhibitor lisinopril and the statin rosuvastatin might confer a cardio protective effect on patients treated with anthracyclines for a range of malignancies.

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"While the exact mechanism of anthracycline related cardio toxicity is not fully understood, animal studies have pointed to oxidative stress and inflammation. Both ACE inhibitors and statins are known to play an important role in reducing oxidative stress and inflammation at the level of the heart muscle cells," says Dr Andreea Parv.

In the prospective study left ventricular ejection fractions and LV diastolic function were compared for the study group of 26 patients treated with the anthracycline epirubicin who were also given the cardio protective treatments Lisinopril 10 mg and Rosuvastatin 10 mg, and a control group of 31 gender and age-matched patients who received epirubicin but had no accompanying cardioprotective treatments.

Results show that in comparison with patients receiving cardio protection the patients who receive no protection showed further deterioration of LV diastolic function, calculated as the ratio of early diastolic filling velocity(E) to filling velocity after atria contraction E/A ( $p < 0.02$ ).

"This is the first human prospective study documenting the cardioprotective effect of lisinopril and rosuvastatin in anthracycline induced cardio toxicity," says Radulescu. Further studies, she adds, are now needed in larger numbers of patients, exploring a range of different types of malignancies.

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