Monitor Patients on Ca Drugs for Cardiotoxicity

BY ROBERT FINN

SAN FRANCISCO — Spotting cardiotoxicity can be a challenge when clinicians follow cancer patients who experience other serious side effects of their treatment as well as the effects of their disease, cardiologist Anju Nohria acknowledged at the annual Oncology Congress presented by Reed Medical Education.

Nonetheless, the cardiac effects of new targeted therapies are often worrisome, and the toxicity of some older agents—notably the anthracyclines—has long been a concern. Dr. Nohria of the cardiovascular division of Brigham and Women's Hospital, Boston, offered the following rules of thumb for monitoring patients on these drugs in the absence of broad consensus panel guidelines on how to follow adult patients. Her suggestions are based on guidelines for following cardiotoxicity in children, she said.

Monitoring should start with a thorough history and physical examination at baseline and continue at every follow-up visit after the start of therapy, according to Dr. Nohria.

"A lot of oncologists and a lot of other practitioners rely on rales and edema as a way of looking for heart failure," she said. "Unfortunately, if you have a slow development of chronic systolic dysfunction, you rarely see rales and edema in more than 20%-25% of patients."

It turns out that the most sensitive physical exam finding for heart failure is an elevation in jugular venous pressure, and testing for this requires no specialized equipment. "If you sit your patient bolt upright in a chair, you should not be able to see [the] jugular venous pulsation above the level of the clavicle," she advised. "If you can see it above the level of the clavicle, that means the patient is intravascularly volume overloaded, and … needs diuresis."

Other symptoms of heart failure include dyspnea, orthopnea, early satiety, and exercise intolerance. Unfortunately, most of those symptoms can also be caused by chemotherapy. Orthopnea is the exception, she said, and it can be assessed simply by asking whether the patient experiences shortness of breath while lying in bed, and whether staying propped up with pillows relieves that shortness of breath.

Electrocardiography is neither sensitive nor specific in detecting cardiac complications of cancer chemotherapy, Dr. Nohria said. Myocardial biopsy, on the other hand, is highly sensitive and specific—especially for anthracycline toxicity, in which common biopsy findings include swelling of the mitochondria and sarcoplasmic reticulum along with myocyte disarray. "Unfortunately, we cannot do this on a regular basis because it's far too invasive and far too expensive," she said.

Therefore, the next step in monitoring patients who take cardiotoxic agents is imaging, either with an echocardiogram or with a multiple-gated acquisition (MUGA) scan. "I prefer echocardiograms over MUGAs," Dr. Nohria said. "The radiation you get with a MUGA is several-fold higher than what you see with an echo. So in terms of thinking of the long-term consequences of screening, you're better off getting an echo for these patients." Use the same modality during subsequent follow-ups, so that the results can easily be compared.

For patients taking anthracyclines, the initial postbaseline monitoring depends on whether the patient has prior cardiac risk factors or underlying heart disease, has received chest irradiation, or is also taking paclitaxel (Taxol). Patients who meet any of those criteria should be monitored once their anthracycline dose exceeds 200 mg/m^2. They should have a history, a physical exam, and an additional echo or MUGA before every subsequent course of therapy.

For patients without those risk factors, Dr. Nohria said that it's safe to delay monitoring until the anthracycline dose exceeds 300 mg/m^2.

At 3-6 months after the completion of therapy, and again at 1 year, patients on anthracycline should get an echo or MUGA. If the test is normal, "they don't need an echo more than once every 2-3 years," Dr. Nohria said. "If they're abnormal, I want to see them in the clinic with special attention to cardiac history

and physical exam every 6 months, at least until they're stable, and then perform an echo or a MUGA every year."

Like the cardiac monitoring that's done with patients on anthracyclines, the cardiac monitoring of patients taking trastuzumab (Herceptin) should include a thorough history and physical, and an assessment of cardiac ejection fraction (EF) at baseline and every 3 months while they're on therapy. "If you get a decline in their EF or symptomatic heart failure, then treat and monitor annually after trastuzumab therapy," Dr. Nohria said.

As for biomarker monitoring, Dr. Nohria said that the evidence is better for troponin I than for brain natriuretic peptide (BNP). An early rise in troponin I can be used as a marker to identify patients who should be monitored more closely and who should receive cardiac therapy. But although several studies have found that BNP does increase after the first dose of chemotherapy, the increase does not appear to correlate well with the development of cardiac toxicity, she said.

Dr. Nohria said she had no conflict of interest related to her talk. Reed Medical Education and this news organization are owned by Reed Elsevier Inc. ■

Cardiovascular Toxicity of Selected Chemotherapy Agents

Heart Failure	Hypertension	Acute Coronary Syndromes	QTc Prolongation
Anthracyclines	Bevacizumab	Fluorouracil	Arsenic trioxide
Trastuzumab	Sorafenib	Bevacizumab	Depsipeptide
Lapatinib	Sunitinib	Sorafenib	Sunitinib
Alemtuzumab	VDAs*	VDAs	Dasatinib
			VDAs

*Vascular disrupting agents

Source: Dr. Nohria

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