Is Chest CT Performed Too Often?

The introduction of computed tomography (CT) of the chest has undoubtedly provided clinicians with a new and valuable diagnostic tool. Compared with plain chest radiography, CT allows greater discrimination between solid mass and fatty, cystic, and vascular structures, and has been shown to be useful in the evaluation of many pulmonary disorders, including pulmonary nodules, interstitial lung disease, and bronchiectasis, to name a few. In particular, chest CT often provides new insight into the evaluation of mediastinal structures due to the superimposition of structures in this region on plain films. Consequently, chest CT is currently in widespread use, being ordered by a wide variety of physicians, including those in various specialties and primary care, as well as residents in training.

Despite the improved imaging that CT scans provide, the specific indications for this study remain vague. Furthermore, the overall utility of this study in enhancing patient-care decisions or improving patient outcome is unclear. In our own experience, data obtained from chest CT scans often provide no new clinical information, and when new information is obtained, it often has little or no impact on patient care. It is our concern, therefore, that the justification for frequent utilization of chest CT scans does not exist.

As with any diagnostic test, if it were low in cost and essentially risk-free, even modest benefits would justify its widespread use. However, chest CT is neither inexpensive nor risk-free. Although charges vary, combined technical and professional fees are approximately $500 (based upon local norms). There are also costs and risks associated with chest CT due to the unnecessary evaluation of false-positive studies and the delay in diagnosis associated with false-negative tests. Unfortunately, the accuracy of chest CT for a wide variety of conditions has yet to be adequately defined.

Perhaps even more significant are the radiation risks. The exact patient radiation dose depends upon several factors, including patient size, the specific machine employed, and the technique used. In general, conventional chest CT results in a radiation dose of approximately 2 rads. To place this value in better perspective, this radiation dose is approximately 100 times that of a standard chest film. While radiation exposure resulting from high-resolution CT can vary considerably depending upon technique, radiation doses can range as high as 12 to 14 rad, or the equivalent of more than 500 chest films! Concern has been focused recently in the literature on the risk of exposure resulting from a single chest film, and most physicians have been confronted by their patients on this issue as well.

A few facts concerning radiation risk are noteworthy. The risk associated with exposure to radiation is cumulative (ie, the risk of each exposure is a lifetime one and is additive with each additional exposure). Consequently, younger patients are at significantly higher risk due to the greater number of years over which they can develop cancer. Risk is also increased by contact with industrial or environmental toxins, such as cigarette smoking. Although cancer mortality risk estimates vary, according to the recent "Biological Effects of Ionizing Radiation" by Beir V, from the National Research Council, an excess of 770 cancer deaths per 100,000 males and 810 per 100,000 females can be expected following a single whole-body exposure of approximately 10 rad.

What can be done? The decision-making process with regard to chest CT should be carefully scrutinized. Ordering physicians should ask themselves whether the findings obtained with chest CT will have a significant impact on patient management and/or outcome and whether such information justifies the cost and risk to the patient—as they would for any diagnostic test. Furthermore, the known potential benefits and risks should be explained to each patient. We suspect that many, if not most, patients are not even aware that radiation exposure is involved with CT scanning. Perhaps patients should be provided with a written record of all radiation exposure during their lifetime to document their exposure history, as suggested previously. Physicians could then review exposure history before ordering tests requiring significant radiation exposure.

Clinical studies evaluating the true yield (ie, obtaining information that will have a beneficial impact on patient outcomes) and accuracy of chest CT are clearly needed. Perhaps then more specific guidelines could be established to assist physicians in the decision-making process. Finally, a few recent studies (each with small sample size) have suggested that chest CT can be performed with lower radiation doses and achieve diagnostic accuracy comparable to that of conventional CT. Such studies should be strongly supported and performed expeditiously.
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Asthma, Lymphocytes, and Dendritic Cells

Perhaps the most important change in our thinking about asthma in recent years has been the realization that airway inflammation is a universal finding, even in the asymptomatic patient. Most investigators now believe that the eosinophil, once thought to play a protective role in the airway, is a key player in this inflammatory response, mediating epithelial injury through release of a variety of cytotoxic substances, including major basic protein, eosinophil cationic protein, eosinophil-derived neurotoxin, and eosinophil peroxidase. The clinical correlate of this eosinophil-dominated inflammation is the late asthmatic response and persistent disease.

What processes initiate this destructive response? The IgE-mediated release from mast cells of histamine, tryptase, and prostaglandin D2 contributes to the initiation of the immediate bronchoconstrictor response, but the role of the mast cell in initiating the inflammatory cell influx characteristic of the late asthmatic response is unclear. In understanding the sequence of events culminating in eosinophil influx and epithelial injury, a key observation has been the realization that cytokines, such as interleukin (IL)-3, IL-4, and IL-5, and granulocyte-macrophage colony stimulating factor (GM-CSF) orchestrate the production, localization and survival of eosinophils at sites of inflammation. This has turned attention to the lymphocyte as a source of these cytokines. Elegant studies such as those by Robinson et al provide convincing evidence for clonal proliferation in the asthmatic lung of a subset of lymphocytes analogous to murine Tced cells, which, through release of these cytokines, result in the “eosinophilic bronchitis” that characterizes the asthmatic airway.

Antigen-specific lymphocyte proliferation requires the presence of accessory cells. What cell is serving this role in asthma? Alveolar macrophages are relatively inefficient antigen-presenting cells, and may serve to limit the IgE-mediated inflammatory response. Studies of cutaneous hypersensitivity suggest an initiating role for dendritic cells, and these efficient accessory cells appear to be present in the lung interstitium.

The study by Bellini et al, which appears elsewhere in this issue (see page 997), examines the role of dendritic cells in initiating the clonal expansion of Tced cells in asthma. The authors describe increased numbers of cells expressing OKT6, a marker for dendritic cells, in bronchial biopsy specimens from atopic asthmatics, compared with atopic nonasthmatics. Epithelial cells and dendritic cells derived from bronchial biopsy specimens were cultured, and cells from asthmatics, but not atopic asthmatics, released GM-CSF into the culture medium and stimulated proliferation of peripheral blood CD4+ memory T lymphocytes in the presence of specific allergens. These cultured cells released IL-4 and IL-5, but not IL-2 or interferon gamma, suggesting expansion of Tced-like lymphocytes. Autologous peripheral blood monocytes also induced proliferation of Tced lymphocytes, but their antigen-presenting capability did not differ between atopics and asthmatics, suggesting that the enhanced antigen-presenting capability of cells derived from asthmatic airways was due to increased numbers of dendritic cells.

There are weaknesses to this study. For example, the authors do not provide convincing evidence that the biopsy samples were rendered completely free of cells such as fibroblasts, which can produce GM-CSF. Nevertheless, this study supports the intriguing possibility that local expansion of Tced lymphocytes in asthmatic airways is driven by dendritic cells in the presence of locally released GM-CSF.

Further work elucidating the steps leading to Tced lymphocyte proliferation in asthma will provide opportunities for refining and targeting treatment strategies. For example, it should be possible to develop specific inhibitors of accessory cell function, thus preventing clonal expansion of lymphocytes in the airway. This may prove more effective than suppressing