A hallmark of noninvasive testing has been the identification of patients with coronary artery disease. Now, with multislice computed tomography (MSCT), information about coronary anatomy can be obtained without the need for catheterization. A major concern with the application of MSCT coronary angiography is the radiation exposure to the patient. Both MSCT and selective coronary angiography share the risks of procedure-related complications, such as allergic contrast reactions, and stochastic risks (i.e., cancer induction) of low-level radiation. There is a substantially higher radiation dose for MSCT angiography (effective dose [$ED$] 14 mSv) than for CCA (ED 6 mSv). These exposures yield lifetimes risks of 0.07% and 0.02%, respectively, of inducing a fatal cancer in the general (i.e., age- and gender-averaged) population. However, CCA poses additional serious risks associated with cardiac catheterization, yielding a non-radiogenic risk of mortality—excluding contrast reactions—of 0.11%. Combining the radiogenic and non-radiogenic risks (0.02% and 0.11%, respectively) yields a 0.13% overall risk of mortality from CCA—nearly two-fold higher than that for MSCT angiography (0.07%). If one were to use the lower, more age-appropriate risk factors for the older patient population in question, the radiogenic risks of both CCA and MSCT would be reduced by about one-half, further widening the overall safety ratio of MSCT relative to CCA. When weighing the relative risks of alternative medical procedures, therefore, it is imperative that one consider the overall risk of the respective procedures. (J Am Coll Cardiol 2006;47:1846–9) © 2006 by the American College of Cardiology Foundation

“Risk is the potential harm that may arise from some present process or from some future event. It is often mapped to the probability of some event which is seen as undesirable. Usually the probability of that event and some assessment of its expected harm must be combined into a believable scenario (an outcome) which combines the set of risk, regret and reward probabilities into an expected value for that outcome.”

—Wikipedia (1)

There are specific elements to an assessment of the value and risk of a procedure. The overall risk is a weighted summation of the risk contribution of each component of the procedure. In the case of contrast X-ray procedures, risk assessment is particularly complex because certain negative outcomes are apparent immediately (such as an extravasation at the contrast injection site, myocardial infarction or stroke during the procedure, decline in renal function, or allergic contrast reaction) whereas others are manifest only years later (such as the statistical risk of cancer induction).

When comparing the risk of selective coronary angiography to that of multidetector computed tomography (CT) coronary angiography, there are risks common to both procedures, such as an allergic contrast reaction and radiation as well as risks unique to each. Typically, 100 to 130 ml of nonionic contrast media containing 300 to 350 mg of iodine per milliliter are injected for CT angiography or a combination of selective coronary intrarterial injections and possibly a ventriculogram for cardiac catheterization studies. Nonionic contrast media causes severe allergic reactions1 in 0.2% to 0.7% of patients (2–5). Additionally, CT coronary angiography poses a risk of extravasation2, which occurs in 0.3% to 0.6% of patients when a power injector is used in a peripheral vascular line. In addition to the 0.37% incidence of contrast reactions, cardiac catheterization has a major complication rate of 1.7%, including mortality in 0.11%, myocardial infarction in 0.05%, neurologic complications in 0.07%, and hemodynamic complications in 0.26% of cases (6,7). Compared with these readily apparent adverse events with the use of either CT or catheterization, the potential low-dose radiation risk is extremely difficult to evaluate.

Risk must be considered in the context of the procedure. Cardiac catheterization has evolved from a diagnostic examination to a procedure often performed with intention to

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1Reactions are divided into mild, moderate, and severe. Mild reactions usually are self-limiting, often do not require treatment, or may be managed with the use of antihistamines and antihistamines. Significant urticaria may require steroids. Moderate-to-severe bronchospasm, laryngospasm, or hypotension requires treatment with oxygen and epinephrine. Anaphylactoid reactions, seizures, or cardiovascular collapse requires a resuscitation team for evaluation and treatment (2).

2Average of 18 ml. The incidence of extravasation is similar with injection rates of 1 to 2 ml/s and 3 to 4 ml/s.
treat. In 2002, an estimated 1,463,000 inpatient cardiac catheterization procedures were performed (8), leading to approximately 1,204,000 angioplasty procedures. Less-invasive procedures have become a gatekeeper, helping to select patients for catheterization in anticipation of treatment. In patients with chronic stable angina, for example, where the diagnosis of coronary disease is established, exercise EKGs were performed in 689,851 patients, whereas stress echocardiography was performed in 303,047 and stress myocardial perfusion imaging in 1,158,389 (9). The value of the noninvasive procedures is improved with the addition of information about coronary artery calcification (10) and is likely to be further enhanced with the addition of information about coronary anatomy.

Contrast-enhanced, gated, multislice computed tomography (MSCT) coronary angiography offers an opportunity to visualize the coronary arteries in patients with chest pain. However, the patient radiation exposure associated with MSCT is higher than that of conventional diagnostic coronary angiography (CCA). The report by Coles et al. (11) in this issue of the Journal, which compares the radiation exposure from MSCT to that of diagnostic selective coronary angiography in the same patients, provides additional objective data about this important and timely issue.

To put the risk of radiation in perspective, in 2002 malignant neoplasms caused the death of 557,271 people (of a total of 2,443,387 deaths) (12) in the U.S. It is unclear how many of these malignant neoplasms were related to radiation exposure. High doses of radiation are clearly linked to immediate and delayed effects (13), whereas the effects of long-term exposure to very low levels of radiation, as used in diagnostic procedures, remain highly controversial. For example, no additional risk of cancer was found in populations exposed to higher levels of background radiation (14,15) or among individuals (such as airline pilots) receiving relatively high occupational exposures (16,17).

Despite such data, various advisory bodies used the conservative assumption that no level of radiation is without excess risk, that is, the zero threshold hypothesis. To estimate the practically immeasurable risk from low-level radiation, various mathematical models are required to extrapolate dose-risk data from highly exposed populations. Currently, a linear relationship between dose and risk is used in the risk model for low-level exposures. The National Council on Radiation Protection and Measurements (NCRP) thus recommends a risk factor of $5 \times 10^{-2} \text{ Sv}^{-1}$ for lifetime cancer mortality for the general population (18). Conceptually, this means that if a randomly selected population of 100 people each received an effective dose (ED; see the Appendix for approaches to calculating the radiation burden) of 1 Sv (100 rem), which is equivalent to a uniform whole-body absorbed dose of 1 Gy (100 rad) of sparsely ionizing radiation (such as diagnostic X-rays), five additional fatal cancers would ensue over the balance of the lifetimes of the irradiated individuals. The BEIR V Committee (19) endorsed a somewhat-higher risk factor of $7.9 \times 10^{-2} \text{ Sv}^{-1}$. Importantly, as lifetime risk factors for the general population, these represent age- and gender-averaged values. However, in the patient population of Coles et al. (11), the population was skewed toward older individuals, with a mean age of approximately 62 years. For such an older population, the risk factor for lifetime cancer mortality is less than one-half of that for the general population and less than one-third of that for a younger population (i.e., younger than 55 years of age) (20). The use of general-population (i.e., age-averaged) risk factors will therefore overestimate the actual radiogenic risk to older patients, that is, patients typically being evaluated for coronary artery disease.

Although modern fluoroscopy systems automatically adjust the amount of radiation delivered for body size, presumably resulting in a uniformly low ED among patients, automatic adjustment of tube current (milliamperem, mA) and tube current-time (milliamper-second, mAs) are not yet incorporated into CT scanning protocols. However, MSCT scanning techniques are being developed to reduce patient radiation dose (21). For example, because the X-ray beam attenuation is less in the shorter posterioroanterior direction than in the longer lateral direction, fewer incident photons will be required to achieve the same degree of projection-image mottle (“noise”) when the tube is anterior and posterior to the patient. The radiation dose may therefore be reduced by decreasing the X-ray tube current when in these positions relative to the patient.

Alternatively, the X-ray tube may be prospectively triggered to generate X-rays only during predetermined portions (e.g., ventricular diastole) of the R-R interval of the cardiac cycle, when cardiac motion artifacts are less likely. For prospectively triggered calcium-scoring CT, for example, the ED is only 1 mSv, 25% to 40% of that for retrospectively triggered calcium-scoring examinations (2.6 to 4.1 mSv), and approximately equivalent to the low ED (~1 mSv) of electron-beam CT calcium scoring and angiography (22).

When weighing the relative risk of any medical procedure, it is imperative that one consider the overall risk of alternative procedures. In the current report, Coles et al.
(11) rigorously analyzed the radiation dose and attendant risk associated with MSCT angiography versus selective diagnostic coronary angiography in the same patients and, consistent with previous reports, found a substantially higher radiation dose for MSCT angiography (ED was approximately 14 mSv) than for CCA (ED was approximately 6 mSv). On the basis of the general-population risk factor of $5 \times 10^{-2} \text{ Sv}^{-1}$ for lifetime cancer mortality (23), the risk of inducing a fatal cancer is therefore 0.07% for MSCT angiography and 0.02% for CCA. However, as reported by Noto et al. (24) in more than 59,000 patients undergoing CCA, the nonradiogenic risk of mortality is 0.11% and of a major complications (excluding contrast reactions) is 1.3%. Most, if not all, of these serious noncontrast adverse events are a consequence of cardiac catheterization and therefore would be avoided with the use of MSCT angiography. Accordingly, combining the radiogenic and nonradiogenic risks (0.02% and 0.11%, respectively) yields an overall risk of mortality of 0.13% for CCA—nearly twofold greater than for angiography (0.07%). Moreover, if one were to use the lower, more age-appropriate risk factors for the patient population in question, as discussed previously, the radiogenic risks of both CCA and MSCT would be reduced by about one-half (to lifetime risks of cancer mortality of about 0.065% and 0.035%, respectively), widening the overall safety ratio of MSCT angiography relative to CCA. For an equivalent clinical diagnostic efficacy of MSCT angiography and CCA (25–33), MSCT angiography emerges as the safer of these two alternatives, despite its higher radiation dose.

If the entire 18,800,000 people comprising the 50- to 55-year-old population of the U.S. (34) were screened for coronary artery disease using MSCT, the anticipated increase in the number of fatal cancers would be 14,900. If this screening were repeated every five years until the population reached the age of 70, the aggregate increased risk would be increased by approximately threefold, to 42,900. Because the average age of patients with their first infarction is 65.8 for men and 70.4 for women (8) and because 94% of patients had >75% stenosis in at least one vessel (35), these sequential procedures should identify patients with significant stenoses before their initial event. If this procedure prevented even 10% of the estimated 355,000 sudden deaths (8) each year, the trade-off would be well worthwhile.

APPENDIX

For the technical aspects of radiation exposure, please see the online version of this article.