



Gender Differences in Radiation Dose From Nuclear Cardiology Studies Across the World

Findings From the INCAPS Registry

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ABSTRACT

OBJECTIVES The aim of this study was to investigate gender-based differences in nuclear cardiology practice globally, with a particular focus on laboratory volume, radiation dose, protocols, and best practices.

BACKGROUND It is unclear whether gender-based differences exist in radiation exposure for nuclear cardiology procedures.

METHODS In a large, multicenter, observational, cross-sectional study encompassing 7,911 patients in 65 countries, radiation effective dose was estimated for each examination. Patient-level best practices relating to radiation exposure were compared between genders. Analysis of covariance was used to determine any difference in radiation exposure according to gender, region, and the interaction between gender and region. Linear, logistic, and hierarchical regression models were developed to evaluate gender-based differences in radiation exposure and laboratory adherence to best practices. The study also included the United Nations Gender Inequality Index and Human Development Index as covariates in multivariable models.

RESULTS The proportion of myocardial perfusion imaging studies performed in women varied among countries; however, there was no significant correlation with the Gender Inequality Index. Globally, mean effective dose for nuclear cardiology procedures was only slightly lower in women (9.6 ± 4.5 mSv) than in men (10.3 ± 4.5 mSv; $p < 0.001$), with a difference of only 0.3 mSv in a multivariable model adjusting for patients' age and weight. Stress-only imaging was performed more frequently in women (12.5% vs. 8.4%; $p < 0.001$); however, camera-based dose reduction strategies were used less frequently in women (58.6% vs. 65.5%; $p < 0.001$).

CONCLUSIONS Despite significant worldwide variation in best practice use and radiation doses from nuclear cardiology procedures, only small differences were observed between genders worldwide. Regional variations noted in myocardial perfusion imaging use and radiation dose offer potential opportunities to address gender-related differences in delivery of nuclear cardiology care. (J Am Coll Cardiol Img 2016;9:376–84) © 2016 by the American College of Cardiology Foundation.

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There are fundamental differences in the pathophysiology, risk factors, and clinical presentation of coronary artery disease (CAD) in women compared with men (1). Indeed, women are more likely to have angina from coronary microvascular dysfunction, whereas men are more likely to have angina from epicardial CAD (2). Women are more likely to be susceptible to psychosocial risk factors than men (3). Further, medical tests used to detect CAD may have limitations associated with sex. For example, the sensitivity and specificity of an exercise test are lower in women than in men (4-6), although the addition of myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) can improve the diagnostic performance of exercise testing regardless of a patient's sex (4-6). With SPECT MPI, breast attenuation artifact is often increased in women compared with men, whereas spatial resolution is decreased (7). Because positron emission tomography (PET) uses attenuation correction routinely and provides higher spatial resolution and lower radiation dose compared with SPECT, it may be preferable to use PET in women who need MPI (8). PET MPI, however, is more expensive and much less available compared with SPECT. Regardless of whether SPECT or PET is used, the benefits of MPI in the diagnosis and risk assessment (9) of CAD are unequivocal in both women and men (7,10-12).

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Controversy exists, however, regarding the long-term health consequences after exposure to ionizing radiation for MPI and medical imaging (13), particularly in women (14,15). An Institute of Medicine report identified ionizing radiation from computed tomography (CT) as a contributing factor for breast cancer in women (15). Similarly, a higher hazard of radiation-related solid cancer has been estimated in women compared with men (16). Such concerns of greater radiosensitivity in women have the potential to affect patterns of use differentially, in particular radiation dose reduction protocols for diagnostic testing, in women compared with men (17).

Given the impact of biological factors, as well as gender differences between women and men that may affect MPI, several questions arise: What is the current proportion of women compared with men undergoing MPI? Are there differences in the way these studies are performed from a global perspective? Does the broader context of social, environmental, and community factors play a role in best practices? Are women more likely to have PET rather than SPECT? To date, gender-based patterns of radiation exposure across nuclear cardiology laboratories have been unknown. Accordingly, in this report, we compared the rates of radiation exposure in women to men through a multinational observational cross-sectional study, INCAPS (International Atomic Energy Agency Nuclear Cardiology Protocols Study), which examined worldwide nuclear cardiology practices (17). The purpose of this report is to determine whether differences in radiation dose from MPI exist between women and men and to examine the use of radiation dose reduction practices in women compared with men in diverse societies across the spectrum of gender equality and human development status.

METHODS

Details of INCAPS have been previously reported (17). In brief, INCAPS was an observational cross-sectional study of protocols used for each of the 7,911 MPI studies performed in 308 participating laboratories in 65 countries (Figure 1) during a single week in March or April 2013. A waiver for Institutional Review Board approval was provided by the Institutional Review Board at Columbia University Medical Center (New York, New York), where all data analysis was conducted.

DATA COLLECTED. Anonymized patient-specific data including gender, age, body weight, scanner, and MPI protocol used were collected from diverse regions of the world including Africa (n = 348), Asia (n = 1,469), Europe (n = 2,381), Latin America (n = 1,139), North America (n = 2,135), and Oceania (n = 439). Protocol

ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

GII = Gender Inequality Index

HDI = Human Development Index

MPI = myocardial perfusion imaging

PET = positron emission tomography

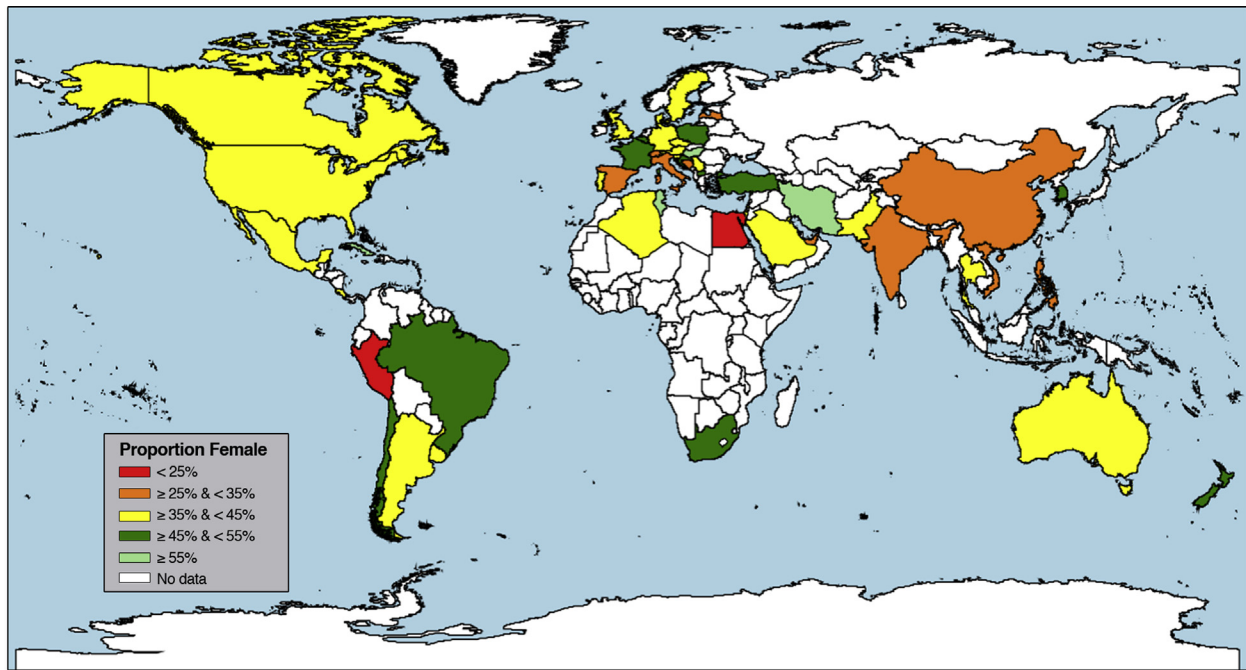
SPECT = single-photon emission computed tomography

^{99m}Tc = technetium-99m

²⁰¹Tl = thallium-201

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FIGURE 1 Proportion of Women Receiving MPI by Participating Country in INCAPS

Countries that contributed <10 patients in INCAPS are not depicted in this figure. MPI = myocardial perfusion imaging.

details obtained included modality (SPECT or PET), 1-day versus 2-day study, imaging position, use of attenuation correction (CT or radionuclide), and the type and dose of radiopharmaceutical used. The whole body effective dose for each subject in this study was estimated on the basis of the type and dose of radiopharmaceutical used, as described previously (17). In addition to patient-level and institutional-level analyses, regional analyses were performed at the level of the geographic regions. Geographic regions were defined as Africa, Asia, Europe, Latin America (including Mexico, Central, and South America), North America (Canada and the United States), and Oceania (Australia and New Zealand).

OUTCOME VARIABLES. The primary outcome variable for this study was the estimated whole body effective dose. The secondary outcome variables were as follows: the use of various types of *protocols* (e.g., 1-day vs. multiday, PET vs. SPECT, as well as different radiopharmaceuticals); the use of *laboratory best practices* to optimize MPI radiation dose; and *laboratory procedure volumes*. Of 8 laboratory best practices pre-specified by an International Atomic Energy Agency expert committee (17), in this study we focused on 4 practices that could be interpreted on a per-patient basis: 1) avoidance of dual-isotope stress

testing in patients ≤ 70 years of age; 2) avoidance of thallium-201 (^{201}Tl) stress testing in patients ≤ 70 years of age; 3) use of stress-only imaging when appropriate; and 4) use of camera-based dose reduction techniques. The use of camera-based dose reduction techniques was defined as at least 1 of the following: 1) attenuation correction (CT or line source); 2) multiple position imaging (e.g., supine and prone); 3) high-technology software (e.g., incorporating resolution recovery or noise reduction, or both); and 4) high-technology hardware (e.g., PET or solid-state SPECT cameras).

SOCIETAL AND ECONOMIC FACTORS. We considered two global societal metrics that have the potential to affect gender differences in the practice of nuclear cardiology: the Gender Inequality Index (GII) (18) and the Human Development Index (HDI) (19), both published annually by the United Nations Development Program. We used the 2013 versions of GII and HDI. Gender inequality in a country was quantified using the GII, a composite index reflecting gender inequalities in reproductive health, empowerment, and economic status, which incorporates diverse data from the United Nations, its agencies such as UNESCO, and related organizations such as the Inter-Parliamentary Union. Designed to measure the

human development costs of gender inequality, a high GII reflects more disparities between the sexes and more loss to human development. A country's human development was quantified using the HDI, a summary measure, that takes into account average achievement in key areas of human development, including life expectancy, education, and standard of living. A high HDI reflects a high level of human development. Details as to how GII (18) and HDI (19) are calculated can be found in the statistical annex to the United Nations Development Program's report "Human Development Report 2015: Work for Human Development" (20).

STATISTICAL ANALYSES. Descriptive statistics were calculated for the outcome variables and were compared between men and women. Continuous variables were described in terms of mean ± SD and median (interquartile range), and were compared using Student *t* tests and Kruskal-Wallis tests, respectively. Categorical variables were compared using chi-square tests. Correlation was evaluated using the Pearson correlation coefficient. A *p* value <0.05 was considered statistically significant.

Comparisons were performed at the world, regional, and country levels, where appropriate. In addition, regression models (linear, logistic, and hierarchical) were developed to determine whether gender was associated with outcome variables. Analysis of covariance was used to ascertain whether a difference in dose according to gender or region existed and to evaluate the interaction between gender and region, with weight included in the model as a continuous variable, to adjust for potential between-group differences in patients' weight. Furthermore, the relationship between GII and HDI, and best practices, were explored using logistic regression models. All analyses were performed using Stata/SE version 13.1 (StataCorp, College Station, Texas) software.

RESULTS

BASELINE CHARACTERISTICS. Of the 7,911 patients in this study, 41% were women. Depending on the region of the world, women represented 38% to 45% of all patients undergoing MPI. The proportion of women in each of the countries that participated in INCAPS is illustrated in Figure 1. There was no significant correlation between GII and the countrywide proportion of MPIs performed on women (*r* = -0.15; *p* = 0.32). Women were on average older (mean age 65.1 ± 12.0 years vs. 63.5 ± 12.0 years; *p* < 0.0001) and lighter (74.3 ± 18.0 kg vs. 84.4 ± 18.1 kg; *p* < 0.0001) when compared with men. Women received a lower effective dose (mean effective dose 9.6 ± 4.5 mSv vs.

10.3 ± 4.5 mSv; *p* < 0.0001) for nuclear cardiology studies when compared with men (Table 1). After using a hierarchical linear regression model to adjust for weight and age, female gender still remained a significant predictor of lower effective dose (Table 2, Simple Model), with a 0.3 mSv lower effective dose in women (beta: -0.305; 95% confidence interval: -0.430 to 0.179; *p* < 0.001).

GENDER-SPECIFIC EFFECTIVE DOSE PATTERNS ACROSS THE GLOBE. The effective dose of MPI in women relative to men varied by country (Figure 2) and by geographic region (Figure 3). The mean effective dose for women versus men in Africa was 9.0 ± 5.5 mSv versus 10.2 ± 5.5 mSv; in Asia it was 10.9 ± 4.8 mSv versus 11.8 ± 4.8 mSv; in Europe it was 7.3 ± 3.5 mSv versus 8.3 ± 3.4 mSv; in Latin America it was 11.4 ± 4.3 mSv versus 12.0 ± 4.0 mSv; in North America it was 10.3 ± 4.5 mSv versus 10.6 ± 4.6 mSv; and in Oceania it was 9.1 ± 3.8 mSv versus 9.4 ± 3.6 mSv. Analysis of covariance adjusting for weight demonstrated a statistically significant difference in the mean effective dose according to gender that varied by geographic region (main effect for region: degrees of freedom 5 and 7,815, *F* statistic 206.1, *p* < 0.001; main effect for gender: degrees of freedom 1 and 7,815, *F* statistic 7.89, *p* = 0.005; and an interaction between gender and region: degrees of freedom

TABLE 1 Representation of Women and Men by Worldwide Region in This Study

| | Women (n = 3,254) | Men (n = 4,657) | <i>p</i> Value |
|-------------------------------------|----------------------|--------------------|----------------|
| Age, yrs | 65.1 ± 12.0* | 63.5 ± 12.0 | <0.001 |
| Weight, kg† | 74.3 ± 18.0 | 84.4 ± 18.1 | <0.001 |
| Regions | | | 0.005 |
| Africa | 39% | 61% | |
| Asia | 38% | 62% | |
| Europe | 40% | 60% | |
| Latin America | 43% | 57% | |
| North America | 43% | 57% | |
| Oceania | 45% | 55% | |
| Total effective dose for MPI ≤9 mSv | 42.1% | 36.4% | <0.001 |
| Effective dose, mean | 9.6 ± 4.5 | 10.3 ± 4.5 | <0.001 |
| Effective dose, median | 9.8 | 10.4 | 0.001 |
| Effective dose, IQR | 5.8-12.5 | 7.5-12.8 | — |
| Radiopharmaceuticals used | | | |
| Technetium-99m | 90.8% | 90.2% | 0.34 |
| Thallium-201 | 4.6% | 6.6% | <0.001 |
| Rubidium-82 | 5.4% | 4.8% | 0.20 |
| Nitrogen-13 ammonia | 0.7% | 0.5% | 0.22 |
| Fluorine-18 fluorodeoxyglucose | 0.3% | 0.7% | 0.02 |

Values are mean ± SD, %, median, or IQR. **p* < 0.0001. †Weights were not available for 83 patients (47 male, 36 female), all in a single laboratory. IQR = interquartile range; MPI = myocardial perfusion imaging.

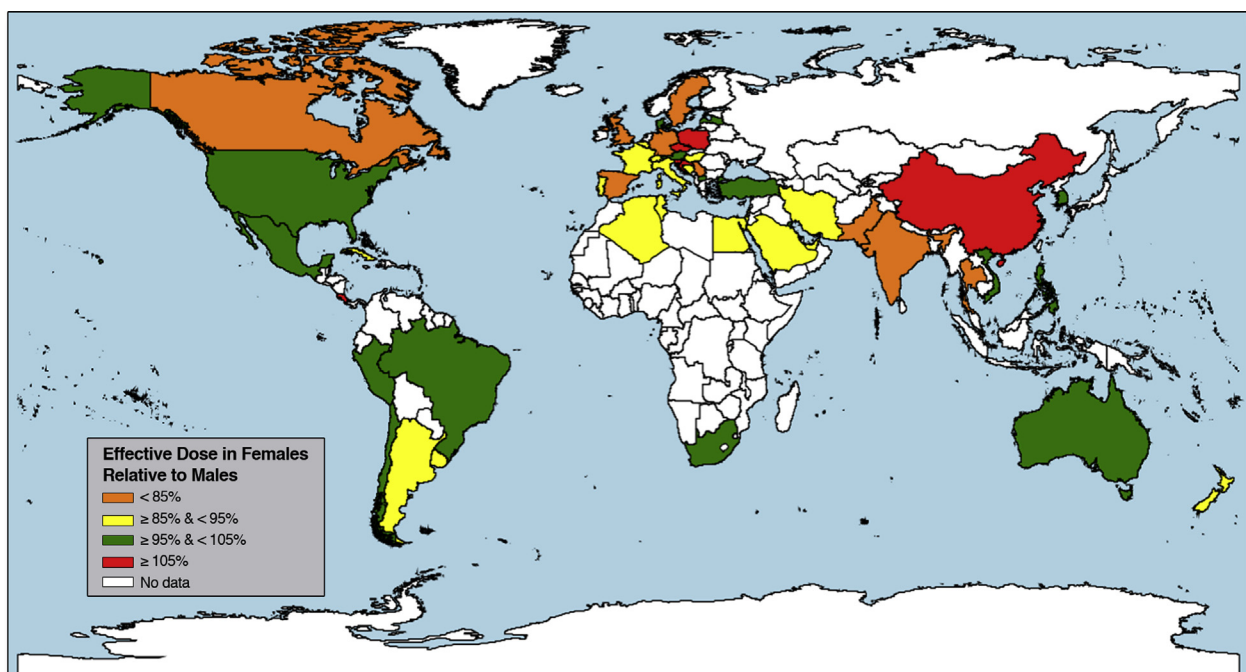
TABLE 2 Impact of Gender on Patient Effective Dose From MPI: Hierarchical Regression Models*

| Factors | Simple Model (Adjusts for Weight and Age) | | Comprehensive Model (Adds Protocols and Best Practices) | |
|--|--|---------|--|---------|
| | Predicted Difference in ED (mSv) (95% CI) | p Value | Predicted Difference in ED (mSv) (95% CI) | p Value |
| Female | -0.303 (-0.429 to -0.178) | <0.001 | -0.055 (-0.150 to 0.040) | 0.26 |
| Weight, per kg | 0.035 (0.032 to 0.039) | <0.001 | 0.035 (0.033 to 0.038) | <0.001 |
| Age, per yr | 0.004 (-0.001 to 0.009) | 0.013 | 0.005 (0.001 to 0.009) | 0.02 |
| 1-day SPECT | — | — | 5.721 (5.420 to 6.022) | <0.001 |
| Multiday SPECT | — | — | 6.744 (6.418 to 7.071) | <0.001 |
| Avoid dual isotope | — | — | -3.490 (-4.042 to -2.938) | <0.001 |
| Avoid stress thallium | — | — | -3.825 (-4.215 to -3.436) | <0.001 |
| Stress-only protocol | — | — | -5.079 (-5.279 to -4.878) | <0.001 |
| Camera-based dose reduction technique(s) | — | — | -0.757 (-1.005 to -0.509) | <0.001 |
| Intercept | 7.710 (7.070 to 8.352) | <0.001 | 9.760 (8.863 to 10.658) | <0.001 |

*In Comprehensive Model, Stata omitted positron emission tomography and assigned a coefficient of 0, as it shows high collinearity with other variables. The between-gender difference in ED after adjusting for age and weight is a modest 0.3 mSv (Simple Model), which is statistically significant. This difference appears to be related to a difference in use of protocols and best practices because after correction for these (Comprehensive Model) the negligible difference of 0.05 mSv is not statistically significant.
CI = confidence interval; ED = effective dose; SPECT = single photon emission computed tomography.

5 and 7,815, F statistic 3.24, $p = 0.006$). Equality between the sexes was seen only in North America and Oceania; elsewhere, women received a slightly lower effective dose associated with MPI than did men, and this difference was most pronounced in Europe.

IMPACT OF MPI PROTOCOLS AND BEST PRACTICES ON EFFECTIVE DOSE AMONG MEN AND WOMEN. The frequency of different patient-specific MPI protocols and estimated effective dose stratified by gender is shown in [Table 3](#). Stress-only imaging was more frequent

FIGURE 2 Distribution of the Relative Mean Effective Radiation Dose for Women Compared With Men in Each of the Countries That Participated in INCAPS

Countries that contributed <10 patients in INCAPS are not depicted in this figure.

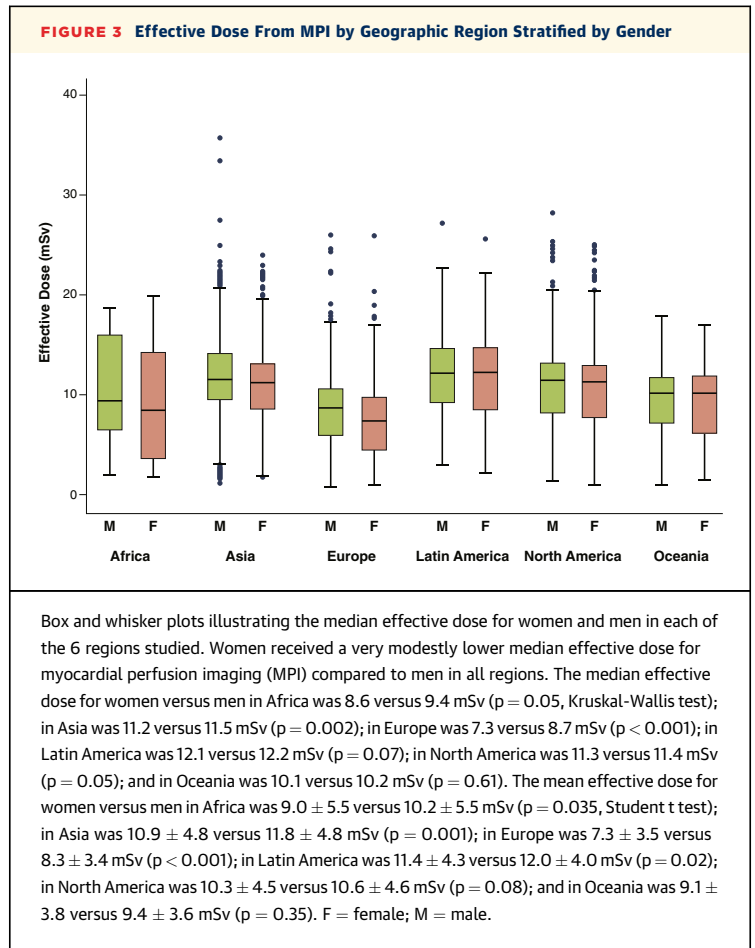
in women compared with men (12.5% vs. 8.4%; $p < 0.001$). Indeed, stress-only imaging occurred in 23.0% of women who underwent MPI in Europe, as compared with only 14.2% of men ($p < 0.001$). Dual-isotope imaging was less frequent in women compared with men (1.0% vs. 1.5%; $p < 0.001$). In women, the mean effective dose ranged from 3.4 mSv for PET to 21.6 mSv for dual-isotope procedures. For men, the mean effective dose ranged from 4.0 mSv for PET to 20.5 mSv for dual-isotope procedures. Multiposition imaging (supine and prone or supine and upright) was more commonly used on men compared with women (9.7% vs. 3.9%; $p < 0.001$). Even after excluding multiposition imaging, camera-based dose reduction methods remained more frequent in men (59.5% vs. 56.1%; $p = 0.003$).

When best practices and protocols were added to the hierarchical linear regression that characterizes the contribution of female gender to patient-specific effective dose (i.e., adding protocols and best practices in addition to the covariates in the Simple Model), no significant difference remained in MPI effective dose between women and men (Table 2, Comprehensive Model; difference in dose 0.05 mSv; $p = 0.26$).

GENDER INEQUALITY INDEX, HUMAN DEVELOPMENT INDEX, AND PATIENT-LEVEL DOSE REDUCTION BEST PRACTICES. We employed separate logistic regression models to evaluate the contribution of GII, HDI, and female gender to patient-level dose reduction best practices and protocols. After adjusting for GII, women were less likely than men to benefit from camera-based dose reduction technology, more likely to receive stress-only imaging, and less likely to receive thallium. After adjustment for GII, there was no statistically significant difference in the avoidance of dual-isotope imaging depending on gender. The impact of GII and HDI on the odds of a patient's receiving best practices was extremely small (Table 4).

DISCUSSION

In cardiology practice, men and women often have different clinical presentations, prevalence of disease, and risk profiles, which may lead to the underestimation of CAD in women. It is important for an investigation strategy to be sensitive to such differences. In terms of nuclear cardiology, the implications of these differences necessitate understanding the current use of best practices between men and women, to ensure that women benefit equally from MPI without undue added risk. In this large, multinational clinical study, we explored gender differences in patient effective dose and laboratory best practices for MPI across geographic regions. On the



basis of our analysis, we found that fewer women underwent MPI than did men in all world regions; however, there was no significant systematic association between the proportion of women undergoing MPI and societal gender inequality as quantified by

TABLE 3 Between-Gender Differences in Frequency and Effective Dose of Specific MPI Protocols and Best Practices

| | Frequency (%) | | | Effective Dose (mSv) | | |
|-----------------------------|-------------------|-----------------|---------|----------------------|----------------|---------|
| | Women (n = 3,254) | Men (n = 4,657) | p Value | Women | Men | p Value |
| Basic protocols | | | | | | |
| 1-day SPECT | 2,262 (69.5) | 3,225 (69.3) | 0.80 | 9.5 ± 4.4 | 10.3 ± 4.3 | <0.001 |
| Multiday SPECT | 786 (24.2) | 1,164 (25.0) | 0.39 | 11.4 ± 3.9 | 11.5 ± 3.9 | 0.52 |
| PET | 206 (6.3) | 268 (5.8) | 0.29 | 3.4 ± 1.8 | 4.0 ± 2.9 | 0.005 |
| Best practices | | | | | | |
| Avoid dual isotope* | 3,222 (99.0) | 4,588 (98.5) | 0.05 | 21.6 ± 1.8 | 20.5 ± 3.5 | 0.10 |
| Avoid stress thallium* | 3,197 (98.2) | 4,540 (97.5) | 0.02 | 15.4 ± 3.3 | 15.6 ± 3.4 | 0.73 |
| Stress-only | 408 (12.5) | 392 (8.4) | <0.001 | 3.8 ± 1.7 | 4.2 ± 2.0 | <0.001 |
| Camera-based dose reduction | 1,820 (55.9) | 2,948 (63.3) | <0.001 | 8.6 ± 4.4 | 9.4 ± 4.3 | <0.001 |

Values are n (%) or mean \pm SD. *Doses listed are those for dual-isotope and stress thallium imaging. PET = positron emission tomography; SPECT = single-photon emission computed tomography.

TABLE 4 Association of Female Gender, Gender Inequality Index, and Human Development Index on Best Practice and Protocol Use*

| | Odds Ratio (95% CI) | | Odds Ratio (95% CI) | | Odds Ratio (95% CI) | |
|--|---------------------|---------|---------------------|---------|---------------------|---------|
| | Unadjusted | p Value | Adjusted for GII | p Value | Adjusted for HDI | p Value |
| Basic protocols | | | | | | |
| 1-day SPECT | 1.01 (0.92 to 1.12) | 0.80 | 1.01 (0.91 to 1.11) | 0.92 | 1.00 (0.91 to 1.10) | 0.99 |
| Multiday SPECT | 0.96 (0.86 to 1.06) | 0.39 | 0.96 (0.87 to 1.07) | 0.48 | 0.98 (0.89 to 1.09) | 0.76 |
| PET | 1.11 (0.92 to 1.33) | 0.29 | 1.11 (0.92 to 1.34) | 0.28 | 1.07 (0.89 to 1.29) | 0.48 |
| Best practices | | | | | | |
| Avoid dual isotope | 1.51 (0.99 to 2.31) | 0.05 | 1.41 (0.92 to 2.16) | 0.11 | 1.33 (0.87 to 2.04) | 0.19 |
| Avoid stress thallium | 1.45 (1.05 to 1.99) | 0.02 | 1.42 (1.03 to 1.96) | 0.03 | 1.34 (0.97 to 1.85) | 0.08 |
| Stress-only imaging | 1.56 (1.35 to 1.81) | <0.001 | 1.54 (1.33 to 1.78) | <0.001 | 1.56 (1.35 to 1.81) | <0.001 |
| Camera-based dose reduction technology | 0.74 (0.67 to 0.81) | <0.001 | 0.72 (0.65 to 0.79) | <0.001 | 0.73 (0.66 to 0.80) | <0.001 |

*Logistic regression models demonstrate the relationship between female gender and use of best practices that are interpretable on the patient level. For example, the odds that camera-based dose reduction technology was used in a woman's study were 0.74 of the odds for a man's study. After adjustment for GII, the odds that camera-based dose reduction technology was used in a woman's study were 0.72 of the odds for a man's study, a finding suggesting that a society's gender inequality, at least as captured by the GII, plays little role in the use of dose reduction technology. Best practices considered are those with patient-level interpretations.
 GII = Gender Inequality Index; HDI = Human Development Index; other abbreviations as in Tables 2 and 3.

the GII. Nevertheless, in several countries women constituted fewer than 35% of patients undergoing MPI (Figure 1); identification of such underrepresentation is a potential actionable finding that can spur efforts to ensure appropriate referral of women for MPI. In addition, women underwent MPI on average at a slightly older age than did their male counterparts.

From a global perspective, the difference in mean radiation effective dose between women and men was very modest, and it was not significant after adjustment for age, weight, and best practices and protocols. It remains uncertain whether the observed modestly lower radiation to women is by intent (i.e., implementation of practices to lower radiation to women) or whether it is dictated by regional differences in resources, access to radiopharmaceuticals, or use of radionuclide imaging within different, possibly gender-related clinical contexts or for assessment of CAD versus viability and differences in patient population. Increased use of stress-only protocols (21) combined with lower use of thallium and dual-isotope imaging in women likely contributed to this overall lower effective radiation dose. Nevertheless, in a few countries women had higher radiation doses from MPI than did men (Figure 2); this should serve as an actionable finding for such countries and laboratories. We found no statistically significant difference in the use of PET in women compared with men across the world, likely at least in part because of limited access to PET scanners on the global market.

Personalizing MPI protocols on the basis of the specific clinical question, the patient's preference, and patient-specific factors is important for the optimal practice of nuclear cardiology (22,23). In terms of the association between sex and gender differences on the choice of MPI protocol, we found that women were

more likely than men to have stress-only imaging. Because stress-only MPI is preferred when the pre-test likelihood of CAD is low or intermediate and because women often have a lower pre-test probability of CAD and a less reliable exercise electrocardiogram than men, it is not surprising that women were more likely to have stress-only MPI for risk stratification.

Stress ²⁰¹Tl and dual-isotope protocols were avoided in both men and women by the majority of the laboratories studied. Further, women had significantly fewer ²⁰¹Tl and dual-isotope studies compared with men. The decreased use of ²⁰¹Tl in women could have been related to several factors. Breast attenuation artifact is often increased in women compared with men, whereas diagnostic sensitivity is reduced in persons with small hearts (24), a factor that is exacerbated by the poorer spatial resolution for a given camera using ²⁰¹Tl compared with technetium-99m (^{99m}Tc). Higher radiation exposure from ²⁰¹Tl compared with ^{99m}Tc could also have contributed to making ^{99m}Tc a more attractive imaging agent. Further, given the higher incidence of previous myocardial infarction in men undergoing MPI, men may have been more likely to have had ²⁰¹Tl MPI to assess for myocardial viability compared with women, who likely had MPI to diagnose CAD. In INCAPS, we could not evaluate whether men received more ²⁰¹Tl imaging because of a higher need for viability evaluation, or whether women received more ^{99m}Tc imaging out of concern for breast tissue attenuation and radiation exposure. Even so, the differences in radiation dose between men and women were very modest.

Interestingly, men were more likely to be assigned camera-based dose reduction strategies than were women. Even after excluding multiposition imaging, which was more frequent in men compared with

women, the use of camera-based dose reduction strategies of novel hardware, novel software, and attenuation correction was still more common in men. Because most of these novel camera-based technologies typically require more expensive equipment, it is possible that more men were scanned in high-end laboratories compared with women, although further data would be needed to confirm this possibility. Notably, even after accounting for gender inequality in society and for human development by country, women were still less likely than men to be assigned camera-based dose reduction technology, but they were more likely than men to benefit from stress-only imaging. Another factor affecting these differences could be the average 10-kg lower body weight in women, which could lead to fewer attenuation artifacts and consequently improved image quality.

Nuclear cardiology tests are increasingly being used globally for the evaluation of CAD. As such, we sought to explore the gender-specific differences in imaging practices related to human development status and gender inequality in society. A recent study (25) reported that CAD prevalence is positively correlated with HDI in developing countries, thus reflecting the growing epidemic of CAD in developing countries. In contrast, HDI was negatively correlated with CAD prevalence in developed countries, a finding reflecting the declining trends of CAD in these countries. A unique strength of INCAPS is the large number of studies evaluated from different regions of the world. To the best of our knowledge, INCAPS allows, for the first time, a study of GII and HDI and their impact on nuclear cardiology procedures in men and in women.

STUDY LIMITATIONS. Despite the large sample size and the global applicability of the results, INCAPS has certain limitations. Practice patterns in the laboratories that participated in INCAPS may not fully be generalizable to practice patterns at the level of the country. Gender differences in the choice of MPI protocol could reflect gender-specific attenuation artifacts (e.g., breast attenuation) or gender differences in pre-test probability of CAD. For example, stress-only MPI was more common in women, and women, particularly those younger than 60 years of age, have a lower pre-test probability of CAD than do men. Measurement of administered activity is not standardized among laboratories internationally, and most laboratories do not exclude residual activity remaining in the syringe and tubing, which can vary among patients. Nevertheless, there is no evidence suggesting or reason to believe that residual activity depends on gender. Effective dose, as defined by the International Commission on Radiological Protection (26), does not reflect patient-specific characteristics such as weight,

anatomy, and biokinetics (27). We did not investigate any possible social context or attributes that may have influenced the slightly lower exposure in women (e.g., perception of women as patients). Imaging using a reduced radiation dose must be balanced by high-quality and diagnostic images to minimize layered testing. The results of nuclear cardiology studies and image quality information were not collected; therefore, we are unable to evaluate whether imaging using a low radiation dose was associated with limitations in image quality or diagnostic accuracy. We hope to address these limitations in further research.

CONCLUSIONS

In the worldwide INCAPS, women underwent MPI with somewhat lower frequency than men, whereas women and men received similar radiation doses when undergoing MPI, with slightly lower doses in women in part reflecting lower body weight. Our findings suggest, reassuringly, that there does not seem to be a large gender bias in radiation exposure from MPI globally. There were some gender-based differences in radiation-related “best practice” use, with a higher proportion of women receiving stress-only imaging but a higher proportion of men undergoing MPI using camera-based dose reduction technology. Regional differences in practice noted, such as a relatively small proportion of MPI studies undertaken in women in some countries, and higher average radiation doses to women versus men in others, serve as potentially actionable areas.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL

SKILLS: Nuclear cardiology imaging using a low radiation dose is essential to maximize the utility of the test. This study explores gender differences in effective radiation dose from nuclear cardiology studies worldwide. An understanding of gender differences in best practices and radiation safety in nuclear cardiology globally is vital so that disparities can be addressed.

TRANSLATIONAL OUTLOOK: Additional studies are needed to define the effects of low radiation dose from nuclear cardiology procedures on image quality and diagnostic accuracy in women compared with men globally.

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KEY WORDS gender, nuclear cardiology, radiation exposure

APPENDIX For a complete list of members of the INCAPS Investigators Group, please see the online version of this article.