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

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Gender Differences in Radiation Dose from Nuclear Cardiology Studies Across the World: Findings from the International Atomic Energy Agency Nuclear Cardiology Protocols Study (INCAPS) Registry

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Abstract

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

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

METHODS—In a large multicenter observational cross-sectional study encompassing 7911 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 utilized 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. We also included the United Nations’ gender inequality and human development indices as covariates in multivariable models.

RESULTS—The proportion of MPI studies performed in women varied between countries, however there was no significant correlation with 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 men, p<0.001), with a difference of only 0.3 mSv in a multivariable model adjusting for patient 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 MPI use and radiation dose offer potential opportunities to address gender-related differences in delivery of nuclear cardiology care.

Keywords
Gender; Radiation Exposure; Nuclear Cardiology

There are fundamental differences in the pathophysiology, risk factors and clinical presentation of coronary artery disease (CAD) in women compared to men.(1) Indeed, women are more likely to have angina from coronary microvascular dysfunction, while 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 is 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 its diagnostic performance regardless of patient sex.(4–6) With SPECT MPI, breast attenuation artifact is often increased in women compared with men, while spatial resolution is decreased.(7) Since PET uses attenuation correction routinely, 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 to 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)

Controversy exists, however, regarding the long-term health consequences following 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 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 to men.(16) Such concerns of greater radiosensitivity in women have the potential to differentially impact utilization patterns, in particular radiation dose reduction protocols for diagnostic testing, in women compared to men.(17)

Given the impact of biological factors, as well as gender differences between women and men that may impact 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, knowledge with regards to gender-based patterns for radiation exposure across nuclear cardiology laboratories is unknown. Accordingly, in this report, we compared the rates of radiation exposure in women to men through a multinational observational cross-sectional study, the International Atomic Energy Agency Nuclear Cardiology Protocols Study (INCAPS), which examined worldwide nuclear cardiology practices.(17) The purpose of this report is to determine if differences in radiation dose from MPI exist between women and men and to examine the use of radiation dose reduction practices in women compared to men in diverse societies across the spectrum of gender equality and human development status.

METHODS

Details of the INCAPS study have been previously published.(17) In brief, INCAPS was an observational cross-sectional study of protocols used for each of the 7911 MPI studies performed in 308 participating laboratories in 65 countries (Figure 1) during a single week in March–April 2013. A waiver for institutional review board approval was provided by the institutional review board at Columbia University Medical Center, 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 details obtained included modality (SPECT or PET), 1-day vs. 2-day study, imaging position, use of attenuation correction (CT or radionuclide) as well as the type and dose of radiopharmaceutical used. The whole body effective dose for each subject in this study was estimated based on the type and dose of radiopharmaceutical used, as described previously.(17) In addition to patient 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 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: the use of various types of protocols (e.g. one- vs. multi-day, PET vs. SPECT, as well as different radiopharmaceuticals); the use of laboratory best practices to optimize MPI radiation dose; and laboratory procedure volumes. Of eight laboratory best practices prespecified by an International Atomic Energy Agency expert committee (17), in this study we focused on four of these which could be interpreted on a per-patient basis: 1) avoidance of dual isotope and 2) $^{201}$thallium ($^{201}$Tl) stress testing in non-elderly patients, 3) use of stress-only imaging as needed, and 4) use of camera-based dose reduction techniques. The latter was defined as at least one 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 and/or noise reduction), 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 impact 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 females and males 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 and HDI 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.”(18, 19)

STATISTICAL ANALYSES

Descriptive statistics were calculated for the outcome variables and compared between males and females. Continuous variables were described in terms of means (±standard deviation) and medians (interquartile range; IQR), and compared using t-tests and Kruskal-Wallis tests, respectively. Categorical variables were compared using chi-squared 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 if gender was associated with outcome variables. Analysis of covariance (ANCOVA) was used to determine if 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 patient weight. Furthermore, the relationship between GII and HDI, and best practices, were explored using logistic regression models. All analyses were performed using Stata/SE 13.1 (StataCorp, College Station, TX).

RESULTS

BASELINE CHARACTERISTICS

Of the 7,911 individuals in this study, 41% were women. Depending on 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 the INCAPS study is illustrated in Figure 1. There was no significant correlation between GII and the country-wide 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 to 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 to men (Table 1). 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 ED in women (beta: −0.305; 95% CI: −0.430–−0.179; p value <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 geographic region (Figure 3). The mean effective dose for women versus men in Africa was 9.0±5.5 mSv vs. 10.2±5.5 mSv; in Asia was 10.9±4.8 mSv vs. 11.8±4.8 mSv; in Europe was 7.3±3.5 mSv vs. 8.3±3.4 mSv; in Latin America was 11.4±4.3 mSv vs. 12.0±4.0 mSv; in North America was 10.3±4.5 mSv vs. 10.6±4.6 mSv; and in Oceania was 9.1±3.8 mSv vs. 9.4±3.6 mSv. ANCOVA 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 df (5,7815), F(206.1), p<0.001; main effect for gender df(1,7815), F(7.89), p=0.005; and an interaction between gender and region df(5,7815), F(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 men and this 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 in women compared to men (12.5% vs. 8.4%, p<0.001). Indeed, stress-only imaging occurred in 23.0% of women who had an MPI in Europe; as compared to only 14.2% of men (p<0.001). Dual isotope imaging was less frequent in women compared to 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. Multi-position imaging (supine/prone or supine/upright) was more commonly used on men compared to women (9.7% vs. 3.9%, p < 0.001). Even after excluding multi-position 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 (GII), HUMAN DEVELOPMENT INDEX (HDI) 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 coronary disease in women. It is important that an investigation strategy is sensitive to such differences. In terms of nuclear cardiology, the implications of these differences necessitates 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 on patient effective dose and laboratory best practices for MPI across geographic regions. Based on our analysis, we found that fewer women underwent MPI than 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 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 which can spur efforts to ensure appropriate referral of women for MPI. Also, women underwent MPI on average at a slightly older age than their male counterparts. From a global perspective, the difference in mean radiation effective dose between women and men was very modest, and 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, utilization of radionuclide
imaging within different, possibly gender-related clinical contexts or for assessment of coronary artery disease vs. viability and differences in patient population. Increased use of stress-only protocols (20) 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 utilization of PET in women compared with men across the world, which is likely due at least in part, to limited access to PET scanners on the global market.

Personalizing MPI protocols based on the specific clinical question, patient preference, and patient specific factors is important for the optimal practice of nuclear cardiology.(21,22) 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, and that this was most common in Europe. Since stress-only MPI is preferred when the pre-test likelihood of CAD is low or intermediate and women often have a lower pre-test probability of CAD and a less reliable exercise ECG test than men, it is not surprising that women were more likely to have stress-only MPI for risk stratification.

Stress $^{201}$TI and dual isotope protocols were avoided in both men and women by the majority of the laboratories studied. Further, women had significantly fewer $^{201}$TI and dual isotope studies compared to men. The decreased use of $^{201}$TI in women could have been related to several factors. Breast attenuation artifact is often increased in women compared with men, while diagnostic sensitivity is reduced in individuals with small hearts (23), a factor that is exacerbated by the poorer spatial resolution for a given camera using $^{201}$TI compared to $^{99m}$Tc. Higher radiation exposure from $^{201}$TI compared with $^{99m}$Tc, could also have contributed to making $^{99m}$Tc a more attractive imaging agent. Further, given the higher incidence of prior myocardial infarction in men undergoing MPI, men may have been more likely to have had $^{201}$TI 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 $^{201}$TI imaging due to a higher need for viability evaluation, or if women received more $^{99m}$Tc imaging due to concerns of breast tissue attenuation and radiation exposure. Notwithstanding, the differences in radiation dose between men and women were very modest.

Interestingly, men were more likely to enjoy camera-based dose reduction strategies than women. Even after excluding multi-position imaging, which was more frequent in men compared to women, using camera-based dose reduction strategies of novel hardware, novel software and attenuation correction, was more still common in men. Since 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. Notably, even after accounting for gender inequality in society, and human development by country, women were still less likely than men to enjoy camera-based dose-reduction technology, but are more likely than men to benefit from stress-only imaging. Another factor impacting 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 (24) reported that CAD prevalence is positively correlated with HDI in developing countries reflecting the growing epidemic of CAD in developing countries. In contrast, HDI was negatively correlated to CAD prevalence in developed countries, reflecting the declining trends of CAD in these countries. A unique strength of the INCAPS study is the large number of studies evaluated from different regions of the world. INCAPS allows, for the first time, a study of GII and HDD and their impact on nuclear cardiology procedures in men and in women.

STRENGTHS AND LIMITATIONS

Despite the large sample size and the global applicability of the results, the INCAPS study has certain limitations. Practice patterns in the laboratories that participated in the INCAPS study may not fully be generalizable to practice patterns at the level of the country. Gender differences in the choice of MPI protocol could be due to gender-specific attenuation artifacts, e.g., breast attenuation, or gender differences in pre-test probability of coronary artery disease; for example, stress only MPI was more common in women, and women, particularly under 60 years of age, have lower pre-test probability of coronary disease than do men. Measurement of administered activity is not standardized between laboratories internationally, and most laboratories do not exclude residual activity remaining in the syringe and tubing, which can vary between 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 (25), does not reflect patient-specific characteristics such as weight, anatomy, and biokinetics. (26) 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 a patient. Reduced radiation dose imaging 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 if low radiation dose imaging was associated with limitations in image quality or diagnostic accuracy. We hope to address these limitations in further research.

CONCLUSIONS

In the worldwide INCAPS study, women underwent MPI with somewhat lower frequency than men, while women and men received similar radiation doses when undergoing MPI, with slightly lower doses in women in part reflecting lower patient 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 utilizing 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 vs. men in others, serve as potentially actionable areas.

Acknowledgments

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ABBREVIATIONS LIST

- **CAD** coronary artery disease
- **MPI** myocardial perfusion imaging
- **SPECT** single photon emission computed tomography
- **PET** positron emission tomography
- **INCAPS** International Atomic Energy Agency Nuclear Cardiology Protocols Study
- **GII** gender inequality index
- **HDI** human development index
- **IQR** interquartile range
- **ANCOVA** analysis of covariance
- **201Tl** thallium
- **99mTc** technetium

References


PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS

Low radiation dose nuclear cardiology imaging 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 to men globally.
Figure 1. Proportion of women receiving MPI by participating country in the INCAPS study
Note: Countries that contributed < 10 patients in INCAPS are not depicted in this figure.
Figure 2. Distribution of the relative mean effective radiation dose for women compared to men in each of the countries that participated in INCAPS
Note: Countries that contributed < 10 patients in INCAPS are not depicted in this figure.
Figure 3. Effective dose from MPI by geographic region stratified by gender
This figure shows the median effective dose for women and men in each of the 6 regions studied. Women received a significantly lower effective dose for MPI compared to men in all regions except for North America.

F= Female; M = Male; * = p<0.05 for between-gender comparison of means; † = p=0.001; ‡ = p<0.001. p = 0.52 for Africa, p = 0.068 for Latin America, and p = 0.61 for Oceania. The mean effective dose for women versus men in Africa was 9.0±5.5 mSv vs. 10.2±5.5 mSv (p=0.035); in Asia was 10.9±4.8 mSv vs. 11.8±4.8 mSv (p=0.001); in Europe was 7.3±3.5 mSv vs. 8.3±3.4 mSv (p<0.001); in Latin America was 11.4±4.3 mSv vs. 12.0±4.0 mSv (p=0.02); in North America was 10.3±4.5 mSv vs. 10.6±4.6 mSv (p=0.08); and in Oceania was 9.1±3.8 mSv vs. 9.4±3.6 mSv (p=0.3496).
### Table 1

Representation of women and men by worldwide region in this study

<table>
<thead>
<tr>
<th></th>
<th>Women (n=3,254)</th>
<th>Men (n=4,657)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>65.1±12.0</td>
<td>63.5±12.0</td>
<td>&lt; 0.001</td>
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<tr>
<td><strong>Weight (kg)</strong></td>
<td>74.3±18.0</td>
<td>84.4±18.1</td>
<td>&lt; 0.001</td>
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<td><strong>Regions</strong></td>
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<td></td>
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<tr>
<td>Africa</td>
<td>39%</td>
<td>61%</td>
<td></td>
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<tr>
<td>Asia</td>
<td>38%</td>
<td>62%</td>
<td></td>
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<tr>
<td>Europe</td>
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<td>60%</td>
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</tr>
<tr>
<td>Latin America</td>
<td>43%</td>
<td>57%</td>
<td></td>
</tr>
<tr>
<td>North America</td>
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<td>57%</td>
<td></td>
</tr>
<tr>
<td>Oceania</td>
<td>45%</td>
<td>55%</td>
<td></td>
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<tr>
<td><strong>Total effective dose for MPI ≤9mSv</strong></td>
<td>42.1%</td>
<td>36.4%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Effective Dose (Mean ± SD)</strong></td>
<td>9.6±4.5</td>
<td>10.3±4.5</td>
<td>&lt; 0.001</td>
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<td><strong>Effective Dose (Median)</strong></td>
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<td><strong>Effective Dose (IQR)</strong></td>
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<td>7.5–12.8</td>
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<td><strong>Radiopharmaceuticals Used</strong></td>
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<tr>
<td>Tc-99m</td>
<td>90.8%</td>
<td>90.2%</td>
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<td>Tl-201</td>
<td>4.6%</td>
<td>6.6%</td>
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<td>Rb-82</td>
<td>5.4%</td>
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<td>N-13 ammonia</td>
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<td>0.5%</td>
<td>0.22</td>
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<td>F-18 fluorodeoxyglucose</td>
<td>0.3%</td>
<td>0.7%</td>
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### Table 2
Impact of gender on patient effective dose from MPI. Hierarchical regression models.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Simple Model (Adjusts for Weight and Age)</th>
<th>Comprehensive Model (Adds Protocols and Best Practices)</th>
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<tr>
<td></td>
<td>Predicted Difference in ED (mSv) (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Female</td>
<td>−0.303 (−0.429, −0.178)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (per kg)</td>
<td>0.035 (0.032, 0.039)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>0.004 (−0.001, 0.009)</td>
<td>0.013</td>
</tr>
<tr>
<td>One-day SPECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-day SPECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid dual isotope</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid stress thallium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress-only protocol</td>
<td>−5.079 (−5.279, −4.878)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Camera-based dose-reduction technique(s)</td>
<td>−0.757 (−1.005, −0.509)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intercept</td>
<td>7.710 (7.070, 8.352)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

ED denotes Effective Dose. In Comprehensive Model, Stata omitted PET 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, since after correction for these (Comprehensive Model) the negligible difference of 0.05 mSv is not statistically significant.
### Table 3

Between-gender differences in frequency and effective dose of specific MPI protocols and best practices

<table>
<thead>
<tr>
<th>Protocols</th>
<th>Women (n=3,254)</th>
<th>Men (n=4,657)</th>
<th>p-value</th>
<th>Effective Dose, mSv</th>
<th>Women</th>
<th>Men</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic Protocols</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-day SPECT</td>
<td>2,262 (69.5%)</td>
<td>3,225 (69.3%)</td>
<td>0.80</td>
<td>9.5±4.4</td>
<td>10.3±4.3</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Multi-day SPECT</td>
<td>786 (24.2%)</td>
<td>1,164 (25.0%)</td>
<td>0.39</td>
<td>11.4±3.9</td>
<td>11.5±3.9</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>PET</td>
<td>206 (6.3%)</td>
<td>268 (5.8%)</td>
<td>0.29</td>
<td>3.4±1.8</td>
<td>4.0±2.9</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td><strong>Best Practices</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid Dual Isotope *</td>
<td>3,222 (99.0%)</td>
<td>4,588 (98.5%)</td>
<td>0.05</td>
<td>21.6±1.8</td>
<td>20.5±3.5</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>Avoid Stress Thallium *</td>
<td>3,197 (98.2%)</td>
<td>4,540 (97.5%)</td>
<td>0.02</td>
<td>15.4±3.3</td>
<td>15.6±3.4</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Stress-Only</td>
<td>408 (12.5%)</td>
<td>392 (8.4%)</td>
<td>&lt;0.001</td>
<td>3.8±1.7</td>
<td>4.2±2.0</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Camera-Based Dose-Reduction</td>
<td>1,820 (55.9%)</td>
<td>2,948 (63.3%)</td>
<td>&lt;0.001</td>
<td>8.6±4.4</td>
<td>9.4±4.3</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

*Doses listed are those for dual isotope and stress thallium.*
Table 4

Association of gender, gender inequality index (GII), and human development index (HDI) on best practice and protocol use

<table>
<thead>
<tr>
<th>Basic Protocols</th>
<th>Odds Ratio (95% CI) Unadjusted</th>
<th>p-value</th>
<th>Odds Ratio (95% CI) Adjusted for GII</th>
<th>p-value</th>
<th>Odds Ratio (95% CI) Adjusted for HDI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-day SPECT</td>
<td>1.01 (0.92, 1.12)</td>
<td>0.80</td>
<td>1.01 (0.91, 1.11)</td>
<td>0.92</td>
<td>1.00 (0.91, 1.10)</td>
<td>0.99</td>
</tr>
<tr>
<td>Multi-day SPECT</td>
<td>0.96 (0.86, 1.06)</td>
<td>0.39</td>
<td>0.96 (0.87, 1.07)</td>
<td>0.48</td>
<td>0.98 (0.89, 1.09)</td>
<td>0.76</td>
</tr>
<tr>
<td>PET</td>
<td>1.11 (0.92, 1.33)</td>
<td>0.29</td>
<td>1.11 (0.92, 1.34)</td>
<td>0.28</td>
<td>1.07 (0.89, 1.29)</td>
<td>0.48</td>
</tr>
<tr>
<td>Best Practices</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid dual isotope</td>
<td>1.51 (0.99, 2.31)</td>
<td>0.05</td>
<td>1.41 (0.92, 2.16)</td>
<td>0.11</td>
<td>1.33 (0.87, 2.04)</td>
<td>0.19</td>
</tr>
<tr>
<td>Avoid stress thallium</td>
<td>1.45 (1.05, 1.99)</td>
<td>0.02</td>
<td>1.42 (1.03, 1.96)</td>
<td>0.03</td>
<td>1.34 (0.97, 1.85)</td>
<td>0.08</td>
</tr>
<tr>
<td>Stress-only imaging</td>
<td>1.56 (1.35, 1.81)</td>
<td>&lt;0.001</td>
<td>1.54 (1.33, 1.78)</td>
<td>&lt;0.001</td>
<td>1.56 (1.35, 1.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Camera-based dose reduction</td>
<td>0.74 (0.67, 0.81)</td>
<td>&lt;0.001</td>
<td>0.72 (0.65, 0.79)</td>
<td>&lt;0.001</td>
<td>0.73 (0.66, 0.80)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Logistic regression models demonstrate the relationship between 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 was 0.74 that for a man’s study. After adjustment for GII, the odds that camera-based dose-reduction technology was used in a woman’s study was 0.72 that for a man’s study, suggesting that a society’s gender inequality, at least insofar as captured by the GII, plays little role in the use of dose-reduction technology. Best practices considered are those with patient-level interpretations.