Opportunities for improvement on current nuclear cardiology practices and radiation exposure in Latin America: Findings from the 65-country IAEA Nuclear Cardiology Protocols cross-sectional Study (INCAPS)

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Background. **Comparison of Latin American (LA) nuclear cardiology (NC) practice with that in the rest of the world (RoW) will identify areas for improvement and lead to educational activities to reduce radiation exposure from NC.**

Methods and Results. **INCAPS collected data on all SPECT and PET procedures performed during a single week in March-April 2013 in 36 laboratories in 10 LA countries (n = 1139), and 272 laboratories in 55 countries in RoW (n = 6772). Eight "best practices" were identified a priori and a radiation-related Quality Index (QI) was devised indicating the number used. Mean radiation effective dose (ED) in LA was higher than in RoW (11.8 vs 9.1 mSv, $p < 0.001$). Within a populous country like Brazil, a wide variation in laboratory mean**

On behalf of Members of the INCAPS Investigators Group.
The members of INCAPS Investigators Group are given in Appendix.
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ED was found, ranging from 8.4 to 17.8 mSv. Only 11% of LA laboratories achieved median ED <9 mSv, compared to 32% in RoW (*p* < 0.001). QIs ranged from 2 in a laboratory in Mexico to 7 in a laboratory in Cuba. Three major opportunities to reduce ED for LA patients were identified: (1) more laboratories could implement stress-only imaging, (2) camera-based methods of ED reduction, including prone imaging, could be more frequently used, and (3) injected activity of ^{99m}Tc could be adjusted reflecting patient weight/habitus.

Conclusions. **On average, radiation dose from NC is higher in LA compared to RoW, with median laboratory ED <9 mSv achieved only one third as frequently as in RoW. Opportunities to reduce radiation exposure in LA have been identified and guideline-based recommendations made to optimize protocols and adhere to the ''as low as reasonably achievable'' (ALARA) principle. (J Nucl Cardiol 2017;24:851–9.)**

Key Words: Nuclear cardiology • SPECT • PET • Latin America • best practices • radiation dose

Abbreviations	
ALARA	As low as reasonably achievable
ED	Effective dose
IAEA	International Atomic Energy Agency
IHD	Ischemic heart disease
INCAPS	IAEA nuclear cardiology protocols study
IQR	Interquartile range
LA	Latin America
MPI	Myocardial perfusion imaging
NC	Nuclear cardiology
QI	Quality index
RoW	Rest of world

See related editorial, 860–861

INTRODUCTION

Ischemic heart disease (IHD) is the leading cause of death in adult men and women worldwide.[1] This is not different in Latin America.[2] Changes in lifestyle, nutrition habits, and obesity are contributing to an increased prevalence of type 2 diabetes mellitus and consequently IHD in the region.[3,4] While mortality rates have progressively decreased over the past 4 decades in the developed world, the same phenomenon is not observed in low to middle income countries, many of them in Latin America.[5] Trying to reduce mortality rates is particularly challenging considering social structure and lack of appropriate financial resources in most of the developing world. Two Latin American countries, Brazil and Cuba, are among the 10 nations in the world with the highest mortality rates due to IHD and the top 2 nations in Latin America considering age 35-74 years old.[6]

Myocardial perfusion imaging (MPI) is an important non-invasive diagnostic test to stratify risk and guide management, widely used in many Latin American countries.[7] In fact, a published registry including patients from Brazil[8] demonstrates a 3 times higher abnormality rate for MPI compared to data from one leading center in the United States.[9] This suggests a ''sicker'', higher probability of IHD population evaluated by nuclear cardiology in Latin America. This finding is consistent with the high mortality rate due to IHD observed in this region.[6]

Although MPI has several demonstrated advantages to help face the challenge of IHD mortality, significant concerns have been raised regarding its associated radiation exposure to patients[10-12] and, in particular, the radiation burden from MPI, that in some settings is the medical test with the highest *per capita* radiation dose.[13,14] A variety of protocols can be used to perform MPI[15,16] and several approaches and ''best practices'' have been developed to lower radiation exposures to patients, in accordance with international standards including International Atomic Energy Agency (IAEA) recommendations and the well-known 'As Low As Reasonably Achievable' (ALARA) principle.

We have recently shown, in the International Atomic Energy Agency Nuclear Cardiology Protocols Study (INCAPS) study, the current patterns of nuclear cardiology practices, worldwide. These findings have provided us an overview of potential opportunities for reduction of radiation exposure to patients in many parts of the world.[17] A better understanding of current practice of nuclear cardiology in Latin America offers the opportunity to identify areas to improve quality of care and to reduce disparities. The present study compares Latin American to rest-of-the-world (RoW) nuclear cardiology practices, and evaluates their impact on radiation exposure to patients, with the objective of decreasing radiation burden from MPI to patients and optimizing protocols in this region.

METHODS

Study Design and Conduct

Details have been published as part of the INCAPS study for the entire 65 countries.[17] Briefly, the International Atomic

Energy Agency (IAEA) organized a needs assessment meeting in 2012, where experts identified knowledge of worldwide nuclear cardiology protocols and practices as a priority. A global study in centers performing nuclear cardiology procedures was performed to identify what laboratories ''around the world [are] doing in terms of tracer utilization, doses used and technology that is available''. Information about all SPECT and PET cardiac imaging procedures over a 1 week period between March 18 and April 22, 2013 was provided by participating laboratories. Approval of this study was provided by the Columbia University Institutional Review Board. As no individually identifiable health information was collected, the study was deemed exempt from the requirements of US federal regulations for the protection of human subjects (45 CFR 46).

Data Collection Instrument

Each site provided information on laboratory demographics. For each MPI study completed, the site also provided patient demographics and clinical characteristics, including age, gender, and weight, and study parameters including radiopharmaceuticals used and injected activities, camera type, patient positioning, additional scanning (CT or nuclear) performed for attenuation correction, and any camera efficiency improving hardware and software.

Radiation Dose Estimation

The patient effective dose (ED) was used to quantify radiation exposure. This is a whole-body measure reflecting

Table 1. Definitions of the 8 best practices[17]

Avoid thallium stress No thallium stress tests were performed in patients ≤70 years old. SPECT MPI performed with thallium-201 is associated with a considerably higher radiation dose to patients than when it is performed with technetium-99m. This excludes thallium rest-redistribution viability studies

Avoid dual isotope No dual isotope (rest thallium and stress technetium) stress tests were performed in patients ≤70 years old. Dual isotope MPI is associated with the highest radiation dose of any protocol

Avoid too much technetium No study was performed with administered activity >1332 MBq (36 mCi) for an injection of technetium, and mean total effective dose was <15 mSv for all studies using just technetium injections. 1332 MBq is the highest recommended activity in guidelines, and 15 mSv is a high radiation dose for a study using technetium-99m

Avoid too much thallium For each nuclear stress test involving thallium, no more than 129.5 MBq (3.5 mCi) was administered at stress. The expert committee maintained that no more than this activity is needed for patients who are good candidates to receive thallium MPI

Perform stress-only imaging The laboratory performed at least one stress-only study, in which rest imaging was omitted, or the laboratory only does PET-based stress tests. If stress images are completely normal, subsequent rest imaging can be avoided to reduce radiation dose by up 75%. PET MPI studies have low radiation dose, the dosimetric advantage of stress-only is less, and there is less evidence regarding stress-only PET MPI

Use camera-based dose-reduction strategies The laboratory performed at least one study using at least one of the following: (1) attenuation correction (CT or line source), (2) imaging patients in multiple positions, e.g., both supine and prone, (3) high-technology software (e.g., incorporating resolution recovery and noise reduction), and (4) high-technology hardware (e.g., PET or a high-efficiency solid-state SPECT camera). Each of these approaches reduces the radiation dose needed or facilitates performance of stress-only imaging

Weight-based dosing for technetium The laboratory had a statistically significant positive correlation between patient weight and administered activity (MBq), for injections of technetium. Tailoring the administered activity to the patient size offers an opportunity to reduce radiation dose

Avoid inappropriate dosing that can lead to ''shine-through'' artifact The laboratory performed no SPECT MPI studies with technetium rest and stress injections on the same day, in which activity of the second injection was <3× that of the first injection. Shine-through occurs in two-injection, single-day technetium studies when residual radioactivity from the first injection interferes with interpretation of images for the second injection. To avoid shine through, it is recommended in guidelines that the activity (mCi or MBq) imaged for the second injection be at least 3–4 times that of the first injection; in some cases this can be achieved with a second injection that has less than 4 times the activity by waiting for some of the technetium-99 m to decay. Reflecting guidelines, we considered a second injection of less than three times the activity of the first injection to constitute dosing that can lead to shine through

A committee of international experts convened at the IAEA, including physicians and medical physicists, developed these criteria to be applied to nuclear cardiology laboratories. *MPI* myocardial perfusion imaging, *SPECT* single-photon emission computed tomography, *mCi* millicurie, *MBq* megabecquerel, *PET* positron emission tomography, *CT* computed tomography. Adapted from Einstein et al[17]

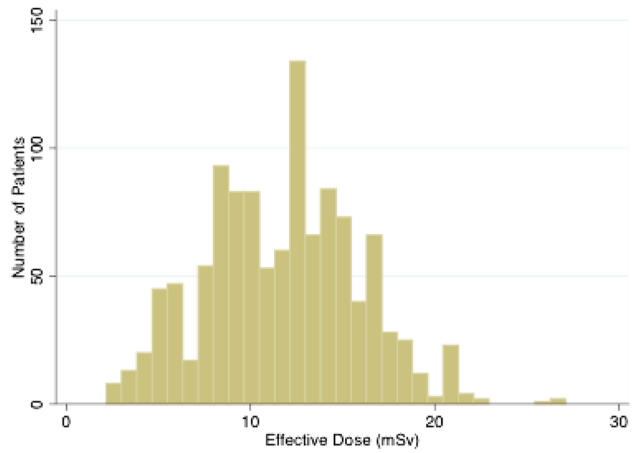

Figure 1. Distribution of patient effective doses for MPI studies in Latin America.

organ doses and their relative sensitivity to the deleterious effects of radiation. The radiopharmaceutical(s) and their activities (MBq) administered to each patient were used to estimate the individual patient EDs. The estimation of ED was based on methods provided by the International Commission on Radiological Protection, as described in the INCAPS study.[17]

Best Practices Quality Index

Prior to data analysis, an expert committee of physicians and medical physicists was convened by the IAEA in order to determine practices that can be implemented by operators to optimize radiation dose from MPI. Using current clinical practice guidelines,[15,18] the committee identified eight measurable laboratory ''best practices'', such as avoiding administering too much isotope, avoiding higher-dose isotopes, and application of dose lowering technologies and protocols. The full list of best practices is detailed in Table 1. A best practices quality index (QI) was developed, a priori, by the committee. The QI score was defined as the number (0-8) of best practices a specified laboratory adhered to during the specified week. A QI score of 6 or greater was determined as a desirable level by the committee. We used data extracted from the INCAPS study to determine each laboratory's adherence to these practices

Statistical Methods

Patient EDs and laboratory QI scores were calculated, as above. We describe continuous variables using means (±standard deviation) and medians (interquartile range; IQR), and categorical variables as proportions. Continuous variables were compared using either analysis of variance or Kruskal-Wallis tests. Chi squared tests were used to compare categorical variables. The primary comparison was between Latin American and RoW laboratories. We also compared laboratories within Latin America. A linear regression model was developed to examine the relationship between laboratory volume and mean laboratory ED. All statistical analyses were performed using Stata/SE 13.1 (StataCorp, College Station, TX, USA).

RESULTS

The INCAPS study acquired data on 7911 patients undergoing MPI in 308 laboratories in 65 countries, including 1139 patients (14.4%) from 10 Latin American countries (Argentina, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Mexico, Peru, Uruguay). Patients undergoing MPI in Latin America were younger (62.4 ± 11.5 vs 64.1 ± 12.0 years, $p < 0.001$). Mean ED for all patients in Latin America was 11.8 ± 4.1 mSv (median 12.1, IQR 8.5-14.6 mSv) compared to 9.1 ± 4.5 mSv (median 10, IQR 6.2-12.4 mSv) in the RoW. The distribution of patient ED is shown on Figure 1. The mean and median EDs both differed significantly between laboratories ($p < 0.001$) (Table 2) and countries ($p < 0.001$). In Latin America, 11% of laboratories had median ED ≤ 9 mSv, which is lower compared to 32% in RoW (Table 3). Only 8 of 36 laboratories adhered to six or more best practices. The proportion of laboratories in Latin America and RoW adhering to each best practice is presented in Table 4. On linear regression analysis, laboratory volume was associated with reduced ED (beta: −0.03, $p = 0.016$), explaining 15.9% of the variance in mean laboratory ED (Figure 2).

DISCUSSION

Our current study indicates that, compared to the RoW, on average, the current practice of nuclear cardiology in Latin America is associated with higher radiation exposure to patients, although there is great heterogeneity in the region. There are certainly regional

Table 2. Latin America laboratory volume, radiation dose, and quality index score

Laboratory	Patients N	ED (mSv) Mean	ED (mSv) SD	QI score
Argentina 1	67	10.1	0.80	5
Argentina 2	6	13.8	2.53	4
Argentina 3	62	9.6	4.95	6
Argentina 4	10	12.6	1.65	6
Argentina 5	76	12.8	3.48	7
Brazil 1	173	8.9	3.72	4
Brazil 2	23	12.0	2.94	5
Brazil 3	7	17.8	2.00	5
Brazil 4	24	12.2	0.03	5
Brazil 5	41	17.4	1.61	4
Brazil 6	127	8.4	2.91	5
Brazil 7	16	16.7	0.45	4
Brazil 8	43	12.7	2.86	5
Brazil 9	81	15.0	1.37	4
Chile 1	11	12.6	1.91	4
Chile 2	11	15.2	0.86	5
Chile 3	2	12.6	0.21	4
Chile 4	4	13.4	0.29	4
Costa Rica 1	9	11.2	1.64	6
Costa Rica 2	9	9.4	1.26	5
Cuba 1	5	18.0	4.52	4
Cuba 2	12	12.2	3.60	7
Cuba 3	10	16.0	3.93	5
Cuba 4	33	11.3	3.51	6
Mexico 1	9	12.3	0.00	5
Mexico 2	7	12.3	0.00	5
Mexico 3	6	14.2	7.79	2
Mexico 4	8	7.8	1.99	4
Mexico 5	12	12.7	0.00	5
Mexico 6	43	14.5	4.12	4
Mexico 7	80	10.1	4.31	6
Other Country 1	8	10.7	0.43	6
Other Country 2	1	18.6	0.00	5
Other Country 3	39	12.9	0.00	5
Uruguay 1	35	16.9	2.49	4
Uruguay 2	29	14.9	2.03	5

Laboratories in Bolivia, Colombia, and Peru—countries in which only a single laboratory participated in INCAPS—are listed above as "Other Country" and presented in random order, so as to avoid providing identifiable information about any individual laboratory

differences in terms of regulation, organized scientific groups, level of knowledge regarding current guideline recommendations, and reimbursement issues which may influence the practice of nuclear cardiology in the region and in consequence the ED delivered to patients.

Brazil is the largest, most populous country in Latin America, where IHD is the number one killer of men and women. This country has contributed the largest number of patients from Latin America in the study (535 of 1139) which in some way reflects the higher utilization of nuclear cardiology compared to some other countries in the region, as previously shown.[19] Among those studied we could find one laboratory delivering a mean ED of 8.4 mSv to 127 patients, which meets the current guidelines recommended goal of ≤9 mSv. Nevertheless, another laboratory in the same country delivered an ED of 17.8 mSv to seven patients (Table 2). It is interesting to note the difference in volume of patients seen within that week, comparing these two laboratories. Evaluating the correlation between mean ED and volume (Figure 2) there is a trend for a higher volume laboratory to deliver lower radiation doses. Considering that these patients are from the same country, working under the same regulations and a population of similar characteristics, it appears that protocol adjustments could be implemented, towards a more homogeneous practice of nuclear cardiology in the region, in order to achieve the guideline recommended goal.

We see opportunities for improvement in the practice of nuclear cardiology in many of these 36 laboratories in these 10 Latin America countries involved in the study and also potentially to other laboratories in the region which were not part of the study. Quite simple adjustments, which are costless to implement, could lead to lower ED and/or improved QI. These include measures such as: (1) *implementing stress only imaging* in at least some patients, when the stress ''first'' imaging is completely normal, therefore avoiding an unnecessary second injection, which is feasible as previously shown;[19,20] (2) *performing prone imaging* as well as supine imaging in some patients, both to improve diagnostic accuracy, preventing potentially unnecessary additional downstream testing which often involves additional radiation exposure, and also to increase the normalcy rate of stress imaging, thereby enabling increasing the rate of stress-only imaging and lowering radiation dose for the particular studies in which rest imaging can be omitted;[21] and (3) *adjusting the injected activity based on patiens weight* instead of using a fixed dose to patient of all weights. One barrier to performing stress-only imaging in Latin America is the low rate at which stress imaging is performed first (38% vs. 49% in the RoW). Additional dose-reduction approaches are available for those Latin American laboratories able to afford software- and hardware-based dose-reduction techniques. For example, high-efficiency cameras with cadmium-zinc-telluride detectors,[22,23] as well as advanced reconstruction software incorporating

Table 3. Patient and laboratory demographics and clinical characteristics

	Latin America	Rest of world	*P* value
Patients (*n*)	1139	6772	
Female, *n* (%)	492 (43%)	2762 (41%)	0.13
Age (years)			
Mean	62.4	64.4	<0.001
SD	11.5	12	
Weight (kg)			
Mean	77.8	80.7	<0.001
SD	16.0	19.1	
SPECT studies, *n* (%)	1139 (100%)	6301 (93%)	<0.001
PET studies, *n* (%)	0	471 (7%)	<0.001
Studies ≤9 mSv, *n* (%)	304 (27%)	2761 (41%)	<0.001
Stress-first, *n* (%)	433 (38%)	3322 (49%)	<0.001
Stress-only, *n* (%)	54 (5%)	951 (14%)	<0.001
Effective dose (mSv)			
Mean	11.8	9.1	<0.001
SD	4.1	4.5	
Median	12.1	10	<0.001
IQR	8.5-14.6	6.2-12.4	
Effective dose (mSv)—SPECT studies			
Mean	11.8	10.1	<0.001
SD	4.1	4.3	
Median	12.1	10.4	<0.001
IQR	8.5-14.6	7.4-12.5	
Laboratories (*n*)	36	272	
Patients/laboratory			
Mean	31.6	24.9	0.23
SD	37.7	30.7	
Median	12	16	0.72
IQR	8-42	8-32	
Quality Index Score			
≥6, *n* (%)	8 (22%)	134 (49%)	0.002
Mean	4.86	5.5	0.0047
SD	0.99	1.3	
Median	5	5	0.0043
IQR	4-6	5-6	
Laboratories with median dose ≤9 mSv, *n* (%)	4 (11%)	87 (32%)	0.01

resolution recovery and noise reduction algorithms,[24] both enable obtaining comparable diagnostic information to scans using conventional equipment while reducing administered activity and thus radiation dose. However, none of the Latin American laboratories reported using high-efficiency cameras or PET, and the rate of advanced reconstruction algorithm use was 20% lower in Latin America than in RoW. This technological difference accounts in part for the higher radiation doses observed in Latin America.

The appropriate use of nuclear technology can potentially help to control costs, important for any country but particularly relevant to those developing nations more financially challenged. Utilization of MPI is heterogeneous worldwide, being underused in many countries.[25] In fact, MPI utilization should still grow in a region like Latin America, helping to reduce high rates of IHD mortality and prevent potential unnecessary invasive procedures in some of these nations. The IAEA remains committed to support the implementation and appropriate use of MPI worldwide as a way to help member states to face these challenges. At the same time, it is committed to quality and optimal use of radiation. This study demonstrated opportunities for

Table 4. Number and proportion of laboratories adhering to each best practice

	Latin America		World		
	N	(%)	N	(%)	*P* value
Laboratories	36		272		
Best practice					
Avoid thallium stress	35	97.2	247	90.8	0.335
Avoid dual isotope	34	94.4	264	97.1	0.33
Avoid too much technetium	23	63.9	240	88.2	<0.001
Avoid too much thallium	35	97.2	271	99.6	0.22
Perform stress-only imaging	7	19.4	86	31.6	0.135
Use camera-based dose reduction strategies	16	44.4	190	69.9	0.004
Weight-based dosing for technetium	11	30.6	77	28.3	0.845
Avoid “shine through”	14	38.9	122	44.9	0.498

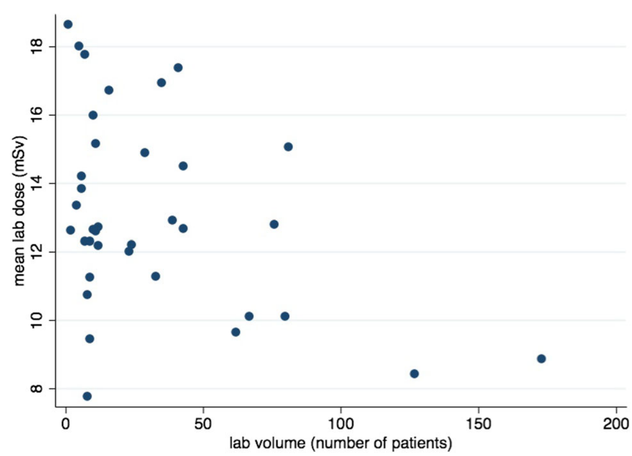

Figure 2. Distribution of mean laboratory ED by patient volume.

improvement and optimization of clinical practice of nuclear cardiology in Latin America and will help to design educational strategies to reduce ED delivered to patients.

STUDY LIMITATIONS

Despite our efforts, we could not reach all laboratories performing nuclear cardiology in Latin America and our conclusions are based on those laboratories replying to our contact. In addition, data reported during a single week may not reflect precisely the entire practice of nuclear cardiology nor all the protocols potentially used in that laboratory. Nevertheless we believe that it reflects general patterns of practice in the region and it serves the purpose of pointing to where adjustments can be made.

NEW KNOWLEDGE GAINED

The current practice pattern of nuclear cardiology in Latin America delivers higher than optimal ED to patients. Adjustments can be made to reduce significantly radiation exposure in the region complying with international accepted standards, guideline recommendations, and the principle of ALARA.

CONCLUSION

Marked variation exists in radiation exposure to patients undergoing MPI in Latin America. On average Latin American countries have higher ED compared to the RoW. Opportunities to reduce radiation exposure can be targeted at expanding the practice of stress-only imaging, using camera-based dose reduction strategies, and reducing injected activity to reflect a patient's habitus.

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APPENDIX

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