REVIEW ARTICLE

Improving Nuclear Medicine Practices in Cardiology in the Emerging Economies: Role of the International Atomic Energy Agency

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Abstract

Low- and middle-income countries (LMICs) are particularly affected by cardiovascular diseases (CVDs), as more than 75% of all CVD deaths occur in these countries. Global prognostic figures are alarming, as an estimated 23.6 million people will die each year due to CVDs by 2030. For this reason, one of the targets of the Sustainable Development Goals (SDGs) of the agenda of the United Nations (UN) aims at reducing premature mortality due to Non-Communicable Diseases (NCDs) by 30% by 2030.

Within the UN family, the International Atomic Energy Agency (IAEA) has the mandate to promote safe, secure and peaceful use of nuclear technologies. The IAEA is strongly committed to accomplish the 2030 UN Agenda and through its Human Health Division, contribute to the attainment of SDGs. One of the key objectives of the Human Health Division is to support Member States to tackle the burden of CVDs through its subprogram of Nuclear Medicine and Diagnostic Imaging. This is accomplished by supporting the establishment and strengthening of capabilities of Member States to provide appropriate and safe use of nuclear cardiology clinical applications. The support ranges from assisting countries in the planning and implementation stages, providing training, maintaining and improving quality of clinical practice, establishing quality management systems and advising on how to comply with international standards, as well as using the technology in an appropriate and safe manner. This review will cover the activities of the IAEA in promoting, implementing, and supporting nuclear applications in cardiology in LMICs.

Keywords

Cardiovascular Diseases/diagnostic imaging; Nuclear Medicine; Myocardium/Radionuclide Imaging; International Agencies; Nuclear Energy.

Introduction

In 2015 the United Nations (UN) adopted the "2030 Agenda for Sustainable Development" which includes seventeen Sustainable Development Goals (SDGs), aimed at ending poverty, fighting inequalities and tackling climate change. The SDGs address a range of social needs, including education, health, social protection, and job opportunities. SDG number 3 focuses on ensuring healthy lives and promoting well-being for all at all ages. This goal addresses all major health priorities, including Non-Communicable Diseases (NCD) which account for an estimated 52% of all deaths among persons under the age of 70, commonly referred to as premature deaths. Cardiovascular diseases (CVDs) represent 38% of the NCD causes of death, followed by cancer with 27%.

The International Atomic Energy Agency (IAEA) was founded in 1957 as the world's "Atoms for Peace" organization within the UN family with the mandate to work with its Member States and multiple partners worldwide to promote safe, secure and peaceful use of nuclear technologies. The objectives of the IAEA's dual mission – to promote and control the Atom – are defined in Article II of the IAEA Statute. "The Agency shall seek to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world. It shall ensure, so far as it is able, that assistance provided by it or at its request or under its supervision or control is not used in such a way as to further any military purpose".[1] This mandate has a special emphasis on Low- and Middle-Income Countries (LMICs), defined

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by the World Bank ranking, which are the target Member States of the work of the IAEA[2] towards the introduction and expansion of nuclear techniques in health care.

The role of nuclear techniques in cardiology

There has been a significant shift in the global disease burden in the past decades from communicable infectious diseases to NCDs. According to the World Health Organization (WHO), more than 38 million people die each year as a consequence of NCDs. Cardiovascular diseases are the largest subgroup of NCDs, killing more than 17.5 million people annually, which account for 31% of all global deaths. More people die due to CVDs worldwide than any other single cause. The epidemic proportions of the global CVD burden go hand-in-hand with the upsurge in common risk factors, including obesity, diabetes, low physical activity and poor diet. LMICs face the highest burden of CVDs, as more than 75% of all CVD deaths occur in these countries.[3]

While in high-income countries the age-standardized death rates for CVDs from 1990 to 2013 declined by 43%, in LMICs declines in CVD mortality have not been as marked (<11%). In addition, there is an upsurge number of people experiencing these diseases at younger and potentially more productive ages, thus limiting their contribution to the economic development of their countries. This is most likely due to an increased prevalence of risk factors, such as tobacco consumption, obesity and physical inactivity. Limited access to basic care for CVD, including management of high blood pressure, high cholesterol, diabetes and acute events (myocardial infarction and stroke), gaps in access to medicines and technology, and limited or lack trained personnel[4] may also contribute.

Medical imaging has revolutionized health care in the past decades as it has enabled the delivery of individual, patient-tailored disease management. The diagnostic and prognostic value of myocardial perfusion imaging (MPI) in coronary artery disease (CAD) is very well established.[5-8] Nuclear techniques not only provide perfusion and functional data, which aid the management decision; they also provide information such as transient ischaemic dilation of the left ventricle (TID) after stress; right ventricular uptake; myocardial stunning, which can also support the decision-making process. MPI is also utilized from the health economics perspective as a gatekeeper to the more costly invasive procedures[9,10] and has led to a rapid use of MPI worldwide, with LMICs being no exception.[11]

The work of the IAEA in nuclear cardiology

Among other Agency's programs, the one dedicated to Human Health is focused on enhancing the capabilities of IAEA Member States in addressing issues related to the prevention, diagnosis and treatment of health problems, supporting the development and application of nuclear techniques in health care, within a framework of quality assurance. As part of the Human Health program, the subprogram in Nuclear Medicine has a special focus on supporting applications in cardiology. This task is accomplished by means of different activities ranging from clinical research to training and education.

Coordinated Research Activities

Research activities at the IAEA are carried out through the Coordinated Research Projects (CRPs), bringing together research institutes from both developing and developed Member States to collaborate on research topics of common interest. The research groups usually comprise 10 to 15 research institutions that work to acquire and disseminate new knowledge.[12] Besides promotion of research through peer reviewed scientific publications, outputs from CRPs include establishment of networks and databases; development of devices / tools for diagnosis and testing; technology transfer through technical cooperation projects; Masters and PhD theses.

Research takes place at those participating institutions that have been identified in the CRP's research, technical and doctoral contracts and cost-free research agreements. The IAEA acts as the sponsoring and coordinating body, with an IAEA staff member, the project officer, assigned to lead each CRP.

Since technology transfer is one of the main goals of the CRPs, they often address clinical topics already explored in high-income countries, where patients may have access to high level therapies and diagnostics. For this reason, they may not be representative of situations found in different settings, such as those of the emerging economies where financial resources are scant and access to top level therapies may not be guaranteed. In some cases, CRPs may lead to slightly different results.

Clinical research in nuclear cardiology: results from IAEA CRPs

The use of MPI in asymptomatic diabetes, a growing epidemic particularly in the developing world due to the adoption of westernized living habits and foods, has been investigated in a CRP. According to an estimate from WHO, more than 400 million people are affected by type 2 diabetes, a number which almost quadrupled in the last 30 years. While other studies on MPI use in this specific clinical setting have already reported a similar incidence of ischemia in asymptomatic diabetics, as compared to non-diabetics with other risk factors,[13] results from the IAEA CRP[14] have shown that such a conclusion does not necessarily apply to populations from the developing world. Perhaps this is due to the lacking control of risk factors and management optimization. This should be considered an important finding: indeed clinical research from countries and high level centres, where patients get the best possible treatments, may have better outcomes. In addition, this CRP stimulated some countries, such as Cuba and Algeria, to carry out detailed study on this subject at national level.

In another study,[15] the association between non-perfusion parameters and ischemia in gated-single photon emission computed tomography (SPECT) MPI has been explored in order to assess whether abnormal left ventricular (LV) function at rest and intraventricular dyssynchrony were associated with inducible myocardial ischemia. This study found that baseline differences in LV volumes and degree of dyssynchrony are associated with inducible ischemia on stress testing in a gated-SPECT MPI and stress-induced ischemia increases the degree of intraventricular dyssynchrony.

Gated-SPECT offers the unique opportunity to assess both myocardial perfusion and cardiac function in one single study. A potential limit, however, is that the delay between peak-stress injection and acquisition, typically between 45 and 60 min, may prevent the detection of transient post-ischemic LV dysfunction due to myocardial stunning in patients with CAD. The aim of a multicenter study supported by the IAEA was to determine whether early post-exercise imaging, i.e. within 15 min post-injection at peak stress, is more likely to detect LV stunning than imaging after the conventional 45-60 min, without adversely affecting image quality or perfusion information. Perfusion was quantitatively assessed, as well as LV ejection fraction (LVEF). Ischemia was assessed using summed differential scores, and stunning as the difference between rest and post-stress LVEF. Results from this CRP[16] showed that both image quality and perfusion information were similar between the early and delayed post-stress studies. A strong association between LVEF and ischemia was also shown, which was stronger at early stress imaging than at conventional timing imaging in the ischemic compared to the non-ischemic population. It was thus concluded that early post-exercise imaging is feasible, and can potentially improve the detection of post-ischemic stunning without compromising image quality and perfusion data.[16]

In another CRP, an international multicenter study[17] undertook a head-to-head comparison of the use of coronary CT angiography (CCTA) and MPI in patients with suspect CAD. The two modalities are often used as alternate studies, although they explore two different aspects of CAD. Indeed, CCTA detects the presence of anatomical disease and its extent, but provides limited information on the presence of ischemia. On the other hand, MPI offers functional data on the effects of possible coronary artery stenosis on myocardial perfusion, but not direct visualization of the atherosclerotic plaque. This randomized study investigated the downstream cascade of other tests triggered by either CCTA or MPI when used for the initial evaluation of possible CAD. This study showed that the MPI strategy may result in less downstream test utilization for clinical decision making, although with a small increase of radiation exposure.

While the relation between the relatively small radiation exposures due to medical studies cannot be fully demonstrated, due to the lack of prospective studies on this topic,[18,19] there is still a growing concern among the public. The reported increase in radiation exposure due to medical studies in the United States in the last decades could be attributed mainly to the increased use of computed tomography (CT), nuclear medicine procedures,[20,21] and for the latter use of MPI. The IAEA also has a mandate to promote the safe use of radiation, therefore the consideration that little was known on the worldwide use of MPI protocols and strategies for effective dose (ED) reduction prompted an international study, titled "IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS)". This study collected detailed information on protocols used in 308 nuclear cardiology laboratories, voluntarily enrolled in 65 countries worldwide. Participating centers were requested to report on MPI studies performed for a single week in March-April 2013. A total of 7911 patients were reported. The level of individual patients' ED was related to a quality index (QI) based on eight best practices[22] previously identified by a panel of international experts. Results[23] provided a better understanding of current practice and opportunities to identify areas to improve quality of care and to reduce disparities, which in turn would decrease the global radiation burden from MPI. Particularly relevant were findings on a wide variation, regionally, of ED.[24] This study has also shown that the use of stress-only protocols, when clinically feasible, may contribute to a significant reduction of ED.[25]

Education and Training

Due to the multidisciplinary nature of nuclear cardiology, all members of the imaging team should be properly trained and prepared to produce high quality results with the potential to affect patient management in a reliable and significant way. In many developing countries, nuclear medicine practitioners have limited access to educational resources and often have few opportunities for peer-to-peer discussion. From a survey through the IAEA Nuclear Medicine Data Base (NUMDAB),[26] it appears that out of the more than 600 centers censored worldwide, as many as 40% do not practice nuclear cardiology at all.

Qualified practice of nuclear cardiology needs sound training and education to make it an effective tool to confront the increasing incidence of CVDs. Well aware of this, the IAEA has started several educational projects to support nuclear cardiology practitioners from countries with limited resources and let them raise the standard of their practice to international standards. Training in nuclear cardiology poses a special challenge since it involves two medical specialties at the same time.

In the last 10 years, through the Technical Cooperation program, the Nuclear Medicine Section has supported training for more than 500 practitioners from IAEA Member States; either as fellows placed in selected training centers or as participants to regional training courses.

Human Health Campus

Attuned to the continuous evolution of the medical field as well as to the advancement and diversity of methods in delivering capacity building efforts in this digital age, the IAEA's Division of Human Health has enhanced its program by incorporating online educational resources for health professionals into its repertoire of projects to further its commitment in addressing the needs of its Member States in the field of radiation medicine and nutrition. The Human Health Campus (HHC) (/www.humanhealth.iaea.org) is the online educational resources initiative towards enhancing professional knowledge of health professionals.

Launched in October 2010, the HHC serves as a 'virtual campus' with over 250.000 regular users from more than 100 countries, this educational website maintains a high quality standard by providing up-to-date technical information. This information is provided in collaboration with medical societies and international health experts, while adhering to robust educational strategies and methods to achieve its goals.

The HHC includes a comprehensive section on nuclear medicine that covers the entire spectrum of clinical practice, with a well-developed section on nuclear cardiology.[27] Here nuclear cardiology practitioners will find directions to:

- Teaching cases
- Lectures from IAEA training courses and meetings
- Guidelines on interpretation and reporting
- E-learning modules covering:
  - Basics of ECG Interpretation for Nuclear Cardiology Practice
  - Eight Best Practices for Nuclear Cardiology
  - Myocardial Perfusion Imaging
  - Gallery of Cardiology Cases: Asymptomatic Patients
  - Atlas of Myocardial Perfusion SPECT Studies

Guidelines/Recommendations, Publications and Conferences

The HHC offers links to the American Society of Nuclear Cardiology (ASNC), which provides a variety of Imaging Guidelines for Nuclear Cardiology Procedures with the corresponding most recent date of approval or endorsement.[28]

The Human Health Series is a publication line with titles in nuclear cardiology that provide comprehensive overview of CVDs as a public health problem in developing countries and on the evidence behind appropriateness and justification of nuclear cardiology methods.[29] A more recent and revised publication provides a detailed analysis of all the steps involved in the delivery of nuclear cardiology services, aiming at supporting the implementation, homogenization and enhancement of MPI practice in those Member States where the technique is under development. The aim is also to help strengthen already existing nuclear cardiology practices, to facilitate their update to currently accepted standards in order to provide better quality services for the population. Clinical scenarios where patients are most likely to benefit from SPECT or positron emission tomography (PET) MPI are clearly identified.[30]

Over the years, the IAEA has become a Continuous Medical Education (CME) provider[31] and has recently implemented awarding of CME credits to selected live educational events, such as conferences and regional training courses intended for practicing medical professionals (including nuclear cardiologists). These are organized by the IAEA Division of Human Health under the stringent rules of the European Accreditation Council for CME of the *Union Européenne des Medecins Specialists* (EACCME/UEMS) guidelines and processes. The awarding of CME credits is an essential component in the maintenance of professional certification in most Member States. The CME credits are recognized worldwide.

Webinars in Nuclear Cardiology

Webinars - a live media presentation over the internet - allows the dissemination of content to many simultaneous listeners/viewers individually or in auditoriums around the world, thereby facilitating the access to even remote locations. Additionally, these webinars are recorded, allowing continuous access to the lectures at the time and place of most convenience to the user. Since 2013, the IAEA in cooperation with the ASNC initiated a series of complimentary webinars designed to provide the best practices in Nuclear Cardiology.

Offered as part of a joint educational series between ASNC and IAEA, these live, interactive webinars allow participants to evaluate and assess their skills and improve their knowledge with regard to best practices in nuclear cardiology. Twenty-one webinars have been broadcasted live and the recorded versions are accessible on-demand and freely available at the HHC. Those webinars cover a wide spectrum of teaching points,[32] from "Basic MPI" and "Coronary Anatomy and the Physician Basis of Hyperemia and Coronary Flow" to "Incorporating Clinical and ECG Findings in to the Interpretation and Reporting of MPI". Attendance to every webinar event has always been in the range of 250-300 registered participants worldwide. In addition, in order to have a broader coverage some of the webinars have been broadcasted in Spanish and French and soon in Arabic.

International Conferences

The IAEA has organized two international conferences on Integrated Medical Imaging in Cardiology (IMIC 2013 and IMIC 2016), both of them in Vienna. IMIC 2013 was attended by 270 participants from 70 countries and IMIC 2016 gathered 350 professionals from 88 Member States; in addition, more than 1000 professionals took advantage of the live streaming. Notably, both conferences had the support of several professional organizations in the field of nuclear medicine, cardiology and radiology. After fulfilling the rigorous requirements of the EACCME/UEMS, the conferences were granted 25 European CME credits.[33]

Quality Assurance/Improvement & Management

Quality management systems are an essential need for continuously improving effectiveness and efficiency of nuclear medicine services, including nuclear cardiology, to achieve the expectations of quality policies, customer satisfaction and improve professionalism in the specialty. Regular quality audits and assessments are vital for modern nuclear medicine services, including clinical, technical, radiopharmaceutical, medical physics and radiation safety procedures. Launched in 2016, the Quality Management in Nuclear Medicine (QUANUM) program[34-36] is being implemented by the IAEA worldwide. In addition to the training of specialised multidisciplinary teams of auditors, more than 50 Quality Management Audits in Nuclear Medicine have been carried-out in 29 countries across the globe. Nuclear cardiology practice is no exception and a special attention from the IAEA is being given to its practice worldwide.[37,38]

Clinical audits

As an outcome-based organization, the IAEA has recently launched a worldwide clinical audit on MPI practice in emerging economies. The aim is to assess the outcome of IAEA activities in NC, through the Technical Cooperation program,[39] considering the substantial level of investment both financially and in human resources from the Nuclear Medicine Section. This project is based on submission of clinical studies from a core lab to share-point as DICOM files of stress/rest MPI studies, together with the relevant clinical and ECG information. Participating centers, enrolled on a voluntary basis, preferably amongst those whose staff attended IAEA training courses, are required to download those studies. Studies are then processed as per local practice and reported back to the core lab on pre-defined forms. After collecting results, the core lab calculates the average of all parameters, SD and the median, and displaying the results distribution for each study. Each centre is assigned a secret code only they know to identify their performance in relation to others. From the graphs, each centre will be able to identify its position in comparison to other centres and to the average values. This project is still undergoing and its results will be published shortly.

Mobile App

In September 2017 the IAEA developed, in cooperation with the Italian Society of Nuclear Medicine, a smart phone app NUCARD that contains a guide to the appropriate use of nuclear cardiology in different clinical scenarios. NUCARD app is available for google and Android systems.

Conclusions

Nuclear cardiology has proved to be an important component of the management of patients affected, or suspected of being affected, by ischemic heart disease. CVDs are rising all over the world, and emerging economies are predicted to bear the highest price in terms of cardiac deaths. Thus the nuclear cardiology area should respond to the challenge with innovations that can be easily put in practice, especially in developing countries. In line with its mission to foster applications of nuclear techniques in human health, over the decades the IAEA is enabling communities around the world to take advantage of the benefits that nuclear cardiology has to offer. The structured support provided has been focused in three main areas: education, research and quality, thus covering different aspects ranging from the planning, establishing and setting up nuclear cardiology facilities; implementation of streamline and emerging clinical applications to the appropriate use of nuclear cardiology techniques; quality management and clinical audits and clinical research.

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Author contributions

Conception and design of the research: Dondi M, Pascual T, Paez D. Acquisition of data: Dondi M. Writing of the manuscript: Dondi M. Critical revision of the manuscript for intellectual content: Dondi M, Pascual T, Paez D. Supervision / as the major investigador: Paez D.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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