*Current Medical Imaging*, 2019, *15*, 661-671

RESEARCH ARTICLE

# A New Relational Database Including Clinical Data and Myocardial Perfusion Imaging Findings in Coronary Artery Disease

Rosario Megna[1,*], Mario Petretta[2], Bruno Alfano[1], Valeria Cantoni[3], Roberta Green[3], Stefania Daniele[1], Wanda Acampa[3], Carmela Nappi[3], Valeria Gaudieri[1], Roberta Assante[3], Emilia Zampella[3], Emanuela Mazziotti[3], Teresa Mannarino[3], Pietro Buongiorno[3] and Alberto Cuocolo[3]

*[1]Institute of Biostructure and Bioimaging, National Council of Research, Naples, Italy; [2]Department of Translational Medical Sciences, University of Naples Federico II, Naples, Italy; [3]Department of Advanced Biomedical Sciences, University of Naples Federico II, Naples, Italy*

ARTICLE HISTORY

Received: December 20, 2017
Revised: June 28, 2018
Accepted: July 12, 2018

DOI:
10.2174/1573405614666180807110829

**Abstract:** ***Background***: The aim of this study was to test a relational database including clinical data and imaging findings in a large cohort of subjects with suspected or known Coronary Artery Disease (CAD) undergoing stress single-photon emission computed tomography (SPECT) myocardial perfusion imaging.

***Methods***: We developed a relational database including clinical and imaging data of 7995 subjects with suspected or known CAD. The software system was implemented by PostgreSQL 9.2, an open source object-relational database, and managed from remote by pgAdmin III. Data were arranged according to a logic of aggregation and stored in a schema with twelve tables. Statistical software was connected to the database directly downloading data from server to local personal computer.

***Results***: There was no problem or anomaly for database implementation and user connections to the database. The epidemiological analysis performed on data stored in the database demonstrated abnormal SPECT findings in 46% of male subjects and 19% of female subjects. Imaging findings suggest that the use of SPECT imaging in our laboratory is appropriate.

***Conclusion***: The development of a relational database provides a free software tool for the storage and management of data in line with the current standard.

**Keywords:** Database, PostgreSQL, cardiac imaging, single-photon emission computed tomography, myocardial perfusion, coronary artery disease.

## 1. INTRODUCTION

Coronary Artery Disease (CAD) remains one of the leading causes of morbidity and mortality in the developed countries [1-3]. Epidemiologic data show that improved control of cardiac risk factors has resulted in a decrement in the incidence and severity of CAD as well as its related mortality [4, 5] In particular, in the United States from 1998 to 2008, the rate of death attributable to cardiovascular disease declined 30.6% [6]. However, the rates of decline of cardiovascular disease decelerated dramatically between 2011 and 2014 [7, 8]. Yet, despite the drop in cardiovascular morbidity and mortality, cardiovascular diseases remain a leading cause of morbidity and mortality in the United States and, therefore, a large area of unmet medical need [9]. Cardiac Single-photon Emission Computed Tomography (SPECT) is a well-established modality for the evaluation of myocardial perfusion and Left Ventricular (LV) function in patients with suspected or known CAD [10-14]. This technique has clinical advantages including high sensitivity and high negative predictive value and can be used for further diagnostic and therapeutic decision-making [15, 16]. Quantitative software programs are used for the evaluation of stress and rest myocardial perfusion and LV function after qualitative analysis of reconstructed images [17, 18]. Scores of the stress and rest images are used to characterize the extent and severity of CAD in a semi-quantitative model [19, 20]. Results produced by cardiac SPECT processing and patient medical history data should be put together in one organized system, containing all the information associated with each subject. In this way, it is possible to have added advantages: firstly, individual patient information is obtainable completely and in real time by a single request; secondly, an orderly data collection of the whole population undergoing SPECT imaging is available for statistical processing. In the light of these considerations, the aims of the present study were to implement and to test a free relational database developed on purpose, including clinical variables and imaging data of a large cohort of subjects with suspected or known CAD undergoing

*Address correspondence to this author at the Institute of Biostructure and Bioimaging, National Council of Research, *Via* De Amicis 95, 80145 Naples, Italy; Tel: +39 081 2203401; Fax: +39 081 2203498; E-mail: rosario.megna@ibb.cnr.it

1875-6603/19 $58.00+.00 

stress SPECT myocardial perfusion imaging. We also assessed the impact of age and gender on imaging findings.

## 2. MATERIALS AND METHODS

### 2.1. Database Description

We developed a relational database including clinical data and imaging findings of 7995 subjects with suspected or known CAD who underwent SPECT myocardial perfusion imaging between January 2006 and December 2016 in our academic center. The review committee of our University provided ethical approval for the study (Protocol number 110/17) and all patients gave written informed consent. The database was implemented by PostgreSQL (version 9.2), an open source object-relational database, with additional object features and widely supported among programming language libraries (*e.g.*, C++, Perl) [21]. As a database server, its primary functions are to store data securely and return that data in response to requests from software applications. PostgreSQL has been employed in many fields of research [22, 23]. In medicine, it is used in systems of data storage and analysis in pediatrics, intensive care, and other medical fields [24-33]. Another important aspect to consider is the use of PostgreSQL in commercial and free PACS systems and for medical image researches [34-40]. PostgreSQL has several interfaces available. We selected pgAdmin III (version 1.18), the most widespread Graphical User Interface (GUI) developed for its management in open source environment, for both Linux and Windows operative systems [41]. PostgreSQL was installed on CentOS 6.5 operative system (Kernel 2.6.32; CPU: AMD Opteron 6238 × 4 @ 2.6 GHz; RAM: 8 GB DDR 3), as a virtual machine on VMware vSphere hypervisor server, and managed from remote by pgAdmin III (Fig. **1**) [42, 43]. Both operative system and hypervisor server are open source.

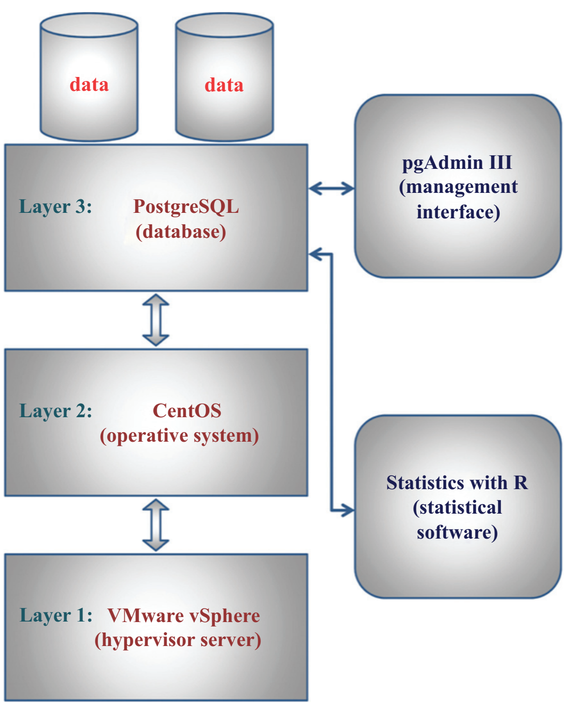


**Fig. (1).** Software architecture of the system completely open source.

PgAdmin III is a GUI with good graphical properties. Its main window [44] consists of three parts: 1) left side shows a tree with all servers and the objects they contain; 2) upper right side shows details of the object currently selected in the tree (properties, statistics, dependencies and dependents); 3) lower right side contains a reverse engineered SQL script. Resize of the main window and change the sizes of the three will be preserved after GUI exit. Through the features of this window is possible to create new objects, delete and edit existing objects if the privileges on the current connection to the database allow this; furthermore, on the lower bar is reported the time necessary for the connection. The query tool has an SQL editor and a graphical query builder on the upper part, while on the lower part has the output panel containing data output, explain, message and history [45]. On the SQL editor is possible to type the commands, instead the graphical query builder is a tool which allows the building of simple SQL queries visually [46].

The database safety is guaranteed by the operative system and software communication protocols. In fact, CentOS has a firewall (called IPTables) that allow the access to the database only to selected Internet Protocol (IP) addresses [47]. Furthermore, PostreSQL has a connection system management configurable by the pg_hba.conf file [48], by which to grant accesses specifying for each user the type of key that must be used for the authentication. Finally, the connections to the database through pgAdmin III [49] are encrypted by Secure Sockets Layer (SSL) [50, 51] or Secure Shell (SSH) [52, 53] protocols, and are necessary credentials (username and password) to establish a connection. This is a robust and also needed safety system, because personal and medical data are stored in the database. At the time of testing, for all subjects the database includes: anamnesis obtained by an interview based on a standard form; other potentially clinical and instrumental (*e.g.*, ECG and echocardiography) features; pre-test likelihood of CAD [54]; post-processing SPECT results (performed one or more times); follow-up information obtained by use of a questionnaire assessed by a phone call.

In total, the maximum number of variables required was 556, while the minimum was 202, depending on the number of SPECT studies performed on subjects. Data were arranged according to a logic of aggregation and stored in a schema with twelve tables, created by the data description language (DDL) PostgreSQL standard; data manipulation (*e.g.*, insert, update) and data query (*e.g.*, select, join) were implemented respectively by DML and DQL PostgreSQL standard languages [55, 56].

We chose PostgreSQL for a large number of data (>3 millions of fields) to be managed by queries also containing many simultaneous constraints (*i.e.*, several personal and anamnestic data, particular range values of blood tests, ECG findings, specific values of SPECT variables and follow-up information). An expansion of the database to clinical variables coming from other departments, with the aim of studying data in a cross-sectional manner, without excluding the possibility of integration with a PACS system is under study.

For specific studies on the data stored in our database, subsets of variables can be easily selected through appropriate query and subsequently analyzed. By pgAdmin III it is possible to create comma-separated values or text file with a subset of data of interest. In addition to the creation of data files by pgAdmin III, several statistical software programs can be connected to the database, downloading directly data from the database server to local personal computer. For this purpose, we used Statistics with R (version 3.4, R Foundation for Statistical Computing, Vienna, Austria) [57], an open source and powerful software for basic and advanced statistical analysis. The connection to database only requires the package RPostgreSQL [58] that provides a compliant driver for access by SSL protocol. The database system was validated by different users, technical features of the computers, operative systems, connections and networks (local and external). In particular, using several subsets of data selected, an epidemiological analysis was performed by R. To obtain the subsets of data for our study, we performed queries to the database by both PgAdmin III and Statistics with R. In the first case, we obtained the required data in text files format, and subsequently they were loaded in the R statistical software and analyzed; in the second case, the data were directly selected from the database and stored as temporary variables in the R statistical software, and analyzed.

Because data collection (anamnesis and instrumental features transcription of data, and follow-up information) and analysis procedures (pre-test likelihood of CAD and post-processing SPECT results) are obtained at different times and by different operators, the database is updated periodically at the end of all these processes, through the insertion of data related to several tens of patients. In the near future, we will develop a web interface for the automatic data entry in our database, currently under study.

### 2.2. Database Validation

PostgreSQL is a validated database with respect to the ACID (Atomicity, Consistency, Isolation, Durability) properties [59, 60]. With the aim of determining the integrity of data retrieval, the validation was done in two ways: 1) in terms of rows, sending queries to the database, we verified that the data retrieval from these and from complementary queries, reproduced the rows number of the whole database; 2) regarding the correctness of fields, we compared the data retrieval with respect to the data inserted into database. This validation was done for simple (*e.g.*, selection of one variable having one constraint) as well as for complex (*e.g.*, selection of more variables by join among tables having multiple constraints, similar to those reported below) queries. These queries were sent to the database by pgAdmin III and Statistics with R. In all cases, the sum of a number of rows was correct, and data retrieved were consistent with the data previously stored in the database, confirming the correct functioning of the system.

For comparing the access and analysis time required for different queries, users and connections, another series of validation test was performed. Regarding the analysis time, pgAdmin III has the time of response as embodied information, while for R we used the Sys.time function [61], both with a precision of 1 ms. For our test, we chose three queries, with an increasing number of variables, tables and constraints, as follows:

1. SELECT sss FROM cardio.exam ORDER BY id
2. SELECT personal.id, personal.age, personal.sex, exam.sss

   FROM cardio.personal JOIN cardio.exam on (personal.id = exam.id)

   WHERE personal.age ≥50 AND personal.sex = 1 AND (exam.sss <1 OR exam.sss >3)

   ORDER BY personal.id
3. SELECT personal.id, personal.age, personal.sex, anamnesis.diabetes, anamnesis.hypertension, exam.sss, exam.sds

   FROM cardio.personal JOIN cardio.anamnesis on (personal.id = anamnesi.id) JOIN cardio.exam on (anamnesis.id = exam.id)

   WHERE personal.age ≥50 AND personal.sex = 1 AND anamnesis.diabetes = 1 AND (exam.sss <1 OR exam.sss >3)

   ORDER BY exam.sss, anamnesis.hypertension

The tests were performed during 10 work sessions by 4 users, 2 connected to the database from the local network (U1 and U2) and 2 from the same external network (U3 and U4); operative systems used were Windows and Linux for both local and remote users; technical features of the computers used were as follows:

- U1 (local user): OS: MS Windows 7 Professional, 64 bit,Version 6.1, Build 7601: Service Pack 1; CPU: Intel i3-2120 @ 3.30 GHz; RAM: 8 GB DDR 3.
- U2 (local user): OS: Centos, 64 bit, Version 6.9, Kernel 2.6.32; CPU: Intel i3-2120 @ 3.3 GHz; RAM: 4 GB DDR 3.
- U3 (external user): OS: MS Windows 7 Enterprise, 64 bit, Build 7601: Service Pack 1; CPU: Intel Core i7-3770 @ 3.4 GHz; RAM: 4 GB DDR 3.
- U4 (external user): OS: Ubuntu, 64 bit, Version 18.04 LTS, Kernel 4.13.0; CPU: AMD Opteron dual core, processor 270 × 4 @ 1 GHz; RAM 4 GB DDR buffered.

### 2.3. SPECT Imaging Protocol

All subjects underwent same-day stress-rest Tc-99m sestamibi gated SPECT myocardial perfusion imaging with exercise or dipyridamole stress testing, according to the recommendations of the European Association of Nuclear Medicine [62]. An automated software program (Cedars-Sinai Medical Center, Los Angeles, CA) was used to calculate Left Ventricular (LV) Ejection Fraction (EF) and the scores incorporating both the extent and severity of perfusion defects, using standardized segmentation of 17 myocardial regions. Each segment was scored from normal (score = 0) to absent perfusion (score = 4). The Summed Stress Score (SSS) is obtained by adding the scores of the 17 segments of the stress images. A similar procedure is applied to the resting images to calculate the Summed Rest Score (SRS). The Summed Difference Score (SDS) represents the difference between the stress and rest scores and is taken to be an index of ischemic burden. A scan was considered normal if the SSS was ≤3, mildly to moderately abnormal if the SSS was between 4 and 10, and severely abnormal if the SSS was >10 [63-65].

### 2.4. Statistical Analysis

For testing our database, a statistics analysis was performed, considering gender, age, the status of suspected or known CAD, the number of SPECT studies performed, the normal or abnormal perfusion pattern and the perfusion defect type found. SPECT was considered abnormal (or positive) when SSS was >3. Descriptive data were summarized and presented as number of subjects, range and mean ± Standard Deviation (SD), number of SPECT studies, abnormal findings and perfusion defect type. Linear regression analysis was used to calculate the increase in abnormal imaging findings in sub-cohort patients stratified by age. Chi-square test was used to determine the difference among ordered groups. The significance level was fixed at 0.05. Statistical analysis was performed by R software.

## 3. RESULTS

### 3.1. Database Validation

All the users used the same version of pgAdmin III (*v.* 1.18) and Statistics with R (*v.* 3.4). In particular, regarding the time of access to the database from local users as well as external users were typical ones of encrypted protocols, that is less than 1 second, also using different operative systems and protocol connections. The test results are summarized in Table **1**. In general, the time responses were less than 0.1 s. The time increased according to query complexity and were very similar between pgAdmin III and Statistics with R. Additionally, as evident from SD, the system was stable and practically independent from the technical features of the computers, connections and networks used. A screenshot of U1 session work regarding the query no. 3, performed by pgAdmin III and R is reported in Fig. (**2**). No anomaly regarding ACID properties or data integrity was found in our database during the validation test as well as for routine operations. Regarding the type of connection to the database, based on statistics with R or pgAdmin III, the users generally preferred using R (~ 70% *vs*. 30%) because did not need to generate a text file for the data analysis.

We also compared our database system with Microsoft Access 2010 [66], installed on the same computer used from U1. The connection for the data import from PostgreSQL was based on Open Data Base Connectivity (ODBC) driver [67]. The tests were performed on the Access server itself. Relatively to the three queries above reported, the time of response calculated as mean ± SD by 10 work sessions were: 48 ± 4 ms, 94 ± 5 ms and 136 ± 4 ms, about twice of those obtained from our database system.

### 3.2. Patients Data Analysis

Characteristics of patients by gender are summarized in Table **2**. Of the overall study population, 69% were men and 31% women. Abnormal findings were observed in 46% of men showing 36% fixed defect, 31% reversible defects and 33% mixed perfusion defects ($p < 0.001$). In women, 19% showed abnormal findings, of these 30% with fixed, 44% with reversible and 26% with mixed perfusion defects ($p < 0.001$).

During the period under study, the mean number of SPECT studies performed was 727 per year (SD 94), with an almost steady proportion between men and women (68% *vs*. 32%, in average). Fig. (**3**) reports the percentages of findings per year found in men and women.

The study population was divided in six sub-cohort stratified by age (<55; 55-59; 60-64; 65-69; 70-74; and >74 years). The results by age group are reported in Table **3**. The number of abnormal SPECT findings increased from 39% to 49% in men (rate ± standard error = 2.0 ± 0.3, p = 0.002) and from 15% to 26% in women (rate ± standard error = 1.7 ± 0.5, p = 0.02). Fig. (**4**) shows the percentages of findings stratified by age for men and women.

**Table 1. Results of the time analysis.**

| - | Query 1 (7995 Rows) | Query 2 (1967 Rows) | Query 3 (728 Rows) |
|---|---|---|---|
| **U1** | | | |
| pgAdmim III | 23±3 | 33±4 | 43±3 |
| Statistics with R | 17±4 | 36±4 | 46±3 |
| **U2** | | | |
| pgAdmim III | 35±4 | 38±4 | 49±4 |
| Statistics with R | 18±3 | 34±4 | 49±3 |
| **U3** | | | |
| pgAdmim III | 27±3 | 33±3 | 47±3 |
| Statistics with R | 18±3 | 37±4 | 48±3 |
| **U4** | | | |
| pgAdmim III | 38±4 | 40 ± 4 | 52±5 |
| Statistics with R | 24±4 | 34±4 | 49±4 |

Time expressed in ms.

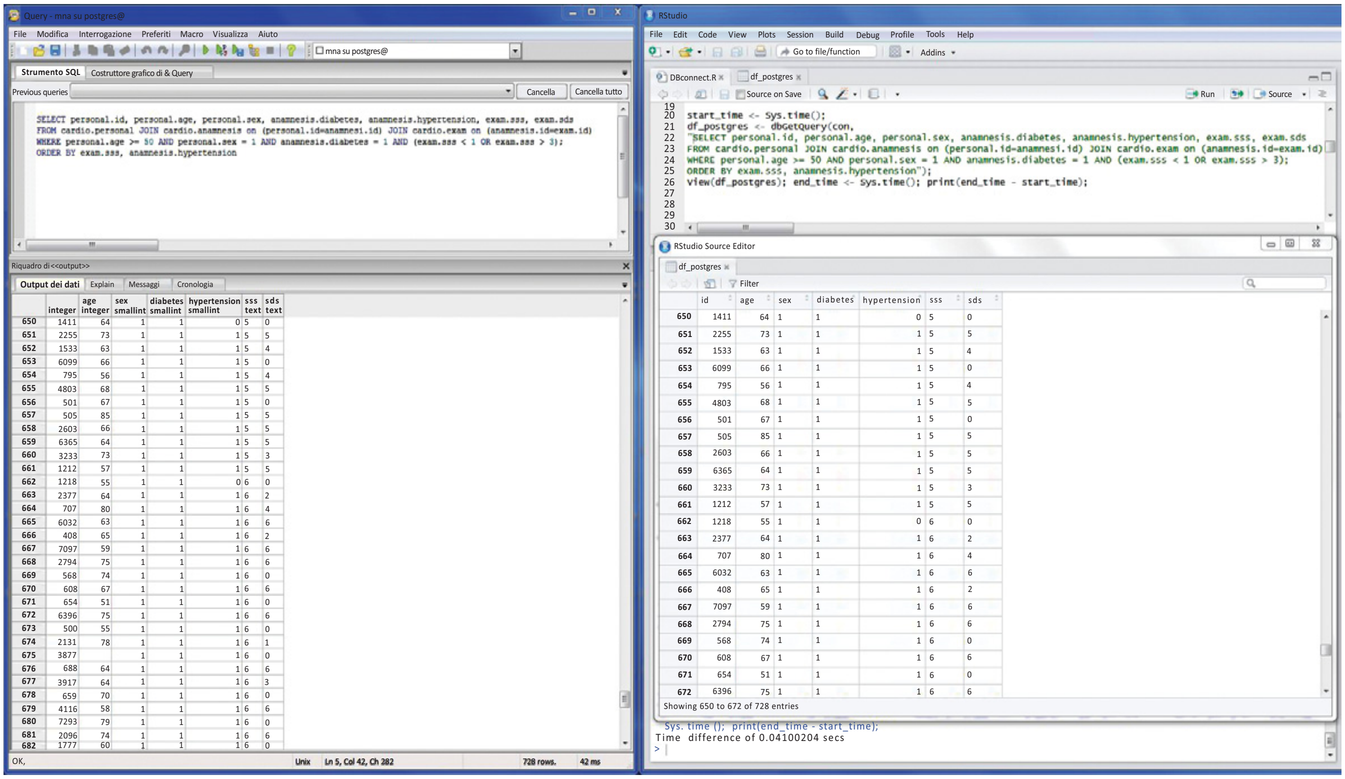


**Fig. (2).** Screenshot of a query from a session work, performed by pgAdmin III (left panel) and R (right panel).

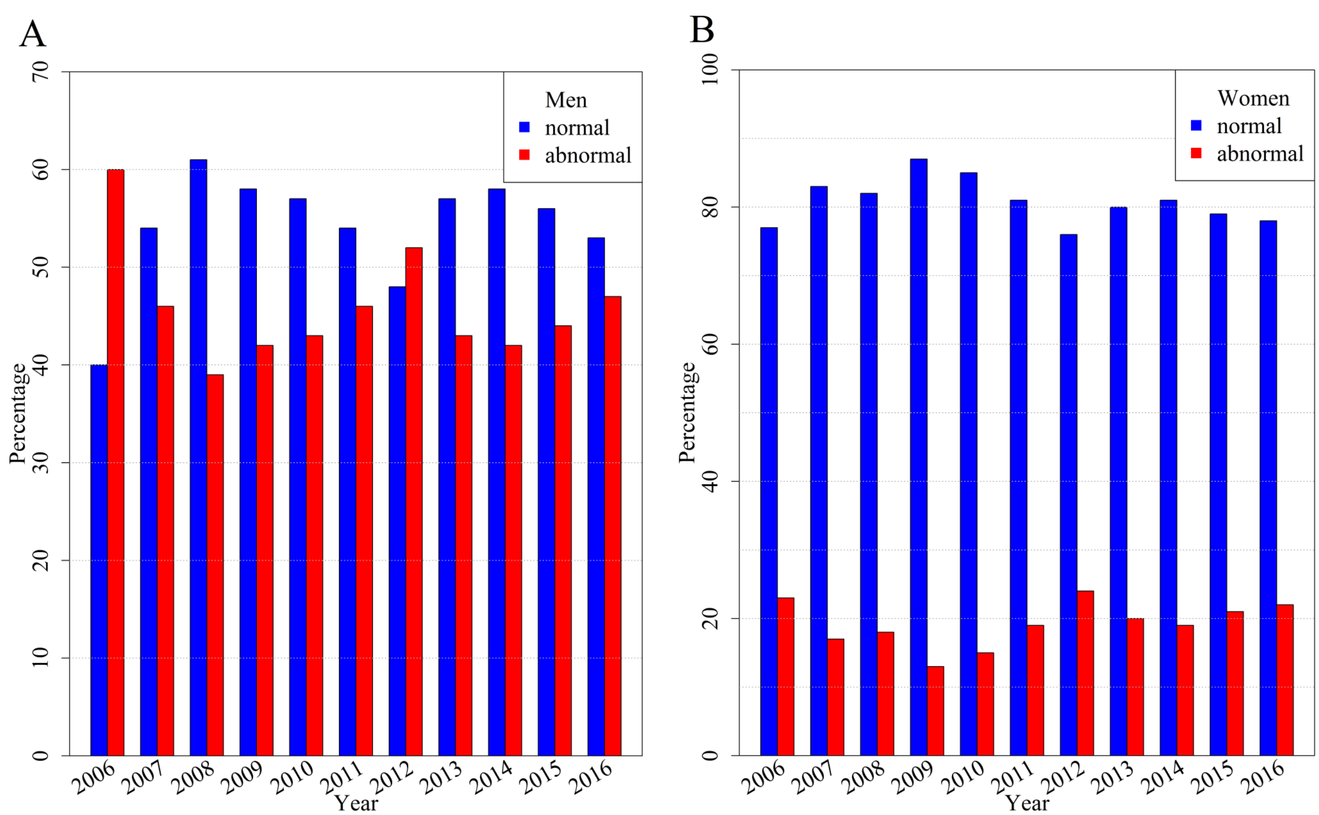


**Fig. (3).** Percentage of SPECT findings per year in men (**A**) and women (**B**). Normal is referred to SSS ≤3 and abnormal to SSS >3.

**Table 2. Demographic data and imaging findings by gender.**

| - | Patients (n) | Age, years (range) | Abnormal SPECT, n (%) |
|---|---|---|---|
| Total | 7995 | 62±11 (18-89) | 2995 (37) |
| Men | 5486 | 62±11 (18-89) | 2513 (46) |
| Women | 2509 | 63±11 (18-89) | 482 (19)* |
| **Suspected CAD** | | | |
| Total | 4678 | 62±11 (18-89) | 942 (20) |
| Men | 2710 | 61±11 (18-88) | 706 (26) |
| Women | 1968 | 62±11 (18-89) | 223 (12)* |
| **Known CAD** | | | |
| Total | 3317 | 62±10 (28-89) | 2054 (62) |
| Women | 2777 | 62±10 (28-89) | 1807 (65) |
| Women | 540 | 66±10 (33-88) | 247 (46)* |

CAD, coronary artery disease.
* p<0.001 *vs*. men.

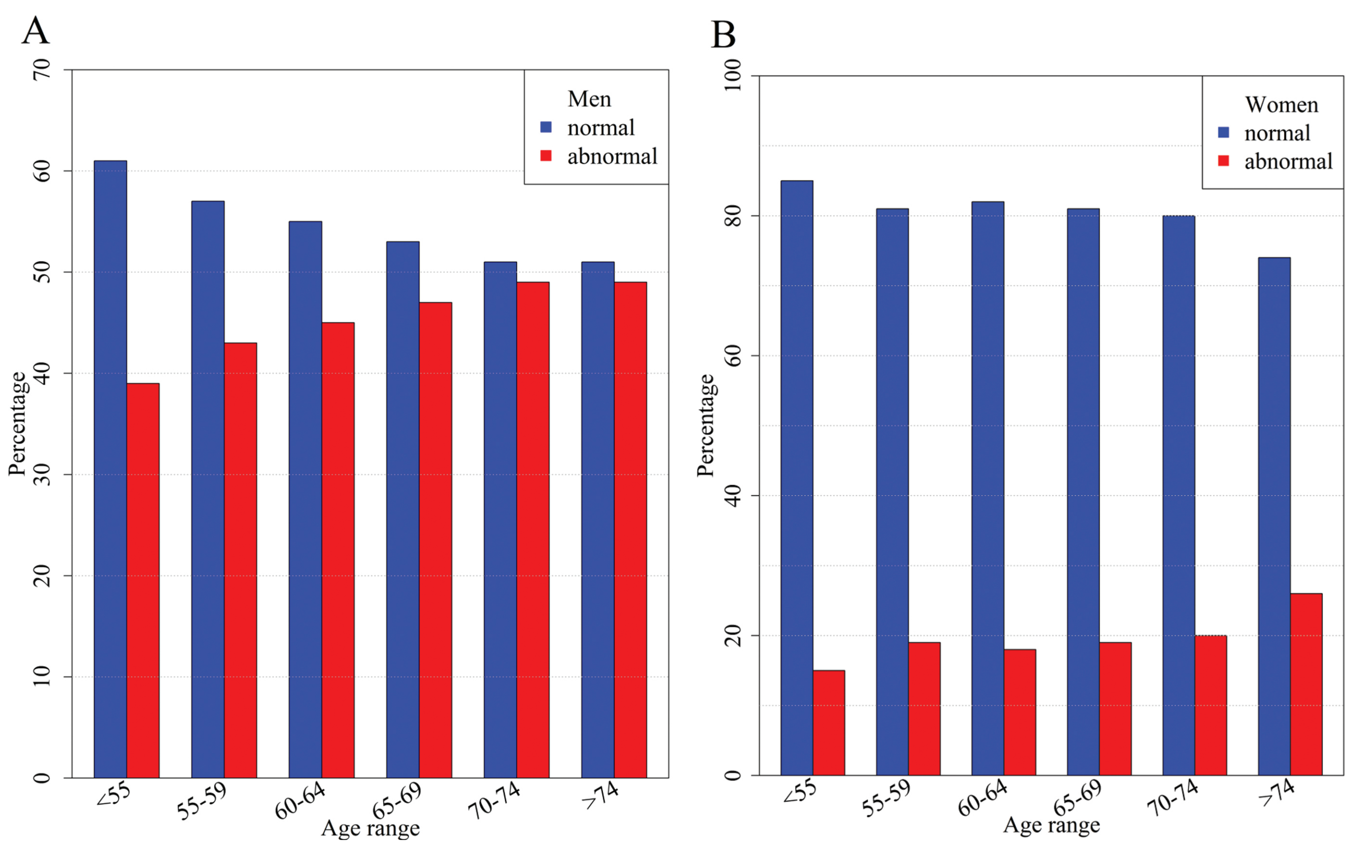


**Fig. (4).** Percentage of SPECT findings in men (**A**) and women (**B**) stratified by age. Normal is referred to SSS ≤3 and abnormal to SSS >3.

**Table 3. Demographic data and imaging findings by age group.**

| - | Patients (n) | Age, Years (range) | Abnormal SPECT, n (%) |
|---|---|---|---|
| **Men** | 1232 | 47±6.4 (<55) | 478 (39) |
| | 822 | 57±1.4 (55-59) | 348 (43) |
| | 1006 | 62±1.4 (60-64) | 430 (45) |
| | 980 | 67±1.4 (65-69) | 416 (47) |
| | 781 | 72±1.5 (70-74) | 337 (49) |
| | 665 | 78±3.1 (>74) | 277 (49) |
| **Women** | 527 | 47±6.7 (<55) | 80 (15) |
| | 375 | 57±1.4 (55-59) | 73 (19) |
| | 445 | 62±1.4 (60-64) | 78 (18) |
| | 441 | 67±1.4 (65-69) | 85 (19) |
| | 370 | 72±1.4 (70-74) | 74 (20) |
| | 351 | 79±3.1 (>74) | 92 (26) |

**Table 4. Distribution of myocardial perfusion defect patterns by gender.**

| - | Reversible Defects (%) | Fixed Defects (%) | Mixed Defects (%) |
|---|---|---|---|
| **Suspected CAD** | | | |
| Total | 53 | 24 | 22 |
| Men | 53 | 24 | 23 |
| Women | 54 | 25 | 21 |
| **Known CAD** | | | |
| Total | 24 | 41 | 35 |
| Men | 23 | 42 | 35 |
| Women | 30 | 36 | 34 |

CAD, Coronary Artery Disease.

The distribution of perfusion defect type in subjects with suspected or known CAD is summarized in Table **4**. Of the 4678 subjects with no history of CAD, 20% had abnormal SPECT findings with a higher prevalence in men compared to women (26% *vs*. 12%, $p < 0.001$). The frequency of reversible perfusion defects was similar in men and women, (53% *vs*. 54%, $p = 0.52$). As expected, in the 3317 subjects with known CAD there was a major occurrence (62%) of abnormal SPECT with a higher prevalence in men compared to women (65% *vs*. 46%, $p < 0.001$). The rate of fixed (42% *vs*. 36%, $p = 0.11$) and mixed (35% *vs*. 34%, $p = 0.69$) myocardial perfusion defects was comparable in men and women.

## 4. DISCUSSION

### 4.1. Database System

The relational database PostgreSQL is a tool that has grown in recent years, and it is among the most popular database management systems [68]. Because PostgreSQL is free and widely supported, it is employed in several fields of research. This tool has been used to monitor and evaluate data quality in institutions with complex and multiple studies [69], and to create a tool for physicians to explore health claims data with regard to adverse drug reactions [70].

The validation tests performed in our database system highlighted that it is stable and maintains the integrity of the data over time. The results of the time analysis obtained for different users, query and connections showed that the system does not depend significantly on computer features, networks and connections tested. The comparison between our database system and Microsoft Access, demonstrated that the execution times of queries by this commercial database are longer than those obtained by our database. The statistical functionalities based on the integration with R, in particular, the great number of software packages available for it, has allowed us to have a system of storage and powerful data analysis without additional costs for academic users with respect to commercial software.

In addition to the economic aspect of the system, another advantage is represented by in-house software development, which has allowed us the database schema creation and the write file script based on the users' needs. On the other hand, our system re-introduces the widespread use of Excel spreadsheets in medical research. In fact, users can write data in spreadsheets that can be easily uploaded in the database as comma-separated values file. Downloading of data from the database is available in the same file format and, if required from users, it can be converted to others file formats (*e.g.* XLS).

### 4.2. Data Analysis

The analysis on data collected in our database, carried out for demonstration purposes, showed that a higher prevalence of men underwent SPECT imaging and this percentage was maintained during each temporal period. No evident trend toward imaging findings was found in both men and women. Previous studies suggested a progressive decline in the frequency of abnormal SPECT results from the early 1990s, however the rate of decline has been minimal in the second half of 2000s [71, 72]. These findings have been related to the appropriateness use criteria first introduced in 2005 and updated in 2009 to reduce the inappropriate use of SPECT imaging as an initial test in low-risk and intermediate-risk subjects [73-75].

In our study, when we considered patients stratified by age, the trend of abnormal SPECT was higher in the elderly, in both men and women. Of note, in patients with suspected CAD the percentage of abnormal findings was not negligible (*i.e.* 20%). This result is somewhat in disagreement with the previous investigation, reporting percentages of 10.4% and 4.4% during 2006-2010 and 2011-2012, respectively [76]. In addition, once men and women were considered separately, a double proportion of abnormal findings between them were observed. Our results also showed a greater prevalence of reversible perfusion defects in subjects with no history of CAD, with no statistically significant difference between genders.

As expected, the incidence of abnormal SPECT findings was higher in subjects with a known CAD, with a significant higher rate in men. Furthermore, in the overall patient population, we found a higher percentage of abnormal imaging studies than that observed in prior investigations [77, 78]. This diversity may be related to the different characteristics in the study population as directed by the appropriateness criteria.

The statistical analysis carried out is a simple example of the system performances. In fact, more articulated analyses may be performed, based on more complex queries and statistical properties of R. On the other hand, currently, our database contains data from cardiovascular patients and it is periodically updated. In the near future, the database system will be automatically updated and will contain clinical data from other departments, able to carry out data mining analysis.

## CONCLUSION

The development of our relational database provides a software tool for the storage and management of data in line with the current standard. Furthermore, software components used to realize the system were open source. During the validation test, no problem was encountered to connect to the database and for query and retrieval of data. The database system was stable and maintained the integrity of the data over time. The time analysis obtained for different users, query and connections showed that the system does not depend significantly on the connections and computer features used. The results obtained from a statistical analysis indicate a higher prevalence of abnormal SPECT imaging findings in male as compared to female gender in both subjects with suspected and known CAD. In particular, for patients without a history of CAD a not negligible percentage of abnormal findings were found. The next tasks will be to develop a web interface for the automatic data entry in our system and to extend our software tools towards medical applications other than SPECT cardiac imaging.

## LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| CAD | = | Coronary Artery Disease |
| DDL | = | Data Description language |
| IP | = | Internet Protocol |
| LV | = | Left Ventricular |
| SPECT | = | Single-photon Emission Computed Tomography |
| SSL | = | Secure Sockets Layer |
| SSH | = | Secure Shell |
| SRS | = | Summed Rest Score |
| SDS | = | Summed Difference Score |
| SD | = | Standard Deviation |

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The review committee of University of Naples Federico II provided ethical approval for the study (Protocol number 110/17), Italy.

## HUMAN AND ANIMAL RIGHTS

No animals were used in this study. The reported experiments on humans were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional national), and with the Helsinki Declaration of 1975, as revised in 2008 (http://www.wma.net/).

## CONSENT FOR PUBLICATION

Written informed consent was obtained from all the subjects.

## AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article will be provided on request.


## FUNDING

This work has been partially funded by the CNR Project: *Invecchiamento*, Italy National Reform Program (NPR 2011-2013).


## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.


## ACKNOWLEDGEMENTS

Special thanks to Mr. L. De Luca, a technician at CNR-IBB, for his contribution in the validation tests.


## REFERENCES


[1] Timmis A, Townsend N, Gale C, *et al.* European society of cardiology: Cardiovascular disease statistics 2017. Eur Heart J 2018; 39(7): 508-79. [http://dx.doi.org/10.1093/eurheartj/ehx628] [PMID: 29190377]

[2] Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med 2016; 4(13): 256. [http://dx.doi.org/10.21037/atm.2016.06.33] [PMID: 27500157]

[3] Mozaffarian D, Benjamin EJ, Alan S. Executive summary: Heart disease and stroke statistics - 2016 update: A report from the American heart association. Circulation 2016; 133: 447-54. [http://dx.doi.org/10.1161/CIR.0000000000000366]

[4] Lloyd-Jones DM, Leip EP, Larson MG, *et al.* Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. Circulation 2006; 113(6): 791-8. [http://dx.doi.org/10.1161/CIRCULATIONAHA.105.548206] [PMID: 16461820]

[5] Stamler J, Neaton JD. The Multiple Risk Factor Intervention Trial (MRFIT)-importance then and now. JAMA 2008; 300(11): 1343-5. [http://dx.doi.org/10.1001/jama.300.11.1343] [PMID: 18799447]

[6] Roger VL, Go AS, Lloyd-Jones DM, *et al.* Executive summary: heart disease and stroke statistics-2012 update: a report from the American Heart Association. Circulation 2012; 125(1): 188-97. [http://dx.doi.org/10.1161/CIR.0b013e3182456d46] [PMID: 22215894]

[7] Sidney S, Quesenberry CP Jr, Jaffe MG, *et al.* Recent trends in cardiovascular mortality in the United States and public health goals. JAMA Cardiol 2016; 1(5): 594-9. [http://dx.doi.org/10.1001/jamacardio.2016.1326] [PMID: 27438477]

[8] Lloyd-Jones DM. Slowing progress in cardiovascular mortality rates: you reap what you sow. JAMA Cardiol 2016; 1(5): 599-600. [http://dx.doi.org/10.1001/jamacardio.2016.1348] [PMID: 27438674]

[9] Meyer RJ. Commentary on R&D trends away from general medicine/cardiovascular drugs: Can the FDA help reverse the trend? Clin Pharmacol Ther 2017; 102(2): 186-8. [http://dx.doi.org/10.1002/cpt.735] [PMID: 28636269]

[10] Iskandrian AE, Dilsizian V, Garcia EV, *et al.* Myocardial perfusion imaging: Lessons learned and work to be done-update. J Nucl Cardiol 2018; 25(1): 39-52. [http://dx.doi.org/10.1007/s12350-017-1093-7] [PMID: 29110288]

[11] Acampa W, Rozza F, Zampella E, *et al.* Warranty period of normal stress myocardial perfusion imaging in hypertensive patients: A parametric survival analysis. J Nucl Cardiol 2018. [http://dx.doi.org/10.1007/s12350-018-1285-9] [PMID: 29679222]

[12] Petretta M, Acampa W, Daniele S, *et al.* Long-Term survival benefit of coronary revascularization in patients undergoing stress myocardial perfusion imaging. Circ J 2016; 80(2): 485-93. [http://dx.doi.org/10.1253/circj.CJ-15-1093] [PMID: 26686993]

[13] Petretta M, Cuocolo A. Screening asymptomatic patients with type 2 diabetes is recommended: Pro. J Nucl Cardiol 2015; 22(6): 1225-8. [http://dx.doi.org/10.1007/s12350-015-0250-0] [PMID: 26391499]

[14] Sabharwal NK. State of the art in nuclear cardiology. Heart 2017; 103(10): 790-9. [http://dx.doi.org/10.1136/heartjnl-2015-308670] [PMID: 27920047]

[15] Green R, Cantoni V, Petretta M, *et al.* Negative predictive value of stress myocardial perfusion imaging and coronary computed tomography angiography: A meta-analysis. J Nucl Cardiol 2017. [PMID: 28205072]

[16] Knuuti J, Ballo H, Juarez-Orozco LE, *et al.* The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. Eur Heart J 2018; 39(35): 3322-30. [http://dx.doi.org/10.1093/eurheartj/ehy267] [PMID: 29850808]

[17] Piccinelli M, Garcia EV. advances in single-photon emission computed tomography hardware and software. Cardiol Clin 2016; 34(1): 1-11. [http://dx.doi.org/10.1016/j.ccl.2015.06.001] [PMID: 26590775]

[18] Alexiou S, Georgoulias P, Angelidis G, *et al.* Myocardial perfusion and left ventricular quantitative parameters obtained using gated myocardial SPECT: Comparison of three software packages. J Nucl Cardiol 2018; 25(3): 911-24. [http://dx.doi.org/10.1007/s12350-016-0730-x] [PMID: 27873167]

[19] Germano G, Kavanagh PB, Waechter P, *et al.* A new algorithm for the quantitation of myocardial perfusion SPECT. I: technical principles and reproducibility. J Nucl Med 2000; 41(4): 712-9. [PMID: 10768574]

[20] Berman DS, Kang X, Van Train KF, *et al.* Comparative prognostic value of automatic quantitative analysis versus semiquantitative visual analysis of exercise myocardial perfusion single-photon emission computed tomography. J Am Coll Cardiol 1998; 32(7): 1987-95. [http://dx.doi.org/10.1016/S0735-1097(98)00501-4] [PMID: 9857883]

[21] PostgreSQL. Available from: https://www.postgresql.org/

[22] Stonebraker M, Hanson EN, Potamianos S. The POSTGRES Rule Manager. IEEE Trans Softw Eng 1988; 14: 897-907. [http://dx.doi.org/10.1109/32.42733]

[23] Stonebraker M, Rowe LA, Hirohama M. The implementation of POSTGRES. IEEE Trans Knowl Data Eng 1990; 2: 125-42. [http://dx.doi.org/10.1109/69.50912]

[24] Silva S, Gouveia-Oliveira R, Maretzek A, *et al.* EURISWEB-Web-based epidemiological surveillance of antibiotic-resistant pneumococci in day care centers. BMC Med Inform Decis Mak 2003; 8: 3-9.

[25] McSparron H, Blythe MJ, Zygouri C, Doytchinova IA, Flower DR. JenPep: a novel computational information resource for immunobiology and vaccinology. J Chem Inf Comput Sci 2003; 43(4): 1276-87. [http://dx.doi.org/10.1021/ci030461e] [PMID: 12870921]

[26] Herskovits EH, Owis MI, Chen R. Integrating data-mining support into a brain-image database using open-source components. Adv Med Sci 2008; 53(2): 172-81. [http://dx.doi.org/10.2478/v10039-008-0009-9] [PMID: 18467275]

[27] Massaut J, Reper P. Open source electronic health record and patient data management system for intensive care. Stud Health Technol Inform 2008; 141: 139-45. [PMID: 18953134]

[28] Staib F, Krupp M, Maass T, *et al.* CellMinerHCC: a microarray-based expression database for hepatocellular carcinoma cell lines. Liver Int 2014; 34(4): 621-31. [http://dx.doi.org/10.1111/liv.12292] [PMID: 24016071]

[29] Austin T, Sun S, Lim YS, *et al.* An electronic healthcare record server implemented in PostgreSQL. J Healthc Eng 2015; 6(3): 325-44. [http://dx.doi.org/10.1260/2040-2295.6.3.325] [PMID: 26753438]

[30] Guien C, Fabre A, Lagarde A, *et al.* OISO, automatic treatment of patients management in oncogenetics. Bull Cancer 2017; 104(7-8): 602-7. [http://dx.doi.org/10.1016/j.bulcan.2017.06.003] [PMID: 28689638]

[31] Singh H, Yadav G, Mallaiah R, *et al.* iNICU - Integrated neonatal care unit: capturing neonatal journey in an intelligent data way. J Med Syst 2017; 41(8): 132. [http://dx.doi.org/10.1007/s10916-017-0774-8] [PMID: 28748430]
[32] Tatikonda VK, El-Ocla H. BLOODR: blood donor and requester mobile application. MHealth 2017; 3: 40. [http://dx.doi.org/10.21037/mhealth.2017.08.08] [PMID: 29184892]
[33] Stripelis D, Ambite JL, Chiang YY, Eckel SP, Habre R. A Scalable data integration and analysis architecture for sensor data of pediatric asthma. Proc Int Conf Data Eng 2017; 2017: 1407-8. [http://dx.doi.org/10.1109/ICDE.2017.198] [PMID: 29731601]
[34] Santesoft PACS and DICOM software. Available from: http://www.santesoft.com/downloads.html
[35] Open Source Clinical Image and Object Management. Available from: https://www.dcm4che.org/
[36] Brown MS, Shah SK, Pais RC, *et al.* Database design and implementation for quantitative image analysis research. IEEE Trans Inf Technol Biomed 2005; 9(1): 99-108. [http://dx.doi.org/10.1109/TITB.2004.837854] [PMID: 15787012]
[37] Lee WJ, Yang CY, Liu KL, Liu HM, Ching YT, Chen SJ. Establishing a web-based DICOM teaching file authoring tool using open-source public software. J Digit Imaging 2005; 18(3): 169-75. [http://dx.doi.org/10.1007/s10278-005-5171-z] [PMID: 15924271]
[38] Evangelista N, Camapum J, Amemiya E. Communication and storage of digital medical images in database. Conf Proc IEEE Eng Med Biol Soc 2005; 5: 5471-4. [http://dx.doi.org/10.1109/IEMBS.2005.1615721] [PMID: 17281491]
[39] Guliato D, de Melo EV, Rangayyan RM, Soares RC. POSTGRESQL-IE: an image-handling extension for PostgreSQL. J Digit Imaging 2009; 22(2): 149-65. [http://dx.doi.org/10.1007/s10278-007-9097-5] [PMID: 18214614]
[40] Prado TC, de Macedo DDJ, Dantas MAR, von Wangenheim A. Optimization of PACS data persistency using indexed hierarchical data. J Digit Imaging 2014; 27(3): 297-308. [http://dx.doi.org/10.1007/s10278-013-9665-9] [PMID: 24402455]
[41] PostgreSQL Tools. Available from: https://www.pgadmin.org/
[42] The CentOS Project. Available from: https://www.centos.org/
[43] vSphere Hypervisor. Available from: http://www.vmware.com/products/vsphere-hypervisor.html
[44] pgAdmin Main Window. Available from: https://www.pgadmin.org/docs/pgadmin3/1.22/main.html
[45] Query tool. Available from: https://www.pgadmin.org/docs/pgadmin3/1.22/query.html
[46] Graphical Query builder. Available from: https://www.pgadmin.org/docs/pgadmin3/1.22/gqb.html
[47] CentOS. Available from: https://wiki.centos.org/HowTos/Network/IPTables
[48] PostgreSQL 9.2.24 Documentation. Chapter 19. Client Authentication. Available from: https://www.postgresql.org/docs/9.2/static/auth-pg-hba-conf.html
[49] Using pgAdmin III. Available from: https://www.pgadmin.org/docs/pgadmin3/1.22/connect.html
[50] SSL. https://www.ssl.com/?s=protocol
[51] 17.9. Secure TCP/IP Connections with SSL. Available from: https://www.postgresql.org/docs/9.2/static/ssl-tcp.html
[52] SSH Protocol. https://www.ssh.com/ssh/protocol/
[53] 17.10. Secure TCP/IP Connections with SSH Tunnels. Available from: https://www.postgresql.org/docs/9.2/static/ssh-tunnels.html
[54] Diamond GA, Staniloff HM, Forrester JS, Pollock BH, Swan HJC. Computer-assisted diagnosis in the noninvasive evaluation of patients with suspected coronary artery disease. J Am Coll Cardiol 1983; 1(2 Pt 1): 444-55. [http://dx.doi.org/10.1016/S0735-1097(83)80072-2] [PMID: 6338081]
[55] Juba S, Vannahme S, Volkov A. Learning PostgreSQL. United Kingdom: Packt Publishing Limited 2016.
[56] Kaur M, Shaik B. PostgreSQL Development Essentials. United Kingdom: Packt Publishing Limited 2016.
[57] The R Project for Statistical Computing. Available from: https://www.r-project.org/
[58] Package 'RPostgreSQL'. Available from: https://cran.r-project.org/web/packages/RPostgreSQL/RPostgreSQL.pdf
[59] Haerder T, Reuter A. Principles of transaction-oriented database recovery. ACM Comput Surv 1983; 15: 287. [http://dx.doi.org/10.1145/289.291]
[60] PostgreSQL 7.3.2 Reference Manual. Available from: https://www.postgresql.org/files/documentation/pdf/7.3/reference-7.3.2-A4.pdf
[61] Sys.time. Available from: https://www.rdocumentation.org/packages/base/versions/3.4.0/topics/Sys.time
[62] Verberne HJ, Acampa W, Anagnostopoulos C, *et al.* EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision. Eur J Nucl Med Mol Imaging 2015; 42(12): 1929-40. [http://dx.doi.org/10.1007/s00259-015-3139-x] [PMID: 26290421]
[63] Hachamovitch R, Berman DS, Shaw LJ, *et al.* Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation 1998; 97(6): 535-43. [http://dx.doi.org/10.1161/01.CIR.97.6.535] [PMID: 9494023]
[64] Klocke FJ, Baird MG, Lorell BH, *et al.* American heart association; American society for nuclear cardiology. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging-executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (ACC/AHA/ASNC Committee to revise the 1995 guidelines for the clinical use of cardiac radionuclide imaging). Circulation 2003; 108(11): 1404-18. [PMID: 12975245]
[65] Berman DS, Abidov A, Kang X, *et al.* Prognostic validation of a 17-segment score derived from a 20-segment score for myocardial perfusion SPECT interpretation. J Nucl Cardiol 2004; 11(4): 414-23. [http://dx.doi.org/10.1016/j.nuclcard.2004.03.033] [PMID: 15295410]
[66] psqlODBC - PostgreSQL ODBC driver. Available from: https://odbc.postgresql.org/
[67] Access 2010. Available from: https://docs.microsoft.com/en-us/previous-versions/office/developer/office-2010/ff604965(v=office.14)
[68] DB-Engines. Available from: https://db-engines.com/
[69] Schmidt CO, Schössow J, Radke D, Krabbe C, Albers M, Henke J. Square$^2$-A web application for data monitoring in epidemiological and clinical studies. Stud Health Technol Inform. 2017; 235: 549-53.
[70] Edlinger D, Sauter SK, Rinner C, *et al.* JADE: a tool for medical researchers to explore adverse drug events using health claims data. Appl Clin Inform 2014; 5(3): 621-9. [http://dx.doi.org/10.4338/ACI-2014-04-RA-0036] [PMID: 25298803]
[71] Rozanski A, Gransar H, Hayes SW, *et al.* Temporal trends in the frequency of inducible myocardial ischemia during cardiac stress testing: 1991 to 2009. J Am Coll Cardiol 2013; 61(10): 1054-65. [http://dx.doi.org/10.1016/j.jacc.2012.11.056] [PMID: 23473411]
[72] Duvall WL, Rai M, Ahlberg AW, O'Sullivan DM, Henzlova MJ. A multi-center assessment of the temporal trends in myocardial perfusion imaging. J Nucl Cardiol 2015; 22(3): 539-51. [http://dx.doi.org/10.1007/s12350-014-0051-x] [PMID: 25652080]
[73] Iskandrian AE, Hage FG. Declining frequency of ischemia detection using stress myocardial perfusion imaging. J Am Coll Cardiol 2013; 61(10): 1066-8. [http://dx.doi.org/10.1016/j.jacc.2012.12.009] [PMID: 23473412]
[74] Brindis RG, Douglas PS, Hendel RC, *et al.* ACCF/ASNC appropriateness criteria for single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI): a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group and the American Society of Nuclear Cardiology endorsed by the American Heart Association. J Am Coll Cardiol 2005; 46(8): 1587-605. [http://dx.doi.org/10.1016/j.jacc.2005.08.029] [PMID: 16226194]
[75] Hendel RC, Berman DS, Di Carli MF, *et al.* ACCF/ASNC/ACR/AHA/ASE/SCCT/SCMR/SNM 2009 appropriate use criteria for cardiac radionuclide imaging: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular

Magnetic Resonance, and the Society of Nuclear Medicine. Circulation 2009; 119(22): e561-87.
[PMID: 19451357]

[76] Jouni H, Askew JW, Crusan DJ, Miller TD, Gibbons RJ. Temporal trends of single-photon emission computed tomography myocardial perfusion imaging in patients without prior coronary artery disease: A 22-year experience at a tertiary academic medical center. Am Heart J 2016; 176: 127-33.
[http://dx.doi.org/10.1016/j.ahj.2016.03.014] [PMID: 27264231]

[77] Jouni H, Askew JW, Crusan DJ, Miller TD, Gibbons RJ. Temporal trends of single-photon emission computed tomography myocardial perfusion imaging in patients with coronary artery disease: A 22-year experience from a tertiary academic medical center. Circ Cardiovasc Imaging 2017; 10(7): e005628.
[http://dx.doi.org/10.1161/CIRCIMAGING.116.005628] [PMID: 28687538]

[78] Beller GA. Decrease in the frequency of stress-induced ischemia over the past two decades. J Nucl Cardiol 2013; 20(3): 322-3.
[http://dx.doi.org/10.1007/s12350-013-9720-4] [PMID: 23636967]