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VALIDATION OF ECG-BASED, POST-MYOCARDIAL INFARCTION (POST-MI) ESTIMATION OF NON-VIABLE MYOCARDIUM THROUGH TECHNETIUM-99M METHOXYISOBUTYLISONITRILE SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (TC-99M MIBI SPECT)

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ABSTRACT

Objective: To validate ECG-based, post-myocardial infarction (post-MI) estimation of non-viable myocardium through Technetium-99m methoxyisobutylisonitrile single photon emission computed tomography (Tc-99m MIBI SPECT).

Study Design: Retrospective, diagnostic accuracy study.

Place and Duration of Study: Nuclear Cardiology Department, Armed Forces Institute of Cardiology & National Institute of Heart Diseases (AFIC & NIHD), Rawalpindi, from Nov 2018 to Feb 2019.

Methodology: This retrospective, diagnostic accuracy study employing consecutive sampling included 142 post-MI patients referred for SPECT myocardial perfusion imaging (MPI). Patients with history of non-ST elevation MI (NSTEMI), bundle branch blocks and unclear/abnormal ECG were excluded. After initial scrutiny, test outcomes data from 105 finally selected patients who underwent the index test (12-lead ECG) and the gold/reference standard (SPECT MPI) were analyzed through 2x2 contingency table.

Results: Age and gender distribution in selected patients (n=105) showed an age range of 29 to 90 years (mean age = 58.16 years ± 10.69) and male to female ratio of 6:1 (90 males and 15 females). A 2x2 contingency table was used to compute different 12-lead ECG (index test) parameters. Calculated values were – Sensitivity (Sn) = 56.25%, Specificity (Sp) = 36.58%, Positive predictive value (PPV) = 58.06%, Negative predictive value (NPV) = 34.88% and Accuracy = 48.57%.

Conclusion: 12-lead ECG – on validation against SPECT MPI – was found to be a bad test for estimation of non-viable myocardium in post-MI patients.

Keywords: ECG, myocardial infarction, Sensitivity and specificity, Single photon emission computed tomography, SPECT, Viable myocardium.

INTRODUCTION

Twelve-lead ECG remains the most frequently used modality for diagnosis of patients with suspected myocardial infarction (MI)/ischaemic heart disease (IHD) and the management of diagnosed post-MI/IHD patients. All clinicians treating post-MI patients are well aware that ECG changes are not always reliable for predicting the presence of non-viable myocardium in post-MI patients[1]. This unpredictability is further compounded in patients with non-ST elevation MI (NSTEMI), bundle branch blocks and other ECG abnormalities and has been recognised and published in scientific literature. However, as generally there is paucity of data from our part of the world in support (or otherwise) of large studies based on European and American populations, if management decisions/guidelines in our population are to rely on ECG findings, it is important to conduct studies analysing the applicability of published international data in our patients and develop consensus; specially in terms of the use of ECG for estimation of non-viable myocardium in post-MI patients.

On literature survey, no studies from our region could be found, which validated the 12-lead ECG based estimation of the presence of

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non-viable myocardium in post-MI patients against positron emission tomography (PET), the gold standard for viability[1]; or myocardial perfusion imaging (MPI) with single photon emission computed tomography (SPECT)[3], the next best functional imaging modality, with close correlation in results with the gold standard[4]. Other tests used for myocardial viability assessment include Dobutamine stress echo (DSE) and cardiac magnetic resonance imaging (CMRI), the most recent arrival in the arena, which is being viewed as another excellent tool for assessment of myocardial viability[5].

As highlighted above, a majority of cardiac patients in today's practice seek partial or complete revascularisation at some stage of follow-up and published studies suggest that up to 50% of the patients with severely impaired ventricles have hibernating myocardium[6], so it is important to assess myocardial viability prior to this expensive and invasive undertaking[7].

Due to limited availability of PET scanning in Pakistan, this study employed MPI with SPECT as the available gold/reference standard. SPECT MPI is known to have very good correlation with PET results[8] and may provide preliminary evidence based on data from the local population about the validity of ECG-based estimation of the presence of non-viable/viable myocardium in post-MI patients and help scientifically evaluate the pros and cons of this approach.

In future, as all centres of excellence in cardiology in the country have attached Nuclear Cardiology departments doing MPI with SPECT, this study may serve as a starting point for multicentre research that may help formulate the best management strategy for cardiac patients in the country.

METHODOLOGY

The study is a retrospective, diagnostic accuracy study employing consecutive sampling, where in data from 142 post-MI patients of any age/gender referred to Nuclear Cardiology Department of the Armed Forces Institute of Cardiology & National Institute of Heart Diseases (AFIC & NIHD), Rawalpindi for MPI through SPECT technique from 4 Nov 2018 to 14 Feb 2019 were included. Patients with history of non-ST elevation myocardial infarction (NSTEMI), bundle branch blocks, unclear ECG trace or any ECG abnormalities which confound the findings seen in post-MI patients were excluded. After initial scrutiny of data and applying exclusion criteria, the final number of patients dropped to 105. Data from these subjects, which constituted 90 males and 15 females (n=105) were finally analysed.

Approval of the institutional ethical committee was obtained. All personal identifiers were removed and the subjects were assigned unique numbers for data analysis. Only the subjects' age, gender, diagnoses and ECG/MPI report details were included in data analysis for the study. As currently recommended, STARD checklist was used for writing this study.

All subjects underwent 12-lead ECG with standard lead placement and voltage standardisation. Representative traces of all limb and augmented limb leads and precordial leads containing at least 4-5 QRS complexes each were obtained. 12-lead ECG of each subject was assessed by an experienced observer, who reported the findings. Presence of significant Q waves in limb or augmented limb leads and/or presence of poor R waves in anterior chest leads were considered a positive test outcome and were accepted as evidence of non-viable LV myocardium. Absence of Q and/or absence of poor R waves was considered a negative test outcome. Subsequent or prior to the ECG, the same day, all subjects underwent Tc-99m MIBI SPECT employing single day Rest-stress or Rest-rest protocols. Either exercise or pharmacological stress protocols, as indicated, were used. Rest-Rest protocol employed nitrate augmentation with sublingual Nitroglycerine. Each subject was injected a maximum of 10.0 mCi (370 MBq) of Tc-99m MIBI intravenously for the rest phase (depending on patient weight), followed by a fatty meal and supine image acquisition using a dual-head, dedicated cardiac SPECT gamma camera system

(Philips Cardio MD ® and/or IS2 Positron ®), interfaced with an acquisition computer. For the stress phase, a maximum of 30.0 mCi (1100 MBq) of Tc-99m MIBI was injected (depending on patient weight) during exercise or adenosine infusion, as indicated; followed by a fatty meal and supine image acquisition. Myocardial perfusion SPECT scan of each subject was assessed by an experienced observer, who reported the findings. A non-viable defect was considered a positive test outcome if it involved more than 10% of the entire LV myocardium. A non-viable defect involving 10% or less of the entire LV myocardium was considered to be a negative test outcome.

Statistical analysis of test outcomes regarding estimation of non-viable myocardium by both tests - 12-lead ECG (index test) and SPECT MPI (reference/gold standard) – was done using 2x2 contingency table and standard formulae were used to calculate different index test parameters. Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and accuracy were all calculated. Descriptive statistics were used to describe rest of the data.

RESULTS

Age and gender distribution of data from 105 post-MI patients (n=105) showed a male to female ratio of 6:1 (90 males and 15 females), with age range of 29 to 90 years (mean age = 58.16 years ± 10.69). Average male age was 58.62 years ± 10.92 (range of 29 to 90 years) and average female age was 55.4 years ± 9.04 (range of 40 to 72 years). Test outcomes, both positive or negative, from each of the subjects who underwent the index test (12-lead ECG) and the gold / reference standard (SPECT MPI) were put in a 2x2 contingency table and these quantities were used to calculate different test parameters.

Table: Statistical analysis of test outcomes by 2 x 2 contingency table.

Tests With Outcomes	MPI + (+ve reference standard)	MPI - (-ve reference standard)
ECG + (+ve index test)	36	26
ECG - (-ve index test)	28	15

Using table and standard formulae, the values of Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and accuracy were found to be: Sensitivity (Sn) = 56.25%, Specificity (Sp) = 36.58%, Positive predictive value (PPV) = 58.06%, Negative predictive value (NPV) = 34.88%, Accuracy = 48.57%.

DISCUSSION

Assessment of non-viable/viable myocardium is integral to the process of taking patient management decisions post-MI as natural outcomes and choice of available revascularization options vary for different patient sub-sets[10]. With tremendous growth in the field of interventional cardiology and advancements in cardiac surgical practice the requirement for an objective, reliable and readily available modality for the assessment of non-viable/viable myocardium has assumed paramount importance[11]. MPI with SPECT technique fits well in this role in most regions of the world but there has always been a school of thought in the cardiology community who put a lot of trust in the conventional 12-lead ECG and do not wish to go beyond stress ECG/ETT and 2-D echo, with/without CT or conventional coronary angiography in taking their patient management decisions. The inadequacy of this approach has been amply highlighted in published international studies, which support the use of MPI based management approach and underscore that this does not add to patient management expenditure but rather proves cost-effective for the health care system in the long run[12].

ECG changes in ST elevation MI (STEMI)/ transmural MI are known to evolve from ST segment elevation seen on acute onset to return of ST segment to baseline over many hours to days, followed by appearance of Q wave with T inversion and subsequent persistence of Q wave with return of T wave to its normal upright form. Typically, ECG from an old STEMI / transmural MI patient (with a few month old history of the event) shows Q waves in leads representing the area of infarct/non-viable myocardium; like leads II, III and aVF in a case of inferior STE/transmural MI and the number of leads showing infarct related changes give a clue to the extent of infarct/non-viable myocardium[13].

Functional and molecular imaging modalities, like MPI, cardiac magnetic resonance (CMR)[14] and the perfusion gold standard, PET[15], are employed for the detection of non-viable myocardium. In MPI and PET, no accumulation of the radiopharmaceutical(s) used despite intact blood supply is seen in the non-viable muscle tissue due to the cessation of metabolic processes at the cellular level. Such areas (termed photopenic due to decreased photon density) stand out against adjacent viable/normal tissue, which takes up the radiopharmaceutical and the gamma rays emitted therefrom are detected by the SPECT/PET scanner to form count based images used for scan interpretation and estimation of non-viable and viable muscle tissue.

This study found a much higher number of male patients in the selected referred patients' dataset (male to female preponderance of 6:1). This may signify the higher incidence of IHD and MI in the male gender but is much different from another local study by Jafary *et al*. published in 2007 evaluating around 1400 patients, which showed a male to female ratio of approximately 2:1[16]. Hence a more cogent reason for this observation may be from the study setting wherein medical treatment entitlement of a majority of veterans is for self only in our military budget funded cardiology institute, with their families' medical treatment primarily being managed by other hospitals run by the respective veterans' welfare organisations.

The study utilized retrospective data from post-STEMI/transmural MI patients and evaluated only those patients as positive whose extent of non-viable myocardium employing MPI (the reference standard) was greater than 10% of the entire LV myocardium, as 12-lead ECG (the index test) could potentially miss smaller areas of non-viable myocardium and this may have led to its compromised diagnostic accuracy assessment. SPECT MPI which was employed as gold/reference standard for the study detected non-viable myocardium in all patients with a history of STEMI / transmural MI but corresponding to the evaluation criteria of only accepting as positive test outcome an extent of non-viable myocardium greater than 10% of the entire LV myocardium (in order to avoid putting the test being validated to a potential disadvantage), small non-viable defects with a size of 2 segments or less out of 20 (employing a 20 segment polar map/model) were disregarded and marked as negative test outcome.

There are difficulties in comparison of results from this study with other studies due to paucity of published data that have evaluated the sensitivity, specificity, accuracy and other parameters of 12-lead ECG for its ability to assess non-viable myocardium but conversely, sizable published validation data are available for its ability to assess myocardial ischaemia. The validation of 12-lead ECG as index test, however, in majority of these studies has been against coronary angiography as gold/reference standard, which is unjustified[17,18], as being an anatomical imaging modality, coronary angiography is unable to detect both myocardial viability and/or ischaemia. Some studies in literature have resorted to PET, MPI, functional MRI, cardiac magnetic resonance (CMR) or stress echo as reference standards for evaluating 12-lead ECG's ability to assess myocardial viability and/or ischaemia and this study is an addition to this pool in our regional context[19].

The values of Sn, Sp, PPV, NPV and accuracy of 12-lead ECG based assessment of non-viable myocardium calculated in this study are similar to present day guidelines and in agreement with current, established medical practice, which do not support the use of 12-lead ECG in isolation for the estimation of non-viable myocardium. However there are studies like a comparative evaluation with CMR on 550 patients published by Lee *et al*. in 2016, which support of the use of 12-lead ECG for estimation of the extent of transmural MI and non-viable myocardium in larger infarcts[20]. The investigators found that infarct size of 9.0 ± 6.4% did not show any ECG changes, compared to infarct size of 14.0 ± 7.7% which showed a single infarct-related ECG change and the number of ECG changes increased with progressively increasing infarct size. These results support our consideration in designing this study about the ECG's potential to miss smaller infarcts and hence our evaluation of test outcomes as positive only if the patients had an infarct size of more than 10% of LV myocardium.

The limitations of this study include a relatively small sample size and non-random sampling technique, ECG and MPI interpretation by only one observer and the use of MPI SPECT with Tc-99m MIBI as gold standard for viability estimation in lieu of PET, which can potentially lead to overestimation of non-viable myocardium.

The study was funded by Nuclear Cardiology Department at AFIC & NIHD, Rawalpindi from its own resources and no external grant was sought.

ACKNOWLEDGEMENT

The authors wish to express their gratitude to Brig Khadija Qamar, Head of the Department of Anatomy, Army Medical College, Rawalpindi & Editor of the Pakistan Armed Forces Medical Journal (PAFMJ) and her editorial staff for their cooperation and assistance extended presently and in the past; and would also like to endorse their appreciation for Mrs. Tasleem Akhter and Mr. Tasswar Iqbal Satti from Nuclear Cardiology Department, AFIC & NIHD, Rawalpindi for their help in data collection and tabulation, which greatly facilitated statistical analysis.

CONCLUSION

12-lead ECG on validation against SPECT MPI – was found to be a bad test for estimation of non-viable myocardium in post-MI patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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