Inovise 12L Interpretive Algorithm Statement of Validation and Accuracy

TECHNICAL REPORT NO. 1

Definitions

STEMI – ST Elevation acute MI as defined by the AHA/ACC guidelines. Angiographic evaluation and coronary catheterization interventions are indicated for patients with resting chest pain whose ECGs are positive for STEMI. ACC/AHA guidelines define ECG lead pairs and threshold limits for identification of STEMI.

nSTEMI – Any Acute MI where abnormal ST deviation does not meet ACC/AHA established thresholds for STEMI. It includes ECGs with borderline ST elevation, minimal ST elevation, marked ST depression, and those ECGs showing no STT abnormalities.

Borderline STEMI – Acute MI with ECG evidencing significantly abnormal ST deviations that do not meet ACC/AHA guideline thresholds for STEMI (e.g. contiguous lead combinations not identified by the guidelines or with ST deviation not quite meeting STEMI thresholds).

Minimal ST Elevation – Acute MI with ECG evidencing minimally abnormal ST deviations well below ACC/AHA guideline thresholds for STEMI.

Marked ST Depression – Acute MI with highly abnormal global ST depression and/or marked STE in lead aVR indicative of left main coronary artery occlusion or severe 3-vessel CAD.

STT Confounders – ECG evidence for one or more pathologies known to perturb the STT segment. The presence of these conditions obscures straightforward evaluation of ECG ST deviation and therefore are considered as "confounding" conditions.

- Left Bundle Branch Block (LBBB)
- Right Bundle Branch Block (RBBB)
- Left Ventricular Hypertrophy with Repolarization Abnormality (LVH w/Repol)
- Right Ventricular Hypertrophy (RVH)
- Bi-ventricular Hypertrophy (BVH)
- Left Anterior Fasicular Block (LAFB)
- Right Atrial Enlargement (RAE)

Performance Metrics – Sensitivity (Se) and Specificity (Sp)

In medical diagnostics, test sensitivity is the ability of a test to correctly identify those with the disease, whereas test specificity is the ability of the test to correctly identify those without the disease. If 100 patients known to have a disease were tested, and 43 test positive, then the test has 43% sensitivity. If 100 with no disease are tested and 96 return a negative result, then the test has 96% specificity. Sensitivity and specificity are prevalence-independent test characteristics, as their values are intrinsic to the test and do not depend on the disease prevalence in the population of interest.

Performance Metrics –Positive Predictive Value (PPV)

For diagnostic testing, the positive predictive value is the proportion of subjects with positive test results who are correctly diagnosed. It is a critical measure of the performance of a diagnostic method, as it reflects the probability that a positive test reflects the underlying condition being tested for.

Population Description

ECGs for evaluating Acute MI positives and negatives were collected from multiple hospitals, including large tertiary care facilities serving ethnically diverse urban populations and smaller community hospitals. Confirmation of acute MI was accomplished through evaluation of cardiac enzymes. ECGs collected for MI algorithm evaluation were acquired within eight hours of onset of chest pain to ensure the algorithm is trained and evaluated on ECGs from the early acute phase (either pre-hospital or upon hospital admission) when cardiac intervention to salvage myocardium is still indicated. The Acute MI negative population was assembled by collecting admitting ECGs from patients who were clinically evaluated and found to be negative for Acute MI on the basis of cardiac enzymes, angiography, or nuclear imaging studies.

STEMI

The Inovise 12L interpretive algorithm system has been demonstrated to effectively identify ST Elevation Acute MI (STEMI) according to the definitions provided by ACC/AHA guidelines. The Inovise 12L interpretive algorithm detects these acute MIs with a proven sensitivity of 77%, specificity of 99% and positive predictive value of 97% . When ECGs exhibiting STT confounders are excluded, sensitivity increases to 89%, specificity is maintained at 99%, resulting in PPV of 98%.

Borderline STEMI (bSTEMI)

Angiographic investigation of acute MI positive patients whose ECGs do not meet ACC/AHA criteria for STEMI reveals many instances where occlusive, culprit lesions were found. It is therefore clinically relevant for Acute MI patients having ECGs that exhibit borderline STE to be accurately identified and interventions to be considered. The Inovise 12L interpretive algorithm discerns, with high-specificity, patterns of borderline

Algorithm Accuracy for Detection of Acute MI

Table 1. Acute MI Performance without confounding conditions present

Total number of test ECGs: 1234
Method used to verify diagnosis: Cardiac enzymes and ST deviation

Diagnosis	N	Se (%)	Sp (%)	PPV (%)
Acute MI, STEMI	193	89	100	98
Acute MI, bSTEMI	45	47	100	88
Acute MI, Minimal STE	44	23	100	77
Acute MI, with Prior MI	141	33	99	84

Table 2. Acute MI Performance including presence of confounding conditions

Total number of test ECGs: 1894
Method used to verify diagnosis: Cardiac enzymes and ST deviation

Diagnosis	N	Se (%)	Sp (%)	PPV (%)
Acute MI, STEMI	359	77	99	97
Acute MI, bSTEMI	97	37	99	80
Acute MI, Marked STD	48	50	99	73
Acute MI, Minimal STE	88	19	99	65

ST elevation associated with acute MI. Borderline STEMI sensitivity is 37%, specificity is 99% and positive predictive value is 80%. When ECGs exhibiting STT confounders are excluded, sensitivity for these acute MIs increases to 47%, specificity is 99%, and PPV increases to 88%.

Marked ST Depression

The Inovise 12L interpretive algorithm evaluates patterns of ST depression following ACC/AHA and other published guidelines for identifying STEMI equivalent ischemia/injury (resulting from left main disease or high-grade 3-vessel CAD). The Inovise 12L interpretive algorithm sensitivity for this group is 50%, specificity is 99% and PPV is 73%.

Minimal STE

ECG identification of acute MI inherently relies upon evaluation of abnormal ST elevation or ST depression. The Inovise 12L interpretive algorithm also evaluates localizing patterns of ST elevation that may not meet definitions for STEMI or borderline STEMI. Algorithm sensitivity for this group is 19%, specificity is 99% and PPV is 65%. When ECGs exhibiting STT confounders are excluded, sensitivity for these acute MIs increases to 23%, specificity is 99%, and PPV increases to 77%.

Prior Myocardial Infarction (Prior MI)

Patients with a history of prior MI have an inherent higher clinical risk than those that have a negative history for MI. Prior MI positive patients have a lower ejection fraction and may be susceptible to developing potentially life-threatening arrhythmias. The Inovise 12L interpretive algorithm ability to identify Acute MI when evidence for prior MI exists on their ECG was evaluated. Sensitivity was shown to be 31%, specificity of 99%, and PPV of 91%.

Algorithm Accuracy for Rhythm Interpretation

Rhythm category	No. of ECGs tested	Sensitivity	Specificity %	Positive predictive value %
Sinus rhythms	1964	98.99	94.63	99.34
Atrial fibrillation	173	93.64	99.07	89.50
1st Degree AV Block	177	66.10	98.72	81.82
Ventricular Premature Complexes	175	87.50	96.66	69.37
Superventricular Premature Complexes	56	85.71	98.24	55.81

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