Evaluation of Orthogonal Vector Projection Method in ST Algorithm for Generating Differential Diagnoses of Chest Pain: A Pilot Study

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Abstract: Diagnosing chest pain can be a challenging process with potential misdiagnoses causing significant morbidity and mortality, and the associated healthcare cost and burden. As a potential solution to increase the diagnostic accuracy and rule out non-life-threatening conditions, we have evaluated the method known as orthogonal vector projection which is a part of the Select and Test (ST) algorithm for medical diagnosis, as a pilot study. Using a knowledgebase consisting of 12 diagnoses and 43 clinical features, we have evaluated 47 clinical cases by comparing the diagnosis given by a senior clinician to the diagnosis arrived by the orthogonal vector projection method.

1 INTRODUCTION

Chest pain is common physical complaint with a lifetime prevalence of 25% in the general population, resulting in common presentations to emergency departments (Thomsett et al, 2018), (Chew et al, 2016), (Cullen et al, 2015). While there are many possible causes of chest pain ranging from benign causes to life-threatening medical emergencies such as acute coronary syndrome (ACS), discriminating them can be difficult (Cullen et al, 2015), (Geyser et al, 2016). For example, it is known that between 50% to 80% of the time, patients with possible ACS are misdiagnosed and sent home without proper treatment (Geyser eta l, 2016); and about one third of patients who didn't have a diagnosis related to their chest pain, are known to be later diagnosed with ACS or die from cardiovascular disease (Fordyce et al, 2016). On the other hand, the benign causes of chest pain still often require evaluation including investigations amounting to healthcare cost of diagnosis which burdens patients and health care services (Cullen et al, 2015). Furthermore, clinicians are known to make diagnostic errors due to number of factors including fatigue and time pressure. Hence, use of diagnostic algorithm to improve diagnostic accuracy, mitigate the errors, and minimise unnecessary investigations, is highly desirable.

In this research work, we have used the method known as orthogonal vector projection of ST algorithm, which was introduced by (Fernando et al, 2016) and has been evaluated in generating differential diagnoses for psychiatric conditions.

In this study, two different evaluations were done to explore the potential use of the method for triaging (i.e., arriving at differential diagnoses prior to conducting investigations) and a diagnostic tool (i.e., arriving at diagnosis with all clinical features including investigation results).

2 ORTHOGONAL VECTOR PROJECTION METHOD (OVPM)

A given clinical presentation with a set of clinical features, requiring a diagnosis, is conceptualised as a binary vector in which, each feature is assigned a binary value to indicate if the feature is present or not in the patient. On the other hand, each potential diagnosis presented as a real vector corresponding to

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the set of clinical features, with each real element corresponding to respective clinical feature, being a relative weight assigned according to its diagnostic importance (i.e., a clinical feature which is highly indicative of the diagnosis is given a higher weight compared to one which is less indicative of the diagnosis). Using these vectors, a similarity measure with respect to each diagnosis is derived as follows.

Let n be the total number of clinical features,

$$\vec{L} = \begin{pmatrix} l_1 \\ \vdots \\ l_n \end{pmatrix} \text{ where, each element } l_i \in \{0,1\},$$

be the vector of clinical features,

$$\vec{D} = \begin{pmatrix} d_1 \\ \vdots \\ d_n \end{pmatrix} \text{ where, each element } d_i \in [0,1],$$

be a potential diagnosis (i.e., a column vector in the knowledge base) which satisfies,

$$\sum_{i=1}^{n} d_i = 1,$$

and we derive, $\vec{X}$ the Hadamard product (element-wise product)

$$\vec{X} = \vec{L} \circ \vec{D}.$$

Then using the similarity measure denoted as r is derived as follows,

$$r = \frac{\vec{X}.\vec{D}}{\left|\vec{D}\right|^2}$$

Where $\left|\vec{D}\right|$ is the length of the vector $\vec{D}$.

Suppose m is the number of total diagnoses, then the knowledgebase is a $n \times m$ matrix which consists of the column vectors corresponding to each diagnosis.

3 STUDY DESIGN AND DATA COLLECTION

A total of 12 diagnoses were carefully chosen along with the list of 43 clinical features consisting of physical symptoms, clinical examination findings and investigations. With the view of two potential use of the method as a triage tool, a separate set of vectors for diagnoses were created excluding investigation findings and redistributing the weights. The weights were assigned to each clinical feature for each diagnosis subjectively using clinical expertise and adjusted using test cases. The two knowledgebases are tabulated in the appendix.

Assuming a prevalence between 5-10% of the chest pain related diagnoses in emergency department, and a predetermined sensitivity and specificity of 80% for each and individual diagnosis, the estimated sample size was 980 participants, which was not feasible to achieve with the time and resources available. However, combining all diagnoses as one general diagnostic entity with their aggregated prevalence be more than 95%, with predetermined sensitivity and specificity of 92% for the general diagnostic entity, and with 8% of maximum marginal error and 95% confidence level, the required sample size was deemed as only 47 participants.

Therefore, evaluation of the orthogonal vector projection method was conducted as a pilot study to determine the general sensitivity and specificity for combined diagnoses as opposed to determining sensitivity and specificity for each individual diagnosis.

The diagnostic data (i.e., list of clinical features and the diagnosis given by a senior clinician) from the patients who were recruited for the study, was collected after obtaining ethics approval from Hunter New England Local Area Health District (John Hunter Hospital and Maitland Hospital) where the study was conducted over a period of 4 months. The recruitment data are summarised in Table-1.

Table 1: Chest pain related diagnoses and number of clinical cases.

Diagnosis	Number of cases
STEMI	6
NSTEMI	23
Unstable angina	4
Pulmonary embolism	4
Pneumonia	9
Gastric ulcer	1
Aortic dissection	0
Pericarditis	0
Pneumothorax	0
Cholecystitis	0
Costochondritis	0
Panic attack	0

4 ANALYSIS AND RESULTS

For each clinical case, the similarity measure r was calculated for each for each 12 diagnoses. We chose arbitrarily the following set of cut-off points for positive diagnoses: $0.6 \geq r, 0.7 \geq r, 0.8 \geq r$. The analysis was conducted separately for the diagnoses with investigations and without investigations.

Without investigation results being included, the OVPM was able to achieve specificity above 90% at all cut-off points with a negative predictive value of 90%, and the maximum sensitivity achieved was 70%. On the other hand, with the investigations being included, the OVPM was able to achieve 87.2% (95% CI 74.3%-95.2%) sensitivity and 99.2% (95% CI 98.0%-99.8%) specificity for the cut-off 0.6>r; and the positive predictive value and the negative predictive values were 93% and 97.5% respectively; Table 2 summarises the results for the three most common diagnoses in the data set.

Table 2: Sensitivity and specificity for the cut-off 0.6>r with investigation results being included.

	STEMI	NSTEMI	Pneumonia
True +	6	21	8
False +	0	1	1
False -	0	2	1
True -	43	23	37
Sensitivity	100%	91.3%	88.9%
Specificity	100%	95.8%	97.4%

The area under the receiver operating characteristic curve (AUROC) for the results of the analysis without and with investigation results were 0.772 and 0.928 respectively (Figures 1 and 2).

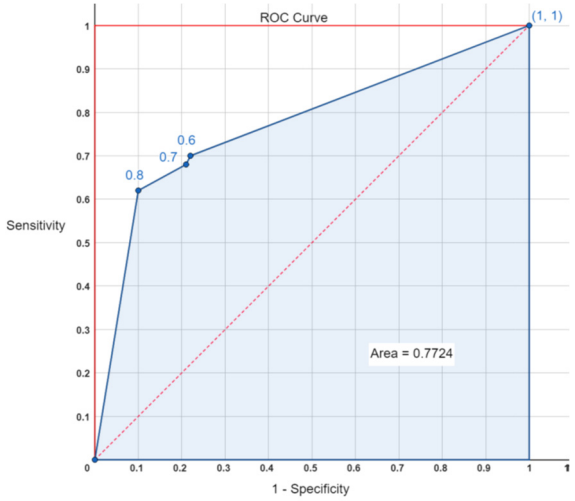

Figure 1: Receiver operating characteristic curve for investigation results being excluded.

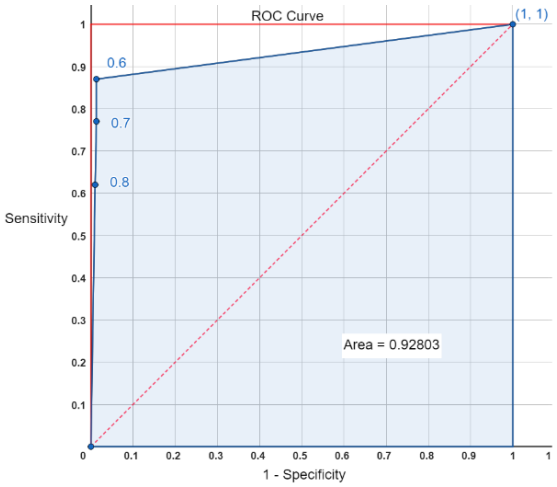

Figure 2: Receiver operating characteristic curve for investigation results being included.

5 DISCUSSION

This pilot study shows that the OVPM has a great potential in triaging chest pain and diagnosis; the results have shown to have an excellent diagnostic accuracy as per the expected standards (Šimundić et al, 2009). Particularly, with high specificity and NPV, OVPM has the potential to use as a triage tool with the utility of ruling out certain diagnoses and thus minimising the cost of unnecessary investigations.

There were number of limitations in the study. Firstly, whilst deriving the optimum weights for each clinical feature for each diagnosis is critical for accurate results, it was done subjectively as a manual process; thus, not necessarily representing the optimum weights. Secondly, the sample size of the study was small and couldn't recruit patients for all the diagnoses, having no patients for 6 diagnoses out of the 12 diagnoses chosen.

Future areas of research involve developing an automated process of deriving weights for each pair of clinical feature and diagnosis; also conducting further evaluation with bigger sample size.

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APPENDIX

	Cardiac					Pulmonary			Digestive		Other	
Clinical Feature	STEMI	NSTEMI	UA	AD	PC	PE	PT	Pneum	Chole	PUD	CC	Panic Attack
Sharp Pain	0	0	0	0	0.1	0.05	0.1	0.1	0	0	0.3	0
Burning Pain	0	0	0	0	0	0	0	0	0	0.2	0	0
Severe Tearing/Ripping Pain	0	0	0	0.4	0	0	0	0	0	0	0	0
Pain Migrates Caudally	0	0	0	0.15	0	0	0	0	0	0	0	0
Dull Pain/ heaviness/ tightness	0.55	0.55	0.55	0	0	0	0	0	0.05	0	0	0.1
Radiation of pain to left arm	0.25	0.25	0.25	0	0	0	0	0	0	0	0	0
Worsened by coughing	0	0	0	0	0.05	0.05	0.05	0.15	0	0	0.1	0
Worsened by inspiration	0	0	0	0	0.1	0.05	0.05	0.15	0	0	0.1	0
Worsened by swallowing	0	0	0	0	0.05	0	0	0	0	0	0	0
Improved sitting and leaning forward	0	0	0	0	0.15	0	0	0	0	0	0	0
Pain elicited with palpation of single point of chest	0	0	0	0	0	0	0	0	0	0	0.5	0
Dyspnea	0.05	0.05	0.05	0.05	0	0.35	0.1	0.05	0	0	0	0
Diaphoresis	0.05	0.05	0.05	0.05	0	0	0	0	0	0	0	0.05
Intense Anxiety and loss of control	0	0	0	0	0	0	0	0	0	0	0	0.7
Pain associated with eating	0	0	0	0	0	0	0	0	0.15	0.4	0	0
Regurgitation	0	0	0	0	0	0	0	0	0	0.4	0	0
cough	0	0	0	0	0.05	0.15	0.05	0.1	0	0	0	0
tachypnea >20	0.05	0.05	0.05	0.05	0	0.1	0.025	0.05	0	0	0	0.1
Tachycardia (>100) (0/2)	0.05	0.05	0.05	0.05	0	0.05	0.025	0	0	0	0	0.05
Hypotension <90 mmHg	0	0	0	0.05	0	0.05	0	0	0	0	0	0
Oxygen Saturation <95%	0	0	0	0	0	0.05	0.05	0.05	0	0	0	0
Fever >38.5 C	0	0	0	0	0.05	0.05	0	0.1	0.3	0	0	0
Orthopnea	0	0	0	0	0	0	0	0	0	0	0	0
Tracheal Deviation	0	0	0	0	0	0	0.2	0	0	0	0	0
Elevated JVP	0	0	0	0	0	0.05	0.05	0	0	0	0	0
unilateral Hyperresonance on percussion	0	0	0	0	0	0	0.15	0	0	0	0	0
Hyporesonance on percussion	0	0	0	0	0	0	0	0.05	0	0	0	0
Basal or Focal crackles	0	0	0	0	0	0	0	0.1	0	0	0	0
reduced breath sounds	0	0	0	0	0	0	0.15	0.1	0	0	0	0
Murphy's Sign	0	0	0	0	0	0	0	0	0.5	0	0	0
Pericardial Friction Rub	0	0	0	0	0.25	0	0	0	0	0	0	0
Jaundice	0	0	0	0	0	0	0	0	0.1	0	0	0
Peripheral oedema	0	0	0	0	0	0	0	0	0	0	0	0
Assymetrical blood pressure or pulse	0	0	0	0.1	0	0	0	0	0	0	0	0

Figure 3: Knowledgebase consisting of clinical features and their assigned values for each possible differential diagnosis, excluding investigations; unstable angina (UA), aortic dissection (AD), pericarditis (PC), pulmonary embolism (PE), pneumothorax (PT), pneumonia (Pneum), cholecystitis (Chole), peptic ulcer disease (PUD).

	Cardiac					Pulmonary			Digestive		Other	
Clinical Feature	STEMI	NSTEMI	UA	AD	PC	PE	PT	Pneum	Chole	PUD	CC	Panic Attack
Sharp Pain	0	0	0	0	0.1	0.05	0.1	0.05	0	0	0.3	0
Burning Pain	0	0	0	0	0	0	0	0	0	0.2	0	0
Severe Tearing/Ripping Pain	0	0	0	0.4	0	0	0	0	0	0	0	0
Pain Migrates Caudally	0	0	0	0.15	0	0	0	0	0	0	0	0
Dull Pain/ heaviness/ tightness	0.15	0.25	0.55	0	0	0	0	0	0.05	0	0	0.1
Radiation of pain to left arm	0.15	0.15	0.15	0	0	0	0	0	0	0	0	0
Worsened by coughing	0	0	0	0	0.05	0.025	0.05	0.15	0	0	0.1	0
Worsened by inspiration	0	0	0	0	0.1	0.05	0.05	0.15	0	0	0.1	0
Worsened by swallowing	0	0	0	0	0.05	0	0	0	0	0	0	0
Improved sitting and leaning forward	0	0	0	0	0.15	0	0	0	0	0	0	0
Pain elicited with palpation of single point of chest	0	0	0	0	0	0	0	0	0	0	0.5	0
Dyspnea	0.05	0.05	0.1	0.05	0	0.05	0.1	0.05	0	0	0	0
Diaphoresis	0.05	0.05	0.1	0.05	0	0	0	0	0	0	0	0.05
Intense Anxiety and loss of control	0	0	0	0	0	0	0	0	0	0	0	0.7
Pain associated with eating	0	0	0	0	0	0	0	0	0.15	0.4	0	0
Regurgitation	0	0	0	0	0	0	0	0	0	0.4	0	0
cough	0	0	0	0	0.05	0.05	0.05	0.1	0	0	0	0
tachypnea >20	0	0	0.05	0.05	0	0.025	0.025	0.05	0	0	0	0.1
Tachycardia (>100) (0/2)	0	0	0.05	0.05	0	0.05	0.025	0	0	0	0	0.05
Hypotension <90 mmHg	0	0	0	0.05	0	0.05	0	0	0	0	0	0
Oxygen Saturation <95%	0	0	0	0	0	0.025	0.05	0.05	0	0	0	0
Fever >38.5 C	0	0	0	0	0.05	0.025	0	0.1	0.3	0	0	0
Orthopnea	0	0	0	0	0	0	0	0	0	0	0	0
Tracheal Deviation	0	0	0	0	0	0	0.2	0	0	0	0	0
Elevated JVP	0	0	0	0	0	0	0.05	0	0	0	0	0
unilateral Hyperresonance on percussion	0	0	0	0	0	0	0.15	0	0	0	0	0
Hyporesonance on percussion	0	0	0	0	0	0	0	0.05	0	0	0	0
Basal or Focal crackles	0	0	0	0	0	0	0	0.05	0	0	0	0
reduced breath sounds	0	0	0	0	0	0	0.15	0.05	0	0	0	0
Murphy's Sign	0	0	0	0	0	0	0	0	0.5	0	0	0
Pericardial Friction Rub	0	0	0	0	0.25	0	0	0	0	0	0	0
Jaundice	0	0	0	0	0	0	0	0	0.1	0	0	0
Peripheral oedema	0	0	0	0	0	0	0	0	0	0	0	0
Asymmetrical blood pressure or pulse	0	0	0	0.1	0	0	0	0	0	0	0	0
T wave inversion across single territory	0	0.1	0	0.05	0	0	0	0	0	0	0	0
ST Elevation and PR Depression across more than one territory	0	0	0	0	0.2	0	0	0	0	0	0	0
ST Depression	0	0.1	0	0.05	0	0	0	0	0	0	0	0
ST Elevation single vascular territory	0.4	0	0	0	0	0	0	0	0	0	0	0
D Dimer Elevated	0	0	0	0	0	0.05	0	0	0	0	0	0
Troponins	0.2	0.3	0	0	0	0	0	0	0	0	0	0
History/Suspicion of DVT	0	0	0	0	0	0.05	0	0	0	0	0	0
Pulmonary Embolism on CT	0	0	0	0	0	0.5	0	0	0	0	0	0
Consolidation/airspace changes CXR	0	0	0	0	0	0	0	0.15	0	0	0	0

Figure 4: Knowledgebase consisting of clinical features and their assigned values for each possible differential diagnosis, including investigations.