Review Article

The Intercept and Slope of breathlessness/chest pain-heart rate relationship in patients with Coronary artery disease using Exercise tolerance test

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Abstract

The most common cause of morbidity and mortality all over the world is Coronary artery disease. The traditional risk factors for Coronary artery disease are hypertension, diabetes mellitus, family history, smoking, dyslipidaemia and obesity. Chest pain and dyspnoea are the two common complaints of patients with Coronary artery disease. The CAD patients are the largest to be recruited in exercise testing. Bruce protocol is most commonly used in exercise testing. Patients developing chest pain and ECG changes are considered ETT positive. Heart rate determines myocardial oxygen demand. The heart rate increases during exercise due to sympathetic activation and parasympathetic withdrawal.

Dyspnoea and pain result from interactions between multiple physiological, psychological, social and environmental factors. Both these sensations strongly motivate adaptive behaviour to regain homeostasis, and patients often experience both conditions. Anterior insula has a strong role that activates in pain and dyspnoea. Pain and dyspnoea which are the major complaints of CAD, can be measured using verbal descriptor or VAS. There is a need of simultaneous recording of chest pain and dyspnoea in patients with CAD. This review includes the studies done previously to record dyspnoea, through VAS and to measure intercept and slope in healthy volunteers and in patients with CAD.

Keywords: ETT, CAD, VAS, Pain, Dyspnoea, Intercept, Slope.

Coronary Artery Disease:

Coronary artery disease is the commonest cause of morbidity and mortality all over the world. The incidence of Coronary artery disease increases with increasing age.[1] In younger age group prevalence is more common in men but it becomes more common in women over 65 years.[2] The traditional risk factors for Coronary artery disease are hypertension,[3] diabetes mellitus,[4] family history,[5] smoking,[6] hypercholesterolemia[7] and obesity.[8] The correlation of these risk factors to pathophysiology of coronary artery disease has been well documented.[9] Previous studies reported that

hypertension, hypercholesterolaemia, diabetes mellitus and smoking promote the endothelial dysfunction by damaging the endothelium of blood vessels. Endothelial dysfunction plays a major role in initiating atherosclerosis.[10]

Atherosclerosis is the process of plaque formation primarily in the intima of large and medium sized arteries. This condition progresses before finally manifesting as an acute ischaemic event.[10] The typical effort induced angina pectoris consists of reversible myocardial ischaemia, caused by obstructive coronary artery disease that limits blood flow during periods of increased myocardial oxygen demand.[9]

Symptoms of Coronary Artery Disease:

The most common presentation of ischaemia in Coronary artery disease is chest pain.[10] Pain frequently radiates to the neck, jaw, left shoulder and left arm.[10] Chest pain is the most frequent indication of Coronary angiography.The other anginal equivalent symptoms include dyspnoea (most common), nausea, vomiting, diaphoresis and unexplained fatigue.[9] Dyspnoea is an unpleasant symptom and it comprises of chest tightness, excessive breathing effort, shortness of breath and air hunger.[11] Patients with undiagnosed Coronary artery disease present with dyspnoea when exertional angina and EKG (ECG) evidence is not present.[11] There is a higher prevalence of angina pectoris in patients who complain of dyspnoea.[11]

Exercise Tolerance Test:

Cardiopulmonary Exercise testing is a tool used to assess the physiological (or pathophysiological) limits of exercise tolerance in health and disease.[12] It is also used for appropriate design of training programmes in sports medicine and rehabilitation.[12] It is a tool used to evaluate the oxygen reserve and exercise capacity. In Clinical Cardiology field, the patients with Coronary artery disease are the largest to be recruited in exercise testing.[13]

Exercise tolerance test is done to assess Coronary artery disease.[11] It indirectly reflects arterial blood flow to the heart during physical exercise. It is the test of choice for patients with medium risk of coronary heart disease. ETT reflects imbalances of blood flow to the heart's left ventricular muscle tissue-the part of the heart that performs the greatest amount of work pumping blood during exercise when compared to blood flow at rest.

In Coronary Artery Disease patients, transient left ventricular contractile dysfunction is frequently observed after exercise, despite myocardial perfusion returning to resting levels.[14] This reversible impairment phenomenon in left ventricular function is known as stunning.[14]

The commonest protocol used for Exercise Tolerance Test is Bruce protocol. Exercise tolerance test can go on till six stages, every stage is of three minutes and at the end of every stage of test, the speed of treadmill and its inclination is increased. Blood pressure, heart rate and ECG are recorded at the end of every stage. The end point of exercise is due to:

1) Achievement of target heart rate (at least 85% of the predicted Maximum heart rate) 2) Pain in the chest or arms 3) Leg pain 4) Exhaustion 5) Maximal dyspnoea 6) ECG changes consistent with ischaemia and 7) Others.

ETT is considered positive when the patient develops pain in the chest or arms and ECG changes with horizontal or down sloping ST depression of 1mm from the baseline 80ms after the J point.[11] ETT is considered negative when the patient achieves target heart rate without complaint of chest pain or any change in ECG.

The elastic and geometric properties of arteries can be affected by exercise[15] so that blood viscosity increases,[16] stiffness decreases,[17] and arterial diameter increases.[18]

The geometric properties of arteries include radius, wall thickness, stiffness and blood viscosity. The large diameter vessels contain a high component of elastic tissue in their walls. They are subjected to the high pressures of 120-160 mmHg. Elastic arteries are the largest arteries and receive the main output of left ventricle. These large arteries are adopted to smooth out the surges of blood flow, as the elastic tissue in their walls provides the resilience to smooth out the pressure wave. During strenous dynamic exercise, systolic blood pressure and mean arterial pressure increase to high levels. Increase in mean arterial pressure during exercise results in proportional increases in mean carotid diameter.[18] Stiffness of arteries is related to collagen-elastin content, arterial wall thickness and arterial radius or diameter.[19] The reduction of arterial stiffness in exercised limbs is observed 30 minutes after moderate intensity cycling.[18] Therefore, the elastic and geometric properties of arteries can be affected by exercise, so that blood viscosity increases, stiffness decreases and arterial diameter increases.

Heart rate is a major determinant of myocardial oxygen demand, and also affects coronary blood flow through diastolic filling time.[20] Heart rate controlling drugs are considered first line treatment for Angina Pectoris.[20] The increase in heart rate during exercise is due to sympathetic activation combined with parasympathetic withdrawal.[21] The chronotropic response to exercise and heart rate recovery 1 min after exercise has a prognostic importance.[21,22] It has been suggested that abnormal cardiovascular autonomic control results in chronotrpic incompetence.[23] In a study done by Huang et al[24] it was reported that subjects with a low chronotropic index had impaired endothelial function, raised markers of systemic inflammation and raised concentrations of N terminal pro BNP as compared to those with a normal heart rate. The previous studies have reported that the

chronotropic incompetence (CI) is an independent predictor of cardiovascular risk profile and all cause mortality.

Coronary Angiography:

Coronary angiography is done to confirm the diagnosis of Coronary artery disease and determine the prognosis. Coronary angiography gives the detail anatomy of Coronary arteries. It depicts the number of arteries stenosed and the percentage of individual stenosis. A negative Coronary angiography confirms the absence of CAD. In case of positive angiography, the decision for angioplasty, CABG or to continue on medicines is made on the basis of percentage of stenosis and number of arteries stenosed and the site of the lesion(s).

Visual Analogue Scale:

A visual analogue scale is a psychometric response scale which can be used in questionnaires. It is an estimate for receptive characteristics or attitudes that cannot be directly measured. A VAS is usually a horizontal line, 100 mm in length anchored by word descriptors at each end. The patient marks on the line the point that they feel represents their perception of their current state. The VAS score is determined by measuring in millimeters from the left hand end of the line to the point that the patient marks.

Intercept and Slope of Linear Relationship:

The intercept and slope of the linear relationship between breathlessness and expired ventilation have been investigated under different experimental conditions. It has been shown for the first time that a repetitive exercise protocol over a period of 10 weeks increased the intercept without change in slope of dyspnoea-expired ventilation relationship using Visual Analogue Scale (VAS/VE).[25] A similar effect has been shown to occur during volitional breathing of an inspiratory resistive breathing pattern.[25] Such a relationship when examined in patients with COPD rehabilitation programme, showed decrease in slope without change in intercept.[26] Since in clinical practice, the recording of heart rate is simpler and easier than that of pulmonary ventilation parameters, the dynamics of VAS-heart rate relationship during progressive exercise in normal healthy volunteers has been shown for the first time to be linear with increase in intercept without change in slope.[25] This means that a representation of both respiratory and cardiovascular control systems can be examined with reference to change in the degree of breathlessness.[25] During exercise, the standard way to measure dyspnoea is to ask the patient after a specific time interval to select a rating on Visual analogue scale that matches the subject's perception of dyspnoea.[27,28]

After having confirmed the relationship of VAS-HR and VAS-VE in healthy exercising volunteers, this relationship was studied by Bokhari et al.[11] in patients with chest pain referred for ETT. This study showed that both the cases and controls showed a linear relationship between VAS and HR during performance of exercise using Bruce protocol. This study showed that intercept was lower in cases with ETT positive than controls with ETT negative.

In a prospective observational study including patients presenting for cardiac stress tests, objective and subjective breathlessness parameters were collected before, during and after stress test exercise. Verbal dyspnoea scores for present dyspnoea was subjective breathlessness parameter. VDS correlated significantly with RR, HR and SBP.[23]

The level of ventilation at a given CO_2 output determines ventilatory efficiency.[29] Ventilatory efficiency is a useful index for assessing patients with heart and lung disease.[30] Increase in ventilation(VE) to increase in CO_2 output (VCO_2) is also an established index reflecting the severity of ventilation perfusion mismatch in heart failure patients.[13] Traditionally an incremental exercise testing to a symptom limited maximum has been used to obtain the VE/VCO_2 slope.[13,29,30] VE increases in tight relationship with the increase in VCO2 during an incremental exercise until the near maximum level i.e ventilatory compensation point. Although slope becomes steeper above the ventilatory compensation point, slope is quite linear below this point. VE/VCO_2 slope becomes steeper in cardiac patients according to severity of heart failure.[13]

In a study,[31] VAS was used and the subjects were asked to judge the relative contributions in relation to opposite in differentiated perceived exertion like central pain or local pain, breathing difficulty or heart pain. It was found that breathing difficulty was greater than heart pain at higher exercise intensities.

Similarities between dyspnoea and pain:

Both dyspnoea and pain result from various interactions between multiple physiological, psychological, social and environmental factors.[32] Dyspnoea is a clinical problem nearly as important as pain. It affects a quarter of the general population and half of seriously ill patients (the latter comparable to pain's impact).[33] Recent research demonstrated that both dyspnoea and pain consists of at least two distinct dimensions: a sensory (intensity) and an affective (unpleasantness) one. Both these sensations strongly motivate adaptive behaviour to regain homeostasis, and patients often experience both conditions.[33,34] The perception of dyspnoea and pain warns the conscious brain of a disturbed physiologic state and motivates adaptive behaviour to modify the aversive situation.[34] Anterior insula is a component in large brain network, that activates in various sensations

including pain and dyspnoea. Anterior insula is an internal alarm center, that alerts the individual to potentially distressing interoceptive stimuli.[33,34]

Conclusion

As dyspnoea is measured in studies by the use of Visual analogue scale and Borg scale, so are the dimensions of pain that can be measured using verbal descriptor or Visual analogue scale. There are many similarities among pain and dyspnoea, both are symptoms of serious disease. Both are "internal sensations" that warn of impending danger. In the field of clinical Cardiology, the measurement of dyspnoea is already done in previous studies using Visual analogue scale in Exercise Tolerance Test. As pain and dyspnoea have many similarities, there is a need to measure chest pain and dyspnoea in the same study and like dyspnoea, chest pain should also be plotted against increasing heart rate and both VAS-cp and VAS-d-HR relationship should be recorded and their clinical correlation should be made.

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