Exercise and Ischemia
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“Confidence is that feeling we have before we fully understand our situation.”
– Unknown

Past: Angina Pectoris was first described by William Heberden in the 1770’s. The physical symptoms he described were later found to be the result of ischemic heart muscle. Myocardial ischemia occurs when oxygen supply to the heart muscle is not sufficient to meet the oxygen demand. In the past it was believed that ischemia occurred due to a fixed narrowing (atherosclerosis, plaque) in the artery, which would restrict blood flow, not allowing enough blood through to meet the demand. This was reproducible; occurring at a consistent fixed work load.

The work load at which ischemia occurs can be measured and quantified by using the Rate Pressure Product (Heart Rate x Systolic Blood Pressure). Generally, ischemia was felt to be represented by ST depression on an ECG. This is usually defined as 1 mm of ST depression from baseline, flat or down sloping, at 80 msec from the j point, lasting more than 1 min., in 1 or more leads. It was believed that the ischemic threshold would only change if and when the plaque progressed. It was also believed that angina occurred with all ischemic events. Those individuals who denied any symptoms with the ischemia denied symptoms leading up to, and during, a heart attack.

Based on this knowledge an exercise prescription for patients with angina was developed, and is still in use today. The American College of Sports Medicine (ACSM) guideline for exercise prescription in patients with Ischemia/angina states:

References:
1. Kelvin L. Lecture to the Institution of Civil Engineers; 3 May 1883; Ireland.

TABLE 2
Estimation of Relative Risk Reduction in All-Cause Mortality in Patients with Coronary Artery Disease – adapted from Iestra JA, et al.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Mortality Risk Reduction % (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacologic</strong></td>
<td></td>
</tr>
<tr>
<td>Low-dose aspirin</td>
<td>18 (1-30)</td>
</tr>
<tr>
<td>Statins</td>
<td>21 (14-28)</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>23 (15-31)</td>
</tr>
<tr>
<td>ACE Inhibitors</td>
<td>26 (16-35)</td>
</tr>
<tr>
<td><strong>Non-Pharmacologic</strong></td>
<td></td>
</tr>
<tr>
<td>Smoking Cessation</td>
<td>35 (CI not given)</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>25 (2-41)</td>
</tr>
<tr>
<td>Moderate Alcohol</td>
<td>20 (17-22)</td>
</tr>
</tbody>
</table>

“Because symptomatic or silent ischemia may be arrhythmogenic, the THR (training heart rate) for endurance exercise should be set safely below (>10 beats/min) the ischemic ECG or anginal threshold. Alternately, the upper heart level can be set as the highest non ischemic workload from a Graded Exercise Tolerance (GXT).”

Typically a patient would undergo a GXT and the point, (heart rate/rate pressure product), at which they developed 1mm of ST depression (as defined above) would be deemed the ischemic threshold. From this the exercise prescription would be developed as 10 beats below that ischemic heart rate. The primary purpose behind this was to avoid having patients exercising while they are experiencing ischemia, and the resulting risk of arrhythmias and sudden cardiac death.

Unfortunately, the early concepts of ischemia/angina, were based on assumptions that were simplistic in their understanding of ischemia and angina. The frequency of “silent” ischemia was not fully appreciated. The importance of vascular smooth muscle control of lumen diameter was unknown and the role endothelium plays in vascular disease was yet to be discovered.

The Ischemic Cascade:

The ischemic cascade refers to a sequence of events that appear to take place during an ischemic episode. This sequence is outlined below and includes the percentage of times during an ischemic event each step is likely to be detected (Berger et al.)

1. Imbalance in the myocardium between supply of oxygen and the demand. (100%)
2. Changes in diastolic and systolic function. (80%)
3. ECG changes may occur. (50%)
4. Patient may experience angina. (30%)

Examples of some factors that are currently believed to influence ischemic episodes:

- Circadian rhythms: the influence of diurnal variation on the frequency of ischemia, angina and MIs is well documented. There is a tendency for a disproportionate number of events to occur during the first few hours of the morning. Ischemic episodes are more common in the first waking hours of the day.
- Endothelial function: it is believed that a dysfunctional endothelium does not produce sufficient Nitric Oxide to stimulate smooth muscle relaxation. In contrast, the direct effect of catecholamines on smooth muscle is vasoconstriction. This may cause “warm up” induced angina/ischemia.
- Effects of smooth muscle constriction; patients with variant angina which is caused by smooth muscle spasm or constriction.

Standard Bruce protocol exercise testing will overestimate the ischemic threshold (rate pressure product) as compared to longer endurance training of activities of daily living. Studies have demonstrated that ischemia routinely occurs at lower rate pressure products when patients engage in longer sustained aerobic exercise than what would have been estimated from standard exercise testing. Ischemic episodes vary with the type of activity being done. Different aerobic exercises cause ischemia in patients at different rate pressure products.

Incidence of silent ischemia:

- Silent ischemic episodes are more common than first believed
- Perhaps as many as 9 episodes of silent ischemia for every episode of angina
- 20%-30% of all individuals with diabetes experience silent ischemia
- About 20% of all elderly people have episodes of silent ischemia

Conclusion:

Lumen diameter is a dynamic construct. Ischemic events during exercise and activities of daily living are far more common and less predictable than we once thought. These episodes are fairly common in people with diabetes and in cardiac patients. The guideline for exercise prescription in patients with angina was written prior to our current understanding of angina and ischemia. Concern for the development of arrhythmias and sudden cardiac death are well founded. It is also known that regular endurance exercise is protective against sudden cardiac death.

“Ischemic events during exercise and activities of daily living are far more common and less predictable than we once thought.”

It is important, and perhaps unsettling, to realize the extent at which ischemic episodes occur during exercise and activities of daily living. There is clear evidence outlining the shortcomings of our current approach for exercise prescription at limiting these occurrences. Clinical experience has shown that after millions of patient-hours of exercise within Cardiac Rehabilitation programs, this approach to prescribing exercise is safe. This begs the question, are these episodes of ischemia as dangerous as we have thought? If they are, then a new approach to prescribing exercise is needed. If these episodes are not as concerning and are to be ignored, then the current
approach to exercise prescription is adequate. More study is needed to address these questions.

References:
5. Berger HJ, Reduto LA, Johnstone DE, Borkowski H, Sands JM, Cohen as primary or secondary prevention measures have resulted in hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, vascular events, most of the remaining risk factors, including age, sex, ethnicity, heredity, and previous history of often initiated by the presence of multiple risk factors.
6. Vascular diseases are the leading cause of increased morbidity and mortality in North America. Together, cerebro- and cardiovascular disease accounted for approximately 40% of all deaths in Canada in 1996, were the leading cause of hospital days (18% of the total) and constituted a significant economic impact both directly and indirectly. As the population of Canada ages and life expectancy increases, the incidence and cost of care for both cerebro- and cardiovascular disease will continue to increase.

It is clear that the progression of vascular disease is most often initiated by the presence of multiple risk factors. Aside from age, sex, ethnicity, heredity, and previous history of vascular events, most of the remaining risk factors, including hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, atherosclerosis, smoking and sedentary lifestyle, are modifiable.

Targeted risk factor management and/or reduction as primary or secondary prevention measures have resulted in significant decreases in both cerebro- and cardiovascular events in large randomized clinical trials. The use of anti-platelet agents, agents used to alter blood pressure, agents used to lower cholesterol, beta-blockers and others have all been shown to be beneficial in both the acute and chronic settings.

Data pertaining to the acute benefit of these agents generally demonstrates improvement in outcome generally between 12 and 36 months after initiation with increasing benefit over time.

The benefits of aggressive disease management as demonstrated by these and other studies has led to the publications of

Saskatchewan Medication Assessment for Risk Reduction Treatment Targets (SMART2 Study)

William Semchuk, MSc, PharmD, FCSHP, on behalf of the SMART2 Investigators, Regina Qu’Appelle Health Region

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“Despite the availability of vast amounts of clinical data and the proliferation of treatment guidelines, a large proportion of patients are not receiving optimal treatment.”

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