Myocardial Coefficient of Oxygen Utilization

By John C. Scott, Ph.D., Sc.D.

The coefficient of oxygen utilization is defined as the arteriovenous difference in oxygen concentration divided by the concentration of oxygen in the arterial blood. Multiplication of the ratio by 100 converts the coefficient into the per cent of arterial oxygen which is removed by the tissue. The term "oxygen extraction ratio" is frequently used as a synonym.

Conflicting reports have appeared in the literature concerning the relationship between the arterial oxygen content and the myocardial coefficient of oxygen utilization. Feinberg et al. have reported a positive relationship, while Hackel and co-workers found a consistent inverse relationship between arterial oxygen content and the coefficient of oxygen utilization during hypoxemia. Both groups used dogs as the experimental animal, but different methods of measuring coronary flow were employed. In the normal range of arterial oxygen values no correlation appeared to exist. Some investigators, however, have been impressed with the constancy of the coefficient under certain experimental conditions and have used this value as an index of coronary flow.

Since the published reports disagree on the relationship of arterial oxygen content to the coefficient of utilization, it may be unwise to use the latter value as an index of coronary flow. In view of the discrepancies found in the literature, a re-examination of the pertinent factors, particularly coronary flow, blood oxygen values, and estimated myocardial oxygen consumption, has been undertaken.

Methods

One hundred and twenty "normal" experiments were selected from several hundred performed in the author's laboratory on the anesthetized dog. The coronary flow was measured by the nitrous-oxide desaturation method. Other data were obtained by methods or calculations previously reported. The cases selected included experiments in which the animal was exposed to several oxygen concentrations in the inspired air, varying from 100 to 10 per cent oxygen. The hematocrit variations were random. In order to restrict the variation in estimated myocardial oxygen consumption, the cases selected were restricted to values between 6 and 12 ml./100 gm./min. The data consisted of: arterial blood oxygen, volumes per cent \(A.O_2\), coronary sinus blood oxygen, volumes per cent \(V.O_2\), the myocardial arteriovenous oxygen difference \(A-V.O_2\), the myocardial coefficient of oxygen utilization, \[ \frac{A-V.O_2}{A.O_2} \] the coronary blood flow \(CBF\), the hematocrit, and the left ventricular oxygen consumption \(L.V.O_2\). Since mean arterial blood pressure and heart rate showed no consistent trends, these values were not tabulated.

The data were grouped in class intervals of 2 volumes per cent arterial oxygen content and the values in each group were averaged. No data were available for the interval 11.00 to 12.99. The \(A-V.O_2\), coronary blood flow, and coefficient of oxygen utilization were examined in relation to the arterial oxygen content, and the statistical significance of these relationships was determined.

Results

Table 1 lists the average values of the results when classified in terms of the arterial oxygen content in volumes per cent.

Figure 1 is a graph of the arterial oxygen content plotted against the myocardial arteriovenous oxygen difference. The regression equation is:

\[ Y = 0.675 \times + 0.928, \]

where \(Y = A-V.O_2\), and \(X = A.O_2\); \(P < 0.001\).

Figure 2 is a graph of the arterial oxygen content plotted against the estimated coronary flow. The regression equation is:

\[ Y = 3.119 \times + 125.7, \]

where \(Y = CBF\) and \(X = A.O_2\); \(P < 0.001\).
Figure 1
Slope was calculated by the method of least squares, using 120 points. Mean values (table 1) are shown on the graph.

Figure 3 is a graph of the arterial oxygen content plotted against the coefficient of oxygen utilization times 100 (U per cent). The regression equation for the left-hand calculated slope, line (a), is:

\[ Y = -1.083 \times X + 92.4, \]

where \( Y = \frac{A-V_02}{A_02} \) or \( U \),

and \( X = A_02 \); 0.01 > \( P > 0.005 \). The regression equation for the right-hand calculated slope, line (b), is:

\[ Y = 0.836 \times X + 52.2, \]

where \( Y = \frac{A-V_02}{A_02} \) or \( U \),

and \( X = A_02 \); 0.07 > \( P > 0.05 \).

**Discussion**

Under the conditions of the above experiments, it would appear that the arterial-blood oxygen content not only influences the coefficient, but also determines the direction of change. Although the coefficient is expressed as \( \frac{A-V_02}{A_02} \), it is derived from the ratio of oxygen consumption to arterial oxygen content:

\[ \frac{A-V_02}{A_02} \]

**High Arterial Oxygen Content**

In the data summarized in figures 1 and 2, there is demonstrated a positive correlation between the arterial oxygen content and \( A-V_02 \), but an inverse relation with coronary flow. The relationships are somewhat surprising at arterial oxygen values in the upper...
Table 1

Average Values of 120 Experiments

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Class interval = 2 volumes per cent oxygen.
N = Number of cases,
A,O₂ = Arterial-blood oxygen (volumes per cent).
V,O₂ = Coronary-sinus-blood oxygen (volumes per cent).
A-V,O₂ = Myocardial arteriovenous oxygen difference.
U (%) = A-V,O₂ × 100.
CBF = Coronary blood flow (ml./100 Gm./min.).
L.V.O₂ cons. = Left ventricular oxygen consumption (ml./100 Gm./min.).

part of the range. Here, at a constant oxygen consumption, increasing levels of arterial oxygen above the normal value would require either a corresponding rise in V,O₂ (constant A-V,O₂) with no change in flow, or a decreasing flow associated with an increase in A-V,O₂. The latter case holds true with our data, and it should be noted that the increase in A-V,O₂ is brought about by the V,O₂ values remaining approximately constant at arterial oxygen levels above 20 volumes per cent. As a result of the decreasing flow, U increases proportionately.

The reduction in coronary flow at high arterial oxygen levels is of practical, as well as theoretical, interest, particularly since the use of oxygen-enriched mixtures of inspired air is an accepted therapeutic procedure. A mechanism responsible for this reduction in coronary flow has not been demonstrated. Other investigators have noted a reduction in coronary flow during administration of 100 per cent oxygen. The high arterial oxygen values in the present data were due to random combinations of breathing 100 per cent oxygen and high hematocrit values. Since the latter values roughly parallel the oxygen-content values, it may be that the reduction in coronary flow was determined primarily by an increased viscosity of the blood. Case et al., using the open-chest dog, found coronary flow to vary inversely with the hematocrit, but they did not find a consistent relationship between U and the hematocrit value; it would appear that relative hypoxia, rather than viscosity, was the primary determinant.

Low Arterial Oxygen Content

Below the normal level, decreasing arterial oxygen values showed an inverse relationship with the coefficient of oxygen utilization. Here an increasing U is correlated with an increasing coronary flow. Several investigators have reported this relationship, and it has been suggested that hypoxia causes vasodilation, either by direct action or through a metabolite which is oxidized under normal conditions. At first glance, it appears paradoxical that at the upper end of the arterial-oxygen scale, an increasing U is associated with a decreasing flow, while at the lower end of the scale, an increasing U is associated with
MYOCARDIAL OXYGEN UTILIZATION

an increasing flow. The latter situation is due to the fact that at arterial oxygen values below the normal level, the \( V_{O_2} \) values decrease at a more rapid rate than the \( A_{O_2} \) values, so that the numerator of the ratio

\[
\frac{A-V_{O_2}}{A_{O_2}}
\]

becomes progressively greater than the denominator, and \( U \) increases. Thus, in spite of a falling \( A_{O_2} \) level, the ratio increases. In more descriptive terms, an increasing coronary flow enables the myocardium to take out more oxygen from a progressively falling arterial oxygen content. The point at which flow increases is apparently triggered by a fall in venous oxygen content and represents the level at which flow fails to maintain a constant \( V_{O_2} \) (or tissue \( p_{O_2} \)).

The validity of a change in slope of the regression lines for \( U \) at high, compared with low, arterial oxygen levels is also supported by substituting the \( A-V_{O_2} \) value obtained in the regression equation for figure 1, i.e., if \( A-V_{O_2} = 0.675 A_{O_2} + 0.928 \), then,

\[
U = \frac{A-V_{O_2}}{A_{O_2}} = 0.675 + \frac{0.928}{A_{O_2}}
\]

This indicates a hyperbolic relation between \( A_{O_2} \) and \( U \), not a linear regression, as has been assumed by other investigators.\(^1\)

An increasing \( U \) with a decreasing \( A_{O_2} \) at the lower levels of arterial oxygen content was also reported by Hackel et al.\(^2\) using the nitrous-oxide method for estimating coronary flow, and changes in the same direction have been obtained with the rotameter\(^7\) in an open-chest dog. On the other hand, Feinberg et al.\(^1\) reported a positive relation between these two factors with hypoxemia. They employed an open-chest preparation in which the systemic venous return to the right heart was bypassed and the output of the right ventricle was measured as an estimate of total coronary flow. The difference in results may be due to difference in methodology. The possibility exists that the right-heart-bypass data may reflect an \( A-V \) shunt through arterioluminal vessels to the right side during hypoxemia. This would increase the \( V_{O_2} \) values and prevent the ratio

\[
\frac{A-V_{O_2}}{A_{O_2}}
\]

from increasing. In another paper\(^8\) from the same laboratory in which the same method was used, "spontaneous" changes in coronary flow were reported which were characterized by an increase in coronary \( V_{O_2} \).

An increase in coronary flow in response to anemic anoxia\(^9\) or to anoxic anoxia\(^10\) has been reported in the experimental dog. The present data do not permit a distinction between the two types, since both hematocrit and the inspired oxygen mixtures were varied indiscriminately. Using an isolated perfused heart, Guz et al.\(^8\) have reported that coronary flow is related to arterial oxygen content even though viscosity and \( p_{O_2} \) remain constant. The possibility exists, however, that the flow changes were initiated at the capillary level by variations in \( p_{O_2} \) which were too small or too rapid to be detected by available methods. Estimates of the \( p_{O_2} \) of coro-
nary-sinus blood from an oxygen dissociation curve have been made on our data. Although these values are admittedly inaccurate, they do indicate a falling pH at points below the normal arterial oxygen levels.

Normal Arterial Oxygen

Under resting conditions at a normal and constant arterial oxygen level, the coefficient approximates 70 per cent. Variations under these circumstances have been erroneously reported to be limited to ± 3.0 per cent. An examination of our data and of the literature indicates that the variation is much greater than this. At a constant level of arterial oxygen, changes in A-V$_{O2}$ indicate the direction of change in U. As has been pointed out before, a change in A-V$_{O2}$ is dependent upon the relative values of oxygen consumption and coronary flow, since A-V$_{O2} = O_{2}$ consumption/flow. In view of these considerations, it does not appear possible to use the coefficient as a reliable index of flow unless the oxygen consumption is known (and this customarily requires an estimate of flow).

If the flow responses were perfectly adjusted to the oxygen demands of the myocardium, A-V$_{O2}$ and, hence, U would not change. The factors responsible for the changes that do occur have not been identified. The experimental methods employed undoubtedly influence flow sensitivity. One would not expect the sensitivity of coronary-flow adjustments to be as great in the open-chest preparation as in the closed-chest dog; in the former case, the flow tends to be higher, the A-V$_{O2}$ smaller, and the adjustments to changing demands for oxygen somewhat less marked. In the intact dog, moderate changes in oxygen demand are readily met by an increase in coronary flow and, in some circumstances, by an over-response with a reduction in the coefficient. With stress of a greater degree, the demands are met by an increase in both flow and the coefficient of oxygen utilization.

Summary

An analysis of blood oxygen values, coronary blood flow, and left ventricular oxygen consumption has been made on data obtained from 120 experiments on normal anesthetized dogs by using the N$_2$O method for estimating coronary flow. The arterial oxygen content was shown to have a positive linear relationship to the myocardial arteriovenous oxygen difference (A-V$_{O2}$), but a negative linear relationship to coronary flow. The coefficient of oxygen utilization showed a positive linear regression with arterial oxygen-content values above 20 volumes per cent, but an inverse relationship with arterial oxygen values below 20 volumes per cent. The significance of these relationships in the regulation of coronary flow is discussed.

References

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