careful retrograde mapping of the atrial exit site of the fast pathway before radiofrequency ablation can help avoid inadvertent heart block in these patients.

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References

1. Sung RJ, Young C, Liem LB, Sanathana-Murthy MG. Localization of retrograde fast and slow atrioventricular node pathway exit with induction of atypical ventriculoatrial Wenckebach periodicity [abstract]. Circulation 1992;86 Suppl I:I-202.
2. Englestein ED, Stein KM, Markowitz SM, Lerman BB. Posterior fast atrioventricular node pathways: implications for radiofrequency catheter ablation of atrioventricular node reentrant tachycardia. J Am Coll Cardiol 1996;27:1098–105.
3. Wilber DJ, Kopp DP, Olshansky B, Kall JG, Lippman N, Lerman BB. Spectrum of atrioventricular nodal reentry [abstract]. J Am Coll Cardiol 1993;21:281A.
4. Lauer MR, Young C, Munsif A, Sung RJ. Identification of patients at high risk of developing complete atrioventricular block during ablation of slow pathway conduction [abstract]. Circulation 1993;88 Suppl I:I-203.
5. Wilber DJ, Kall JG, Olshansky B, Kopp D, Lippman N, Lerman BB. Fast-slow atrioventricular nodal reentry: anterior versus posterior retrograde pathways [abstract]. J Am Coll Cardiol 1993;21:355A.

Supplemental Oxygen Administration and Congestive Heart Failure

We read with concern the interesting work of Haque et al. (1), and we wish to raise two important points.

1. Should we be surprised by a diminution of cardiac output (CO) secondary to supplemental oxygen administration? It seems sensible that the increase in arterial oxygen content (Cao_2) obtained in this way could consequently permit a decrease in CO to maintain constant oxygen delivery (Do_2) at a given work load. Moore et al. (2) described such a variation in CO secondary to an increased inspired oxygen concentration in patients with chronic congestive heart failure undergoing exercice tests. Interestingly, the decrease in CO observed in their case was associated with reduced subjective scores of fatigue and breathlessness. It would have been appropriate for Haque et al. (1) to provide more information about the evolution of the clinical status of their patients during oxygen administration. In other words, we have to be sure that the reported observations truly reflect the detrimental effects of oxygen therapy. The formula of Do_2 permits prediction of the theoretic variation in CO that should be expected in response to a given increase in Cao_2. For example, in the case of the patients of Haque et al., and assuming a normal hemoglobin concentration of 15 g/dl, it can be calculated that the expected decrease in CO would be 8.92% in experiment 1 and 8.16% in experiment 2. Undoubtedly, the reported decrease in CO remains greater (16.22% and 23.68%, respectively), but the significance of the results should be discussed in light of this fundamental notion.

2. It can be calculated from the data of Haque et al. that oxygen consumption (Vo_2) was not constant during the investigation. In fact, Vo_2 values varied from 370.7 ml/min at 21% fraction of inspired oxygen (FIo_2) to 317.8 ml/min at 100% FIo_2 in experiment 1 (Vo_2 (21%) − Vo_2 (100%)/Vo_2 (100%) = 14.27%), and from 354.2 ml/min at 21% FIo_2 to 281.3 ml/min at 100% FIo_2 in experiment 2 (Vo_2 (21%) − Vo_2 (100%)/Vo_2 (100%) = 20.58%). Even if these calculated Vo_2 values are the result of a formula that includes CO, which implies a certain amount of mathematical coupling between Vo_2 and oxygen delivery (Do_2) calculated values, there is no guarantee that an external factor did not modify Vo_2 and, secondly, Do_2 and CO. It has been previously hypothesized (3) that hyperoxia-related vasoconstriction could decrease Vo_2 by increasing peripheral shunting, which could explain the increased mixed venous oxygen saturation (Svo_2) and decreased oxygen extraction ratios (ERo_2) reported in the study of Haque et al. (1). Another explanation could be that their patients were already on the oxygen supply/Vo_2 dependency slope of their Vo_2/Do_2 relations. This could explain the fact that Vo_2 decreased in response to any reduction of CO and Do_2. Some factors support this hypothesis, such as the extremely poor ejection fraction of the study patients or the relatively low Svo_2 measured. In contrast, the values of Do_2 calculated in both experiments (Do_2 (21%) = 386.86 ml/min per m^2 and Do_2 (100%) = 355.64 ml/min per m^2 in experiment 1 and Do_2 (21%) = 401.56 ml/min per m^2 and Do_2 (100%) = 333.5 ml/min per m^2 in experiment 2, assuming a mean surface body area of 1.8 m^2) remain greater than the previously described Do_2 critical limit of 330 ml/min per m^2 (4) below which oxygen supply/Vo_2 dependency appears. The same can be said for ERo_2 (ERo_2 (21%) = 53.23% and ERo_2 (100%) = 49.65% in experiment 1 and ERo_2 (21%) = 49.00% and ERo_2 (100%) = 46.86% in experiment 2), which remains lower than the reported critical ERo_2 limit of 70% (5). The latter two argue for a oxygen supply/Vo_2-independent situation. If Haque et al. (1) had reported the lactate serum levels of their patients, the question of oxygen supply/Vo_2 dependency or peripherical shunting would have been avoided. Actually, lactate serum level usually increases in situations of oxygen supply/Vo_2 dependency, as well as in any form of Do_2 insufficiency (6), and should have been used as the final tracer of oxygen imbalance. Despite these remarks, Haque et al. (1) have opened an important and exciting debate that merits further development even if the clinical implications of such a study are not obvious. Indeed, in a patient with severe heart failure steady state, why should oxygen therapy be initiated? In contrast, if the same patient develops any form of Do_2 insufficiency, he or she will undoubtly take advantage of supplemental oxygen administration.

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References

1. Haque WA, Boehmer J, Clemson BS, Leuenberger UA, Silber DH, Sinoway LI. Hemodynamic effects of supplemental oxygen administration in congestive heart failure. J Am Coll Cardiol 1996;27:353–7.
2. Moore DP, Weston AR, Hughes JMB, Oakley CM, Cleland JGF. Effects of increased inspired oxygen concentrations on exercise performance in chronic heart failure. Lancet 1992;339:850–3.
3. Reinhart K, Specht M, Föhring U, Mayr O, Eyrich K. Einflu der präoxygenierung auf hämodynamik und sauerstoffverbrauch. Anaesthesist 1989;38:233–7.
4. Shibutani K, Komatsu T, Kubai K, Sarchala V, Kumar V, Bizarri DV. Critical level of oxygen delivery in anesthetized man. Crit Care Med 1983;11:640–3.
5. Samsel RW, Nelson DP, Sanders WM, Wood LDH, Schumacker PT. Effects of endotoxin on systemic and skeletal muscle O_2 extraction. J Appl Physiol 1988;65:1377–82.
6. Haupt MT, Gilbert EM, Carlson RW. Fluid loading increases oxygen consumption in septic patients with lactic acidosis. Am Rev Respir Dis 1985;131:912–6.

Reply

We appreciate the keen interest of Broka et al. in our work on the hemodynamic effects of oxygen. They raised two concerns. The first relates to the importance and mechanism of our observation demonstrating a diminished cardiac output in response to supplemental oxygen. The second relates to the calculated oxygen consumption values in our study and the fact that oxygen consumption decreased as supplemental oxygen was added.

With regard to the first concern, the majority of subjects did not become symptomatic as we gave supplemental oxygen. However, one subject became short of breath and diaphoretic in response to this intervention. Another subject who was studied after completing this project also became diaphoretic as oxygen was delivered. We did not include these data in the original report because we did not systematically examine symptoms and considered these data to be too anecdotal. However, as we emphasized in our report, pulmonary capillary wedge pressure increased, confirming the finding that oxygen had a detrimental hemodynamic effect. We agree that measurements of plasma lactate would have been useful. Unfortunately, at the time of these studies, we did not think of performing these measurements.

What is the mechanism for the decrease in cardiac output? We would expect a change in cardiac output to be associated with either a change in loading conditions or a change in inotropy. As mentioned above, pulmonary capillary wedge pressure increased in response to oxygen, providing evidence that preload increased. This would suggest that cardiac output diminished at a time when Starling forces would dictate that cardiac output should increase. Therefore, one could only conclude that there must be a change in either inotropy or systemic resistance. Although we did not measure inotropy directly, a decrease in inotropy is typically accompanied by evidence of reflex sympathoexcitation. We found no changes in heart rate or peroneal nerve muscle sympathetic nervous system activity. Thus, we would surmise that inotropy did not decrease. We did calculate system vascular resistance and found it to increase fairly dramatically. Therefore, our data support the contention that oxygen acted as a direct vasoconstrictor, thereby increasing peripheral vascular resistance.

We have further pursued the issue of changes in systemic resistance in our experiments in patients with a left ventricular assist device. We have performed studies in six such patients and found a consistent relation between increased systemic resistance and the administration of oxygen (unpublished observations). Further, in normal subjects, we have performed experiments on forearm blood flow in response to 10 min of forearm ischemia. We have observed that peak vasodilation is reduced with the administration of supplemental oxygen (1). The exact mechanism for this change in systemic resistance is currently unknown.

In terms of the insightful discussion on oxygen delivery of Broca et al., we completely agree that the change in calculated oxygen consumption in our data would bring into question the dependency of oxygen consumption on oxygen delivery. Ideally, one would measure oxygen consumption during such experiments. Measuring oxygen consumption during oxygen delivery is fraught with a number of inaccuracies and, accordingly, we did not pursue these measurements. The work cited in their letter was performed in anesthetized patients with coronary disease (2). These subjects differed considerably from those in our study in that they were anesthetized, and there is no comment on the presence or absence of congestive heart failure. These are important considerations because spontaneous ventilation in the presence of increased filling pressures would substantially increase the work of breathing and total oxygen consumption. This could substantially alter the relation between oxygen consumption and oxygen delivery so aptly described in your letter.

With regard to the estimated oxygen consumption values in the letter of Broca et al., there were some assumptions made that would overestimate the calculated oxygen delivery. In reviewing the data in experiment 2, we found that oxygen delivery ranged from 333 ml/min on room air to 270 ml/min with 100% oxygen. Accordingly, we were in the previously described range where there is a dependency of oxygen consumption on oxygen delivery. Additionally, from the data that Broca et al. referenced, one would predict a 21% decrease in oxygen consumption. Based on our patients, a 29% change was observed. As mentioned above, because the patient groups and clinical conditions are different, it would be inappropriate to directly apply the previous data to our patients.

In conclusion, our work dealt primarily with the hemodynamic effects of supplemental oxygen in conscious humans with severe heart failure. We agree with Broca et al. that other "clinical" measures during oxygen administration in patients with heart failure are warranted.

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References

1. Crawford P, Good PA, Gutierrez E, Feinberg JH, Silber DH, Sinoway LI. The effects of oxygen on forearm dilator capacity [abstract]. FASEB J 1996;10:A590.
2. Shibutani K, Komatsu T, Kubai K, Sarchala V, Kumar V, Bizarri DV. Critical level of oxygen delivery in anesthetized man. Crit Care Med 1983;11:640–3.

Selection Bias in Thrombolytic Trials

Jha et al. (1) compared the characteristics and mortality outcomes of Canadian patients who participated in two thrombolytic trials (GUSTO and LATE) with those in patients with acute myocardial infarction who did not participate. Administrative discharge data were used for nonparticipants to obtain demographic and "comorbidity scores." No physiologic data were available for nonparticipants. The authors found that trial participants were younger, more likely to be male and had a lower comorbidity score. Participants also had lower in-hospital mortality "after adjustment for age, gender, revascularization and comorbidity scores." The authors conclude that there is selection bias in the recruitment of trial participants, with favoring of lower risk patients.

In essence, what the authors have described are differences in demographics, comorbidity scores and mortality between a population of patients who are eligible for thrombolysis (participants) compared with an unselected group of all patients with acute myocardial infarction (nonparticipants). Nonparticipants thus include both thrombolysis eligible and ineligible patients. It is well known that many patients with acute myocardial infarction are ineligible for thrombolysis on the basis of late presentation, absence of chest pain, nondiagnostic electrocardiographic findings, uncontrolled hypertension or other contraindications (2). Data reveal that these patients are older, more likely to be male and more likely to have a higher degree of comorbidity (3).