Studies on the Changes in Myocardial Oxygen Tension

Tadashi NAKAMURA, Yoshito WAKAO, Makoto MUTO, and Mitsugi TAKAHASHI

Department of Veterinary Surgery, School of Veterinary Medicine, Azabu University, Fuchinobe, Sagamihara 229, Japan

(Received 30 June 1988/Accepted 6 October 1989)

ABSTRACT. An arterial oxygen tension (PO_2) sensor was used to measure the myocardial PO_2 at three sites in the left ventricle supplied by the paraconal interventricular branch of the left coronary artery, cranial descending coronary artery (CDCA): a subendocardial site, a subepicardial site and an intermediate point in the left ventricular wall. At first, the PO_2 sensor had been compared with the values from a blood gas analyzer. The regression equation $Y=1.4\times-4.9$ with a correlation coefficient of 0.993 indicated a high correlation between these two measurements. The PO_2 of the arterial blood in the left ventricular cavity was assigned an index value of 100%. The PO_2 was about 70% in the subendocardial myocardium, about 15% in the mid-ventricular wall myocardium and 9% in the subepicardial myocardium, demonstrating a decreasing PO_2 gradient from the endocardial to the epicardial surface. A transient occlusion of the CDCA confirmed the pathway of myocardial oxygen supply. In the mid-ventricular and subepicardial myocardium, marked hypoxia occurred after occlusion of the CDCA. Release of the occlusion resulted in a rapid return to the normal PO_2 level. The oxygen supply to these sites is strongly influenced by coronary artery blood flow. The PO_2 in the subendocardial myocardium was not dependent on the cranial descending coronary artery. Oxygen appears to be probably supplied through arterial blood in the left ventricle via the endocardium.—KEY WORDS: hypoxia, myocardium, oxygen tension.

Jpn. J. Vet. Sci. 52(1): 79–84, 1990

Hypoxia has been defined as a failure of the oxygen supply necessary for normal function of cells in the living organism [16]. Tissues within the living organism exhibit different sensitivities to hypoxia. The central nervous system exhibits serious disturbances at the earliest stages of hypoxia, whereas skeletal muscles may remain relatively undamaged for long periods of anoxia [15]. In addition, the influence of cardiopulmonary function as well as intrinsic blood properties and the process of blood supply has an important role in the pathogenesis of hypoxia tissue damage [14].

In experimental cardiac arrest induced by phlebotomy in dogs, the oxygen tension (PO_2) in the bone, liver, brain and subcutaneous tissue rapidly decreases with the subsequent appearance of significant hypoxia of organs and tissues [8]. This description suggests close relation between cardiac function and hypoxia.

The active heart consumes large amount of oxygen, normally supplied by oxygenated blood from the coronary arteries. The mode of blood supply from the coronary artery to the myocardium has not been fully explained. In addition, the relationship between myocardial hypoxia and cardiac function remains unclear.

Using a small, highly accurate PO_2 sensor, the authors attempted to clarify the relationship between PO_2 in the three layers of the left ventricular (LV) myocardium and coronary arterial blood flow.

MATERIALS AND METHODS

In the present study, 6 adult healthy mongrel dogs (3 males and 3 females) of which body weight ranging from 7.0 to 14.0 kg were used. General physical examina-

tion, cardiac function studies and chest X-ray were performed to evaluate the condition.

In order to measure myocardial PO_2, a newly developed PO_2 sensor system, M-HOS™, and an analytical system, PO-2080™ (Mitsubishi Rayon Co., Ltd.), were used. The PO_2 sensor system consisted of an 80 μm platinum electrode covered by polypropylene and a thermocouple microprobe for thermal adjustment of oxygen tension. The PO_2 sensor was used after confirmation of a high correlation with the values obtained using a blood gas analyzer (IL-meter Micro 13, Instrumentation Laboratory) and arterial blood.

The myocardial PO_2 measurement is illustrated in Fig. 1. The dogs underwent thoracotomy under halothane (OF) anesthesia (100% oxygen inhalation) and the PO_2 sensor was inserted into the exposed left ventricular (LV) wall. Three sites were selected for insertion of the electrode, the area supplied by the paraconal interventricular branch of the left coronary artery, the cranial descending coronary artery (CDCA). The tips of the three PO_2 sensors were inserted into the subendocardium, the subepicardium and an intermediate in the ventricular wall, which enabled us to measure the PO_2 at points through the cross-section of the LV wall. The PO_2 at each site was measured using a simultaneous recording. The sites of insertion of the PO_2 sensors were confirmed by autopsy.

After the initial measurement, the basal portion of the CDCA was reversibly occluded for 5 min by using surgical thread and then was released to study the influence of reversible myocardial hypoxia on the PO_2 within the three layers of the myocardium compared to intraventricular blood.

RESULTS

Responsiveness of the PO_2 sensor: The correlation between the PO_2 sensor and the arterial blood gas measurement was evaluated. The PO_2 was measured 30 min after insertion of the PO_2 sensor into the carotid artery under OF anesthesia. At the same time, the PO_2 of blood obtained from the abdominal aorta was measured with a blood gas analyzer. The actual measured values are shown in Fig. 2. The regression equation was $Y=1.4X-4.9$, and the correlation coefficient was $r=0.993$ ($N=26$).

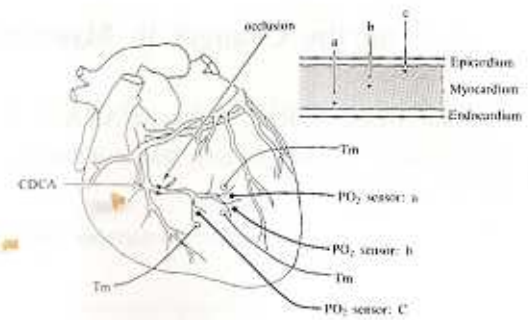

Fig. 1. Mesurement of myocardial oxygen tension in myocardial hypoxia. A, The PO_2 sensors, 80μm ø platinum electrodes, were inserted in the myocardium of left ventricle around the cranial descending coronary artery (CDCA). Thermocouple microprobe (Tm) was inserted near each PO_2 sensor for thermal adjustment of PO_2. B, The tips of PO_2 sensors were at the subendocardium (a), the subepicardium (c), and the mid-ventricular myocardium (b). Myocardial hypoxia was induced by transient occulusion of CDCA.

Oxygen tension in the subendocardium of the left ventricle: The PO_2 obtained from the subendocardial myocardium of the LV wall ranged from 261 to 342 mmHg, with the mean and standard deviation (SD) of 291.0±38.5 mmHg ($N=5$). The simultaneous PO_2 in the arterial blood in the LV cavity was 308 to 500 mmHg, with the mean and SD of 411.5±68.3 mmHg ($N=4$). The mean PO_2 in the subendocardium was lower than that in arterial blood by about 120 mmHg.

The CDCA was occluded to induce a reversible hypoxia in the myocardial tissue. The PO_2 changes in the subendocardial myocardium were observed (Fig. 3). For 5

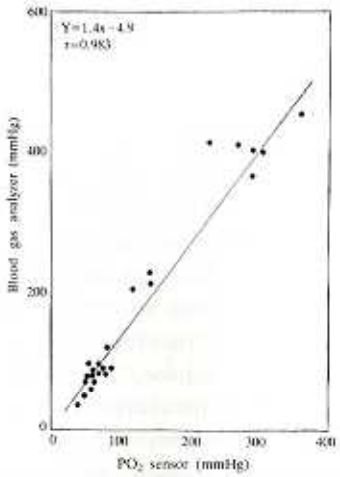

Fig. 2. Relationship between arterial oxygen tension determined by blood gas analyzer and by PO_2 sensor.

min after the arterial occlusion, the PO_2 in the subendocardial myocardium remained approximately 300 mmHg. Even after the release of the occlusion, little change was noted in the subendocardial PO_2. The induction of temporary myocardial hypoxia resulted in little change in the PO_2 at this site.

Oxygen tension within the mid-ventricular myocardium in the left ventricle: The PO_2 of the mid-ventricular myocardium ranged from 34.0 to 76.0 mmHg, with the mean of 61.0±16.7 mmHg (N=5). This result was approximately 350 mmHg and 230 mmHg lower than those in the blood in the LV cavity and in the subendocardial myocardium, respectively.

Fig. 3 shows the PO_2 after the induction of transient myocardial hypoxia. Within 2 min of the arterial occlusion, an average decrease of approximately 20 mmHg occurred, which was approximately one-third of the PO_2 prior to the arterial occlusion. The value remained stable for approximately 5 min. When the occlusion was released, a rapid recovery was observed and the PO_2 rose to a level higher than the pre-ligation value within 1 min.

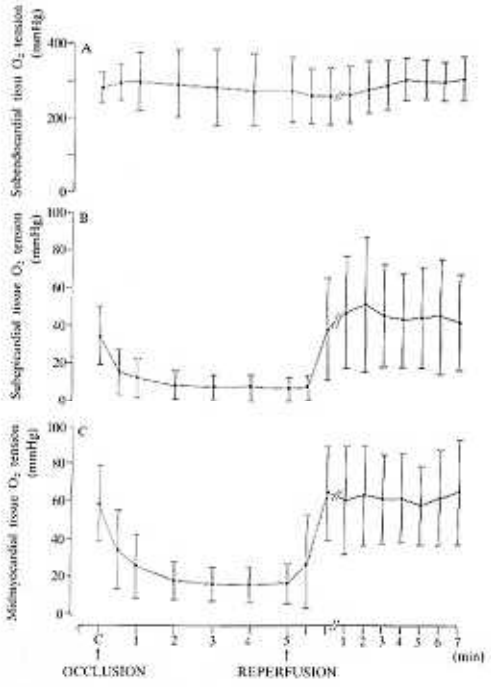

Fig. 3. Changes of myocardial tissue oxygen tension during coronary artery occlusion and after reperfusion. A, subendocardial tissue oxygen tension. B, subepicardial tissue oxygen tension. C, mid-ventricular myocardial tissue oxygen tension.

The PO_2 in the mid-ventricular myocardium averaged approximately 60 mmHg. This is approximately 85% and 79% lower than those of blood in the LV cavity and of the subendocardium, respectively. After the induction of a transient myocardial hypoxia by arterial occlusion, the PO_2 rapidly decreased in the mid-ventricular myocardium but recovered promptly after releasing the occlusion.

Oxygen tension in the subepicardial myocardium in the left ventricle: The PO_2 in the subepicardial myocardium ranged between 22.0 and 58.0 mmHg, with the mean of 35.8±13.9 mmHg (N=6). This is approximately 380 mmHg lower than the PO_2 in the LV cavity, 250 mmHg lower than that in the subendocardial myocardium and 25 mmHg lower than that in the mid-ventricular myocardium.

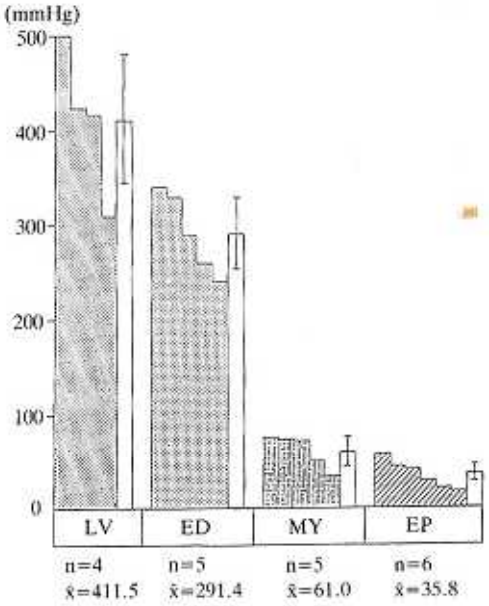

Fig. 4. Analysis of left ventricular blood oxygen tension and myocardial tissue oxygen tensions. The PO_2 in the subepicardial myocardium is the lowest among the three layers. LV: left ventricular blood oxygen tension, ED: subendocardial tissue oxygen tension, MY: mid-ventricular myocardial tissue oxygen tension, EP: subepicardial tissue oxygen tension.

A rapid fall of the PO_2 was noted within 2 min of the arterial occlusion. The mean value decreased about 10 mmHg, a fall approximately one-third of the level prior to the arterial occlusion. When the occlusion was released after 5 min, a rapid recovery took place within 1 min and the rebound of the PO_2 was higher than the pre-occlusion levels.

The PO_2 in the subepicardial myocardium averaged 36 mmHg. This value was 91% lower than that in the blood of the LV cavity, 88% lower than that in the subendocardial myocardium and 41% lower than that in the mid-wall myocardium. The PO_2 in the subepicardial myocardium was the lowest in each layer of the myocardium. When myocardial hypoxia was induced by arterial occlusion, a sudden decrease in the PO_2 was noted, with recovery immediately after the release of the occlusion.

DISCUSSION

The data obtained using the newly developed microcapillary platinum PO_2 sensor, N-HOS™ and PO-2080™ system and a blood gas analyzer indicated an extremely high correlation. With the high accuracy the PO_2 sensor enables us to measure precisely the PO_2 in the intracardiac tissue.

Utilizing this sensor, the PO_2 in the myocardium was measured at three sites: the subendocardial myocardium, the subepicardial myocardium and the mid-ventricular myocardium of the left ventricle.

In comparision of each PO_2 value, the subendocardial, mid-ventricular and subepicardial myocardium were about 30%, 85% and 91% lower than that in the blood of the LV cavity. The subepicardial myocardium was the lowest value among the three layers of the myocardium studied.

In one published study, the PO_2 in the myocardium was measured after insertion of a 0.83 mm ϕ PO_2 sensor at a depth of about 3 mm in the LV wall between the CDCA and the diagonal branch of the left coronary artery. The mean value of the myocardial PO_2 obtained in that study was 26.2 mmHg (N=5). The PO_2 of arterial blood measured with the same PO_2 sensor averaged 113.6 mmHg (N=5) [3]. In another study, the PO_2 in the myocardium and arterial blood under controlled respiration with 40% oxygen averaged 27.6 and 113.3 mmHg, respectively. Under controlled ventilation with 100% oxygen, the PO_2 of the myocardium and arterial blood were 33.8 and 404.4 mmHg, respectively [12].

The PO_2 in the myocardial tissue of dogs described in those reports appear to be lower than our results obtained in the subepicardial myocardium of the LV wall. While, the PO_2 in the arterial blood under controlled ventilation was almost equal.

This is probably due to differences in the response of PO_2 to tissue changes [1, 2, 4, 6, 7, 9–11, 13]. The arterial blood response was little influenced by the size of the PO_2 sensor, but tissue injury increased. The accuracy of the 80 μm PO_2 sensor used in the present study appears to be superior to other reported PO_2 sensors.

Since the PO_2 in the ventricular wall decreased from the endocardial to the epicardial sides, uniform insertion of the PO_2 sensor to a depth of 3 mm from the heart surface may cause a measurement variation depending on the thickness of the ventricular wall. In a thin wall, for example, placing the sensor at a depth of 3 mm will be led to placement nearer the endocardium than in thick wall. In the human heart, the PO_2 is lower in the superficial layer than in the deep layer of the anterior wall of the LV, and the measurements vary depending on the site of the PO_2 sensor insertion [3].

When blood flow was blocked and released at the CDCA with resulting transient hypoxia, the PO_2 at the mid-ventricular myocardium suddenly fell, reaching about one-third of the level before arterial occlusion. When the occlusion was released and blood flow was restored, the PO_2 rapidly recovered and exceeded the level prior to the arterial occlusion within 2 min. The oxygen supply to this site appears to be dependent on the blood flow through the coronary artery. Introduction of transient myocardial hypoxia resulted in a sudden fall of the PO_2 measured at the subepicardial myocardium. After release of the occlusion, a recovery to a level exceeding the preocclusion value was noted. The oxygen supply to the subepicardial myocardium of the LV wall also appears to depend on the blood flow through the left coronary artery in a manner similar to the mid-ventricular myocardium.

Coronary artery occlusion causes the myocardial PO_2 to fall, but PO_2 increased again in response to application of balloon pumping. This may be due to recruitment of capillaries acting as a collateral circulation for the coronary artery system [5, 12]. In the authors' studies, coronary artery ligation results in a sudden fall of PO_2 in the mid-ventricular and subepicardial myocardium. This state persists during the blockade of blood flow in the coronary artery, but rapidly recovers after release of the occlusion. This recovery phenomenon is due to a transient increase of blood flow caused by vascular dilation in response to the rapid increase of blood flow in sleeping vessels as collaterals.

Introduction of transient myocardial through ligation and release of the CDCA resulted in little change in the PO_2 in the subendocardial myocardium of the LV wall. It has been considered that all the myocardium was supplied with oxygen by coronary artery. In authors' study, however, oxygen supply to the subendocardial myocardium appeared to be independent of coronary artery blood flow [3]. This result suggested that the oxygen may be supplied from intracardiac blood via the endocardium, which protects the conduction system from localized hypoxia.

REFERENCES

1. Albanese, R. A. 1973. On microelectrode distortion of tissue oxygen tension. *J. Theor. Biol.* 38: 143–154.
2. Baumgartl, H., Grunewald, W., and Lubbers, D. W. 1974. Polarographic determination of the oxygen partial pressure field by pt-microelectrodes using the O_2 field in front of a pt-macroelectrode as a model. *Pfluegers Arch. Gesamte Physiol. Menschen Tiere* 347: 49–61.
3. Burch, G. E. 1953. A Primer of Cardiology., Lea &Febiger, Philadelphia.
4. Endo, M., Hino, T., Itaoka, T., Hayashi, H., and Wada, J. 1978. Continuous mesurement of human myocardial tissue oxygen tension. *Resp. Circ. (Kokyu to Junkan)* 26: 881–887 (in Japanese, with English summary).
5. Fatt, I. 1964. An ultramicro oxygen electrode. *J.*

Appl. Physiol. 19: 326–329.
6. Gradner, T. J., Brantigan, J. W., Perna, A. M., Bender, H. W., Brawley, R. K., and Gott, V. L. 1971. Intramyocardial gas tension in the human heart during coronary artery-saphenous vein bypass. *J. Thorac. Cardiovas. Surg.* 62: 844–850.
7. Grunewald, W. 1970. Diffusionsfehler und Eigenverbrauch der Pt-Elektrode bei PO_2-Messungen im steady State. *Pfluegers Arch. Gesamte Physiol. Menschen Tiere* 320: 24–44.
8. Grunewald, W. 1973. How "local" is PO_2 measurement? pp. 160–163. *In*: Oxygen Supply (Kessler, M., Bruley, D. F., Clark, L. C., Jr., Lubbers, D. W., Silver, I. A., and Strauss, J. eds.), Urban & Schwarzenberg, Munchen.
9. Kobayashi, A. and Murakawa, K. 1979. Cerebral, liver and renal tissue gas changes with hemorrhagic shock. *Jpn. J. Acute Med. (Kyukyu Igaku)* 3: 681–684 (in Japanese).
10. Kreuzer, F. and Kimmich, H.-P. 1976. Recent developments in oxygen polarography as applied to physiology. pp. 123–158. *In*: Measurement of Oxygen (Degen, H., Balslev, I., and Brook, R. eds.), Elsevier Sci. Pub., Amsterdam.
11. Lubbers, D. W. 1966. Methods of measuring oxygen tensions of blood and organ surfaces. pp. 103–127. *In*: Oxygen Measurements in Blood and Tissues and Their Significance (Payne, J. P. and Hill, D. W. eds.), Churchill, London.
12. Lubbers, D. W. 1969. The meaning of the tissue oxygen distribution curve and its measurement by means of Pt electrodes. *Prog. Resp. Res.* 3: 112–123.
13. Monma, M., Miyake, Y., Shiroma, T., Mikawa, M., Yamamoto, Y., Nakamura, Y., Sakurai, N., Okamura, T., and Sugai, J. 1975. Studies on the pathophysiology of the ischemic heart disease (Measurement of intramyocardial oxygen gas tention). *J. Jpn. Coll. Angiol.* 15: 623 (in Japanese).
14. Schneiderman, G. and Goldstick, T. K. 1976. Oxygen fields induced by recessed and needle oxygen microelectrodes in homogeneous media. *In*: Oxygen Transport to Tissue, Vol. II (Grote, J., Reneau, D., and Thews, G. eds.), Plenum Pub., Oxford.
15. Sezai, Y. 1970. Respiratory failure and circulation. pp. 487–496. *In*: Surgical Physiology, Vol. 1 (Ishiyama, S., Wada, T., Nakamura, N., and Hori, M. eds.), Nankodo, Tokyo (in Japanese).
16. Sporri, H. and Stunzi, H. 1969. Pathophysiologie der Haustiere. Paul Parey, Berlin.
17. Sunada, T. and Seki, S. 1970. Diagnosis and treatment of acute respiratory failure. pp. 481–485. *In*: Surgical Physiology, Vol. 1 (Ishiyama, S., Wada, T., Nakamura, N., and Hori, M. eds.), Nankodo, Tokyo (in Japanese).

要　約

心筋組織酸素分圧の変動に関する研究：中村　志・若尾義人・武藤　眞・高橋　貢（麻布大学獣医学部獣医外科学教室）——新しく開発された微小電極，PO_2 センサー（M-HOS, PO-2080：三菱レイヨン社）による動脈血中の酸素分圧測定値について，従来からの血液ガスアナライザーによる動脈血液中の酸素分圧測定値と比較検討した．その結果，回帰直線は $Y=1.4X-4.9$ ($r=0.993$) であり，両者間では極めて相関性が高く，PO_2センサーによる酸素分圧の測定値は，血液ガスアナライザーの測定値に匹敵することが確認された．PO_2センサーを使用して心筋組織内の酸素分圧を測定した．測定部位は左冠状動脈前下行枝の支配領域で3カ所を選び，PO_2センサーの先端を左心室心内膜下，左心室心外膜下ならびに心室壁中間点に位置するように刺入して当該部位における心筋組織内の酸素分圧を測定した．その結果，左室腔内動脈血中の酸素分圧を100％（平均411.5±68.3mmHg）とした場合，心内膜下の心筋組織では約70％，心室壁中間点の心筋組織では15％，心外膜下の心筋組織では約9％であり，心内膜側から心外膜側に向って酸素分圧の勾配がみられることが確認された．冠状動脈前下行枝の血行を遮断または解除して心筋組織に供給される酸素供給経路を確認した結果，心室壁中間点ならびに心外膜下の心筋組織では，前下行枝の血行遮断によって顕著な低酸素状態を呈し，血行遮断を解除することによって速やかに回復を示すことから，この部位における酸素供給は，明らかに冠状動脈の血液から供給されることが確認されると同時に，冠状動脈の血行動態に大きく影響されることがわかった．一方，心内膜下の心筋組織では，冠状動脈の血行にほとんど影響されなかった．したがって，この部位における酸素供給は冠状動脈よりもむしろ心腔内動脈血中から心内膜を介して供給されるものと考えられた．