Experimental coronary artery occlusion
I. Measurement of infarct size

Experimenteller Koronarverschluß
I. Bestimmung der Infarktgröße

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With 5 figures

(Received August 1, 1978)

Summary

We studied the size of infarcts in 25 dogs 48 hrs after proximal occlusion of the left anterior descending coronary artery. In one group of animals infarct size was measured by histologic criteria, in another group the infarct was measured macrohistochemically using p-NBT and malate to incubate unfixed slices of myocardium. In both groups infarct size was expressed as percentage of the area of perfusion of the occluded artery. Infarct size was 72% of the area-at-risk in the group studied by histology and 74.5% in the macrohistochemical group. The satisfactory agreement of both methods favors the p-NBT technique because of its ease and speed. It is suggested that the expression of infarct size as percentage of the perfusion area is a good definition and should be used in experiments designed to manipulate infarct size. In this way differences in the size of occluded arteries and their respective perfusion areas have no or only a negligible influence on infarct size.

Interventions to reduce the size of jeopardized tissue after coronary artery occlusion has become a major research undertaking with obvious clinical implications. Efforts to salvage ischemic myocardium depend, however, critically on the accuracy to measure infarct size.

The pioneering work of Braunwald and his group (1, 2, 3) has shown that infarct size can be estimated from epicardial electrograms (4), precordial mapping (5) and from the kinetics of the CPK plasma concentration (6, 7). These measurements are, however, indirect (epicardial EG) or they respond relatively slowly to interventions (CPK). In experimental animals infarct size can be measured more directly and with a high degree of precision by histologic means. The disadvantages of conventional histology are that the animal cannot serve as its own control in drug studies and that the animal has to survive the intervention 24 to 48 hours in order to obtain a sharp delineation between living and necrotic tissue. Finally, a quantitative histologic determination is time consuming and the result is usually not available one week after coronary occlusion at the earliest. It is therefore desirable to have a faster method with a similar degree of precision.
Another problem in the determination of infarct size is the area of reference. Often the amount of necrotic tissue is expressed in absolute units (cm$^3$ or g) or as percentage of left ventricle. Both methods suffer from the disadvantage that the size of the occluded artery influences infarct size. We have shown repeatedly (8, 9) that the best method of reference is to express the area of necrosis relative to the area-at-risk, i.e. the perfusion area of the occluded artery. In this way the size of the occluded artery does not influence infarct size significantly. We will show later (10) that this is correct in principle but that the occlusion of very small arteries produces relatively smaller infarcts.

**Materials and Methods**

Mongrel dogs of either sex weighing between 20 and 30 kg were premedicated with subcutaneous piritramide (5 mg/kg) and Haloperidol (0.5 mg/kg). Anesthesia consisted of 5 mg/kg intravenous sodium pentobarbital and nitrous-oxide-oxygen (70 + 30). Piritramide was constantly infused at a rate of 2.5-5.0 mg/kg/hr.

The animals were artificially ventilated with intermittent positive pressure using a Bird Mark 7 – Mark 4 combination.

The chest was opened in the 5th left intercostal space and the heart was suspended in a pericardial cradle. The left anterior descending coronary artery was prepared and proximally ligated. Thirty minutes after occlusion the chest was closed in layers and the animals were allowed to recover. Occasionally it was necessary to defibrillate the heart with DC-shocks. This occurred almost always within the first 30 minutes after occlusion which was the reason why the chest was left open during that period.

Forty-eight hours after coronary artery occlusion the animals were again anesthetized as described above. The chest was opened, the heart was stopped by AC shock (50 Hz, 60 V) and excised. Thereafter the heart was either processed in our own laboratory (“Nauheim-Method”) or it was put in crushed ice and transferred to the Department of Pathology, University of Marburg (“Marburg-Method”).

![Fig. 1. Illustration of the “Marburg”-Method. Left panel: arteriogram of a heart slice. Right panel: histologic section of an entire heart slice. The perfusion area of the occluded coronary artery is taken from the arteriogram and drawn into the histologic section. The infarcted area is outlined (under the microscope) in the section and both areas are determined by planimetry.](image-url)