Experimental Myocardial Infarction in Dogs

Description of a Closed Chest Technique

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SUMMARY

A closed chest technique for production of myocardial infarction in dogs is described. After isolation of the left carotid artery, selective coronary cineangiography is performed. A guide wire is then inserted into the catheter and advanced into the circumflex or anterior descending branch of the left coronary artery. The catheter is temporarily removed. A specially designed, siliconized, stainless steel cylinder is then inserted over the guide wire. The catheter is reinserted and is used to push, direct, and lodge the stainless steel cylinder into the anterior descending or the circumflex artery. The dogs are heparinized before, and for 3 days subsequent to, constriction. Ventricular arrhythmias are treated with procainamide. Coronary cineangiograms and serial electrocardiograms are obtained after coronary artery constriction. This technique provides an accurate model for research in the field of myocardial infarction.

Additional Indexing Words:
Myocardial ischemia
Animal model for myocardial infarction

The production of acute myocardial infarction or ischemia in animals is of particular importance in research related to coronary artery disease. In this regard a reliable and accurate experimental model should closely simulate the clinical situation. Ideally, an animal model should provide the following conditions: (1) The technique of producing myocardial infarction or ischemia should not need thoracotomy. (2) The technique should have the versatility of producing the lesion in various sites of coronary arteries. (3) Physiological studies, such as determination of coronary blood flow, especially distal to the narrowing (by injection of isotope indicators into the narrowed vessel and precordial counting or serial coronary sinus sampling), and cardiac metabolic studies should be feasible.

It is the purpose of this preliminary communication to describe a closed-chest technique for producing myocardial infarction in dogs. Narrowing of the coronary artery and subsequent occlusion were produced by insertion of a stainless steel cylinder into a branch of the left coronary artery.

Methods

Stainless steel cylinders were polished and siliconized. They measured 4 mm in length, 3.25 mm in external diameter, and 2.0 mm in internal diameter. They were smoothly tapered for ease of insertion into the coronary artery.

Sixteen mongrel dogs, weighing between 25 and 30 kg, formed the material for this study. During general anesthesia with intravenous injection of 10 mg/kg of pentobarbital and intramuscular injection of 90 mg of morphine, the left carotid artery was isolated. Heparin sodium, 1.5 mg/kg, was administered intravenously. A

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Schematic demonstration of production of coronary artery narrowing. Stainless steel cylinder is at the left coronary ostium. The catheter will push and eventually lodge the cylinder (which is already inserted over the guide wire) into the branches of the left coronary artery.

no. 7½ F-radiopaque J-shaped polyethylene catheter was inserted into this artery, and selective left coronary cineangiograms were obtained. This served as control for subsequent coronary cine-

angiograms after production of narrowing in the coronary artery. A Teflon-coated guide wire * was inserted into this catheter and advanced into the circumflex or anterior descending branches of the left coronary artery. The catheter was then removed and the stainless steel cylinder was inserted over the guide wire. The catheter was reintroduced and served to push and direct the cylinder into the desired position in the coronary artery (fig. 1). After positioning of the cylinder, the catheter was withdrawn, and the guide wire was removed. The stainless steel cylinder was positioned in the anterior descending branch in five dogs and in the circumflex branch in 11 dogs. Selective coronary cineangiograms were repeated in all dogs. After this initial period, the dogs were kept in kennels, under the supervision of a veterinarian. Anticoagulation with heparin, 1.5 mg/kg given intravenously every 4 hours, was continued for 3 days after insertion of this cylinder. At night concentrated heparin, 100 mg, was administered subcutaneously. Coronary cineangiograms were repeated periodically in subsequent days and weeks in several animals, and limb lead electrocardiograms were serially recorded in all. Necropsy was performed in each dog after spontaneous death or sacrifice.

*Picker X-ray Corp., White Plains, New York, Catalog No. 290554.

Coronary cineangiograms immediately after constriction of the coronary artery. Left lateral views. (A) Narrowing (transparent Ameroid cylinder) of anterior descending branch of left coronary artery. Radiopaque material has passed through the lumen of the artery, and the vessel is visualized distally. Myocardial infarction involving the anterior wall of the left ventricle developed. (B) Narrowing is produced in the circumflex branch. Radiopaque material opacified the narrowed vessel distally. Myocardial infarction involving the inferior wall of the left ventricle developed.
Serial electrocardiographic tracing (lead II) in a representative experiment before and after narrowing of anterior descending branch of the left coronary artery. Ventricular arrhythmia was treated with procainamide.

Figure 3

Results

Figure 2 demonstrates the narrowing in the anterior descending and circumflex branches of the left coronary artery. Initially, the constriction was produced by Ameroid cylinders of the same shape and dimensions as the stainless steel cylinders in the hope of producing gradual occlusion. For demonstration of narrowing, the illustration with the Ameroid cylinder is shown, since constriction produced by the stainless steel cylinder frequently cannot be visualized because of the opacity of the metal. The distinctive feature of the present technique is that it does not occlude the coronary artery acutely. The infarctions in the dogs followed a fairly uniform pattern. There were no electrocardiographic abnormalities until 6 to 8 hours later. After this period, ventricular extrasystoles or intraventricular conduction defects appeared. These were treated with repeated intramuscular injections of procainamide (fig. 3).
Subsequent to this arrhythmic period, some of the animals developed signs and symptoms of heart failure.

Figures 4 and 5 demonstrate coronary cineangiograms 1 week and 2½ months after production of constriction in anterior descending and circumflex arteries, respectively. In this series, the overall mortality rate was 50%; however, only three dogs died during the first 24 hours. There was no immediate death due to arrhythmias. Of five dogs in which infarction was produced in the area of the anterior descending branch, three survived. After the first week the mortality of the animals was markedly decreased. Late complications of myocardial infarction were seen in one of the animals, who had ruptured chordae tendineae and died 3 weeks after the production of myocardial infarction (obstruction was produced in the circumflex artery).
EXPERIMENTAL MYOCARDIAL INFARCTION

Figure 5

Coronary cineangiogram, left lateral view, 2% months after insertion of stainless steel cylinder into circumflex branch (large arrow). Most of the radiopaque material was injected into anterior descending branch of the left coronary artery. There is retrograde visualization of the distal part of the circumflex branch via collateral channels (small arrows) from the anterior descending branch.

In addition to the ruptured chordae tendineae, necropsy revealed an extensive old myocardial infarction and fibrosis involving the inferolateral wall of the left ventricle.

Discussion

Several techniques are used to produce myocardial ischemia or infarction in animals. In an open chest animal, ligation of the coronary artery or its branches is the easiest and most widely used technique. This, indeed, has a high mortality rate because of ventricular arrhythmias. For gradual occlusion of coronary arteries, Ameroid sleeves1,2 have been used in open-chest animals. By treating Ameroid with petroleum, the rate of hygroscopic action decreases, and constriction is further delayed. These animals usually recover and, in fact, had they not been subjected to thoracotomy, would be good models for coronary artery narrowing. In closed chest animals, acute myocardial infarction or ischemia has been produced by embolization of microspheres of various sizes. Gensini and associates3 have selectively occluded the anterior descending branch of the left coronary artery in experimental animals by radiopaque spheres delivered through a Sones catheter. Harris4 has produced occlusion of the coronary artery by a two-stage technique. This technique results in delayed production of arrhythmia; however, the need for thoracotomy makes this technique less desirable as an experimental model. Salazar5 has produced experimental myocardial infarction in dogs without using thoracotomy by passing direct electrical current into the coronary arteries. This technique continues to be a good model for experimental myocardial infarction, although subsequent lysis of the clot may be a shortcoming.
In the present study, continuous telemetering of the electrocardiogram was performed in some animals, and the pattern of development and evolution of arrhythmia and myocardial infarction was observed. This technique enables one to produce occlusion or narrowing of the coronary arteries at various sites, depending upon the size of the stainless steel cylinder and coronary arteries. We have been able to produce occlusion in secondary branches of the anterior descending and circumflex arteries. Coronary blood flow, although not measured in this study, can easily be measured by selective injection of a radioisotope substance (xenon-133 or krypton-85) through the lumen of the cylinder into the constricted vessel for radioactive counting. Indeed, the effects of various pharmacological agents, especially anticoagulants, anti-arrhythmic medications, and β-adrenergic receptor-blocking agents, can be studied. In this study, heparin was used mainly to delay the clotting. In some preliminary experiments, when heparin was not used, acute occlusion of the cylinder with subsequent ventricular tachycardia and fibrillation occurred. This usually led to the animal's early death. Heparin, as used in these experiments, delayed rather than prevented the formation of the clot. Although dogs were used as experimental animals in this study, pigs may be a better model for experimental myocardial infarction, since their coronary arteries are more nearly similar to the human coronary vascular system.

References
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