A Conscious Porcine Model for Sudden Cardiac Death

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INTRODUCTION

Sudden cardiac death is a major challenge to our health care system. Hundreds of thousands of lives annually claimed by sudden cardiac death – including more than 10000 fatalities in Finland – and the 60 % of all cases caused by coronary heart disease demonstrate the vast magnitude of the disease (*Lown* 1984, *Reunanen* 1984). Until 25 years ago sudden cardiac death was considered the final, inevitable and ultimate expression of irreversible coronary atherosclerosis. Since then it has been shown that ventricular fibrillation, the basic mechanism of sudden cardiac death, can be both prevented and reversed.

Sudden cardiac death has been studied in numerous clinical and experimental investigations. Experimental studies have almost invariably been done with dogs and cats. These species have, however, many anatomical (*Lumb & Singletary* 1961) and physiological dissimilarities with other species, including man, and even with each other.

It is generally known that the pig like man, but unlike the dog, has few collaterals, and the collateral blood flow in the anterior descending branch of the left coronary artery is very small (*Schaper* 1971, *White & Bloor* 1981) and that interspecies differences in the coronary blood flow may alter both the arrhythmogenesis and drug effects in various arrhythmia models (*Szekeres & Papp* 1971). Furthermore blood flow distribution in the ischemic area of the dog also differs considerably from that observed in the pig. The myocardial blood flow in the pig is much smaller per unit of muscle mass and more uniform than in the dog (*Most, Williams & Millard* 1978).

The most commonly used preparation in cardiovascular research has been an open-chest anaesthetized animal. This preparation makes it possible to study the intact cardiovascular system, but the preparation has two serious drawbacks.

The anaesthesia as such has for quite some time been known to affect the circulatory system directly and/or though an interaction with the nervous system (*Ferguson, Shadle & Gregg* 1953, *Olmsted & Page* 1966, *Epstein, Wang & Bartelstone* 1968, *Horwitz et al.* 1969, *Giles & Birch* 1970, *Sawyer, Lumb & Stone* 1971, *Halinen, Hakumäki & Sarajas* 1978, *Manders & Vatner* 1976, *Nevalainen et al.* 1980, *Friström* 1983). Open chest necessitates the use of machined ventilation and causes a change in the dynamic geometry of the heart (*Rushmer, Finlayson & Nash* 1954, *Sandler* 1975). Intermittent positive pressure ventilation tends to affect the cardiac output, aortic stroke volume and venous return (*Morgan, Martin & Hornbein* 1966). While the use of chronic awake animals circumvents the problems of anaesthesia, open chest, and artificial respiration, it also creates some new problems.

The question of what type of measurements can be made in the unanaesthetized animal can be answered with advanced instrumentation and skilful training and handling of the animals. Conciousness as such means that the animal is well aware

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of its surroundings, to which it reacts with its individual and species-specific manner. Only recently has the use of conscious, trained and chronically instrumented animals in studies of cardiac arrhythmias by coronary occlusion been emphasized. *Skinner, Lie & Entman* (1975) investigated the effects of adaption and beta-blockage on ventricular fibrillation with conscious swine instrumented with coronary occluder. Their study showed that the incidence of ventricular fibrillation in pigs undergoing coronary artery occlusion in an unfamiliar environment was substantially higher than in a familiar laboratory setting.

According to the foregoing the majority of experimental studies on sudden cardiac death has been carried out with anaesthetized carnivore species. The specific aims of this study were to develop a conscious model for sudden cardiac death in a species with a close resemblance to man and evaluate its performance and applicability.

MATERIALS AND METHODS

Animals

This study was carried out with a total of 7 Göttingen miniature swine. Five of these animals belonged to an uncoloured line, three were females and four were uncastrated males. The age of the animals varied from 152 to 439 days (mean ± SD = 261.1 ± 105.3) and the corresponding weight range was 24–39 (mean ± SD = 29.1 ± 6.4) kg.

The animals were produced within the University, reared at seven weeks of age and subsequently housed in pens, 3–5 animals of the same sex together. No bedding was used and the pens were washed daily with water. The animals were fed with commercial hog chow (Emakko-Pekoni, Vaasanmylly Oy, Finland) with precalculated doses twice daily and municipal tap water from water nipples ad libitum.

Surgical Procedure

Prior to anaesthesia the animals were fasted for 24 hours. Sedation and premedication were achieved using azaperone (2 mg/kg Stresnil, Janssen Pharmaceutica N.V. Belgium). 15–20 minutes after azaperone i.m. injection the animal was anaesthetized with thiopental sodium i.v. (7 mg/kg, Hypnostan, Leiras Huhtamäki Oy, Finland) and subsequently intubated. The skin of the ventral neck and left chest was clipped and scrubbed with chlorhexidine-ethanol (Klorheksidiinisprii, Rohto, Finland). The animal was connected to a volume controlled ventilator (Engström 150, Mivab, Sweden) fed with equal volumes of oxygen and room air. A temperature corrected methoxyflurane vaporizer (Pentec 2, Cyprane Ltd, England) was connected into the oxygen line. Using a 0.5–1.0 % concentration of methoxyflurane (Penthrane, Abbott, USA) a considerably stable anaesthesia and a 24 hour postoperative analgesia was achieved (*Greene* 1979).

A midline incision was made on the ventral neck. The left carotic artery was located and freed of surrounding tissues. A small skin incision was made behind the left ear. A catheter made of a size 5 F PVC feeding tube (C. R. Bard, USA, I.D. = 1.2 mm) was drawn underneath the skin from the main incision to the incision behind the ear, where the protective box (Figure 1) was to be placed. A small incision through the arterial wall was made. The catheter was forwarded into the lumen to a 10–15 cm depth. The artery was tied with silk ligatures around the catheter. The lumen of the catheter was filled with heparinized saline (5000 IU heparin in 100 ml of physiologic saline). A disposable cut 18G needle, which fitted snugly into the lumen, was placed to the other end of the catheter, and subsequently this was coupled to a plastic three-way-stopcock.

A skin incision about 25–30 cm long was made along the caudal shoulder muscula-

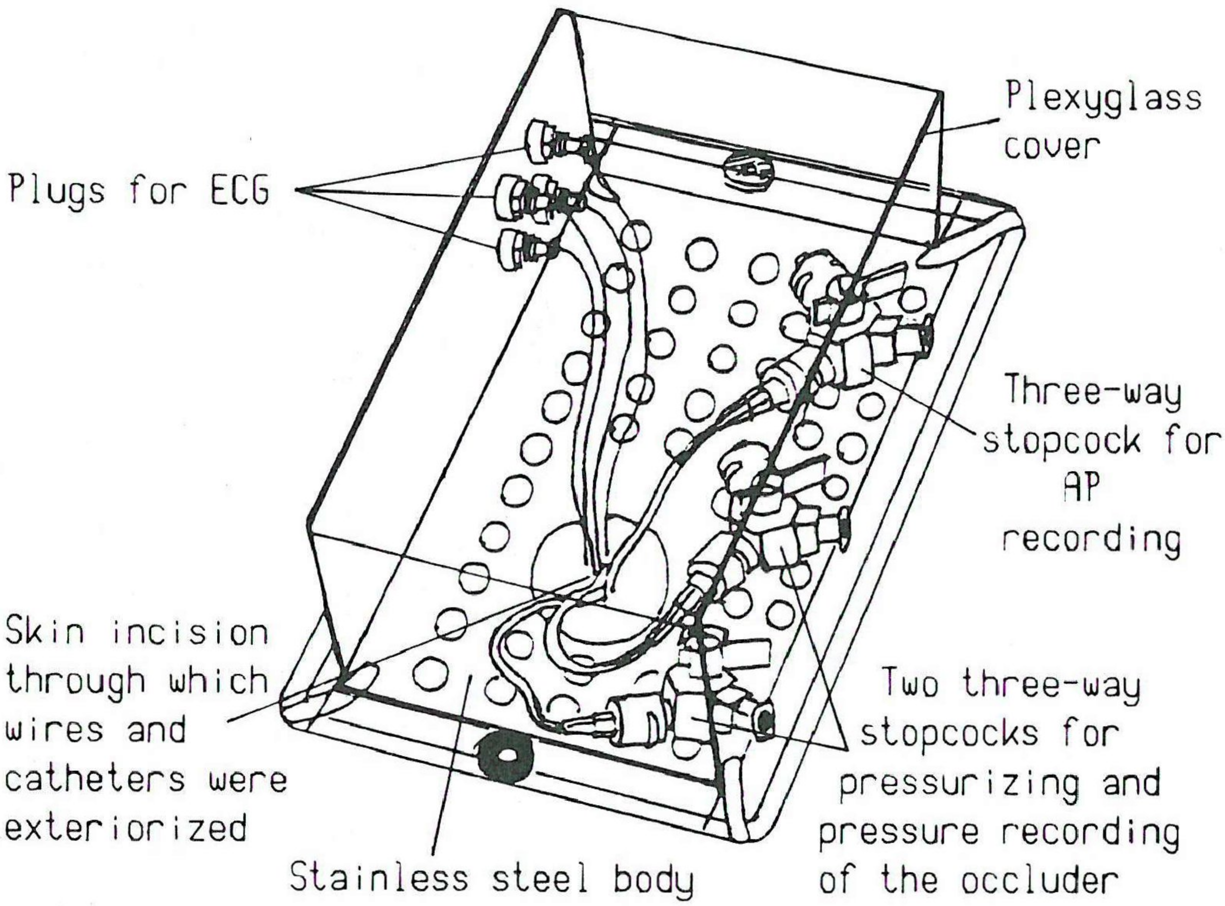

Figure 1. Design and components of the protective box used. Dimensions of the box are 100 mm × 70 mm × 30 mm.

ture contour 3–5 cm behind it. The latissimus dorsi muscle was partly cut. The entrance into the thorax was achieved through the left fourth intercostal space. In order to decrease the susceptibility to cardiac arrhythmias and irritability of the heart during manipulation, the animals were given intravenously 1 mg/kg lidocaine hydrochloride (Lidocard, Orion-Yhtymä, Finland). The pericardium was cut 5–7 cm to expose coronary arteries. The anterior descending (LAD) branch of the left coronary artery was carefully freed from surrounding tissue for a 5 mm distance at about 1 cm below the corner of the left auricule. Pericoronary fascias and nerves were separated from the artery in order not to be included below the occluder. A tunnel wide enough to allow the passing of the occluder was made with a blunt dissection below the coronary artery. A hydraulic occluder made of silicone rubber tubing and sheet was constructed according to the description of *Dallmer et al.* (1979).

Electrodes made of teflon-coated multifilament stainless steel wires (size 0, Flexon, Davis+Geck, USA) sutured to the pericardium cranially and caudally were used for the recording of the pericardial ECG. The tubings of the occluder as well as the wires were passed under the skin to the incision behind the ear. Both silicone rubber tubings of the occluder were attached to plastic three-way-stopcocks with 18G cut disposable needles. All the instrumental connections were fixed with plastic ties (3M) on the protective box. The protective

box as such was sutured to the skin with stainless steel multifilament wires at each corner. Figure 1 illustrates the protective box and the fixing of the three-way-stop-cocks.
The closing of the thorax incision was commenced with the approximating of the fourth and fifth rib leaving the pericardial incision unclosed. The intercostal space was closed with interrupted surgical gut. The fascias of the latissimus dorsi muscle were sutured together with interrupted surgical gut. The skin was closed with nonabsorbable suture material.

Postoperative Care

The animal was moved to the recovery room where it was held until it was able to walk. A single (im) injection of antibiotic consisting of penicillin (20000 U/kg) and streptomycin (25 mg/kg) was given after recovery from anaesthesia.
After the surgery the swine was allowed a five-day recovery. During this time it was held in an individual pen and the arterial catheter was flushed daily with five ml of heparinized saline.

Training of animals

The animals were all exposed to a familiarization schedule. This consisted of two half-an-hour visits to the recording laboratory during the third and fourth day after the surgery. During these visits the animals were kept in a movable plywood box, which was the same where they were kept during the experiments. The top of the box was opened and the swine were exposed to handling simulating the actual recording.

Experimental session

During the experiments the swine were kept in a transportable box (120 cm × 45 cm × 53 cm), which allowed certain freedom to the animals; they could move half a meter back and forth, but could not turn around. Figure 2 shows the design of the box and instrumentation connections.
The experimental periods consisted of a 20-minute occlusion which was preceded by a 5-minute control period. The recording was not continued beyond the point of ventricular fibrillation. All the graphic illustrations are provided with indicators showing when occlusion was on.
The occlusion of the left coronary artery was accomplished by pressurizing either one of the silicone rubber tubings and measuring the pressure from the other tubing. Pressure was created with a disposable 30 ml syringe, and a standard acetylene pressure gauge was used for pressure measurement. Throughout the occlusion a pressure of 100 kPa was maintained.
Only the experiments resulting in a consistent ECG-change (Figure 3) were considered successful and consequently included into experimental groups. The exteriorized arterial catheter was connected with a 70 cm long PE-50-tubing to a pressor transducer (Hewlett-Packard 267BC) and amplifier (Hewlett-Packard 8805B), and the signals were stored on a Racal-7D instrumentation tape recorder.

Data Processing

The pressure recordings were used for the calculation of the systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP = SBP-DBP), mean arterial pressure (MAP = DBP + PP/3), heart rate (HR), tension time index (TTI = SBP × HR) and pulse-time index (PTI = PP × HR). Throughout the experiment these parameters were calculated for every 15-second interval. The end DBP and SBP were digitized from the ink jet recorder paper using a Bit Pad One digitizer and Data General Eclipse 130S minicomputer. The heart rate was calculated from the end diastole to end diastole intervals (T_{dd}) as follows

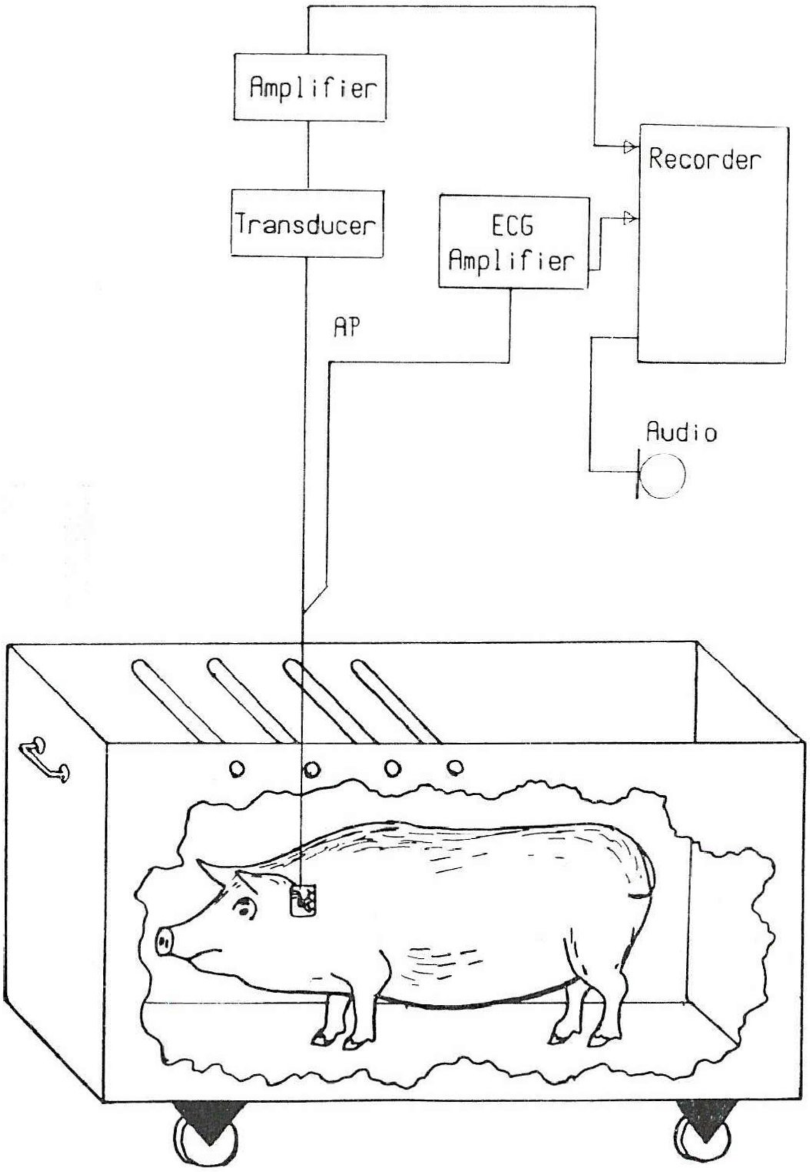

Figure 2. Plywood box where the swine were kept in experiments and connections diagram for recording of the signals.

$$HR = \frac{60\ s \times N_{15}}{\sum_{i=1}^{N_{15}} T_{dd,i}}\ min^{-1}$$

where N_{15} is the number of complete T_{dd}-intervals in the 15 sec period. The means were calculated for the heart rate, systolic pressure and diastolic pressure.

Ventricular extrasystoles were calculated from ink jet recorder paper. Primarily both ECG- and arterial pressure recordings were used. When the ECG-recording showed ventricular extrasystole, a simultaneous compensatory break and decrease in the diastolic pressure were noticed (Figure 3). In the few recordings with a too noisy ECG-recording compensatory break and the lowering of diastolic pres-

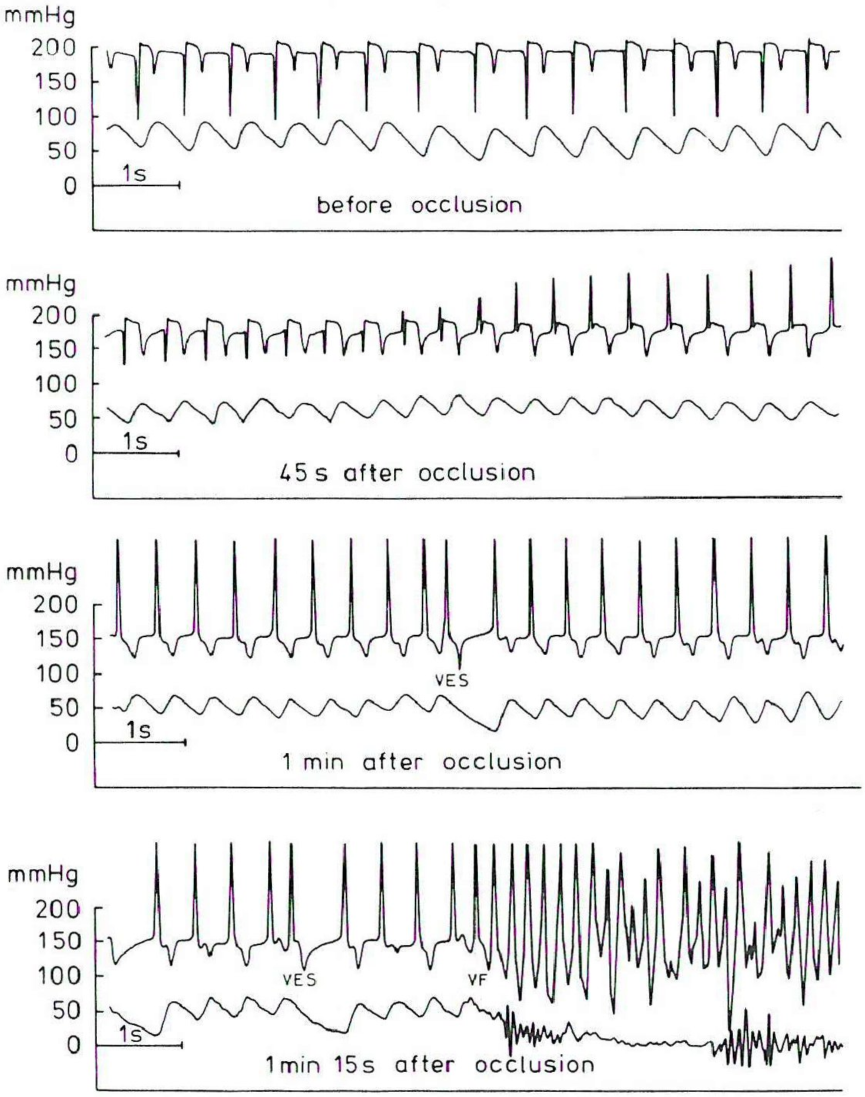

Figure 3. ECG- and arterial pressure recording of a typical experiment. Samples are picked from preocclusion period, 45 s, 1 min and 1 min 15 s after the occlusion was placed on. The beginning of the strip represents the time point indicated at the botom of each strip. The recordings illustrate ECG (pericardium)- and pressure changes, ventricular extrasystoles (VES) and ventricular fibrillation (VF).

sure in the arterial pressure recording were considered indicative of ventricular extrasystole. The extrasystoles were calculated at one-minute intervals after the occlusion.

Statistical Analysis

The Mann Whitney U-test was used for evaluation of the effect of sex and line on the occurrence of ventricular extrasystoles. The normal distribution of all haemodynamic parameters was tested with the Kolmogorov-Smirnov test prior to any covariance analysis. Intragroup comparisons for the seven haemodynamic parameters processed were tested with the analysis of covariance between periods. The main effects used were period, sex and line and the covariates were age and time.

Time was the absolute time elapsed since the beginning of the experiment. A SPSS-package on PDP 11/70 computer was utilized for all statistical analysis (*Morrison* 1982).

RESULTS

Surgical procedure

The preparation of the tunnel for the occluder caused on a few occasions rupture of an intramural branch of the coronary artery. A ligation of the branch was not attempted, and in case of large branches the preparation had to be suspended.
After a pilot study with another type of occluder, the occluder described by *Dallmer et al.* (1979) failed to operate properly only in one experiment. In this case the occluder could be pressurized adequatly, but no ECG-change of any kind could be seen.

Ventricular fibrillation

All the seven animals underwent ventricular fibrillation during occlusion. Ventricular fibrillation latencies are indicated in all figures (Figures 4–7) of ventricular extrasystoles and haemodynamic parameters.

Ventricular extrasystoles (VES)

The relative occurrence of ventricular extrasystoles is presented in Figure 4. Sex did not have any significant effect on the occurrence of extrasystoles, but VES were significantly ($p < 0.01$) fewer in coloured animals.

Haemodynamic parameters

Occlusion of the anterior descending branch of the left coronary artery caused significant decreased of SBP ($p < 0.01$), DBP ($p < 0.001$), MAP ($p < 0.001$) and PTI ($p < 0.01$) and significant increase of HR ($p < 0.001$). All the changes are shown in Figures 5–7.

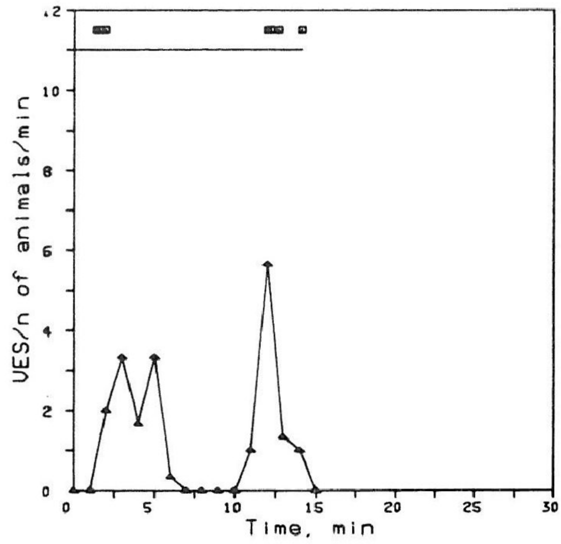

Figure 4. Relative occurrence of ventricular extrasystoles (VES) in conscious swine during left coronary occlusion. Solid line represents the occlusion. Small squares (□) illustrate cases terminating in ventricular fibrillation.

DISCUSSION

As spontaneous models of sudden cardiac death are not readily available, various methods have been used in the induction

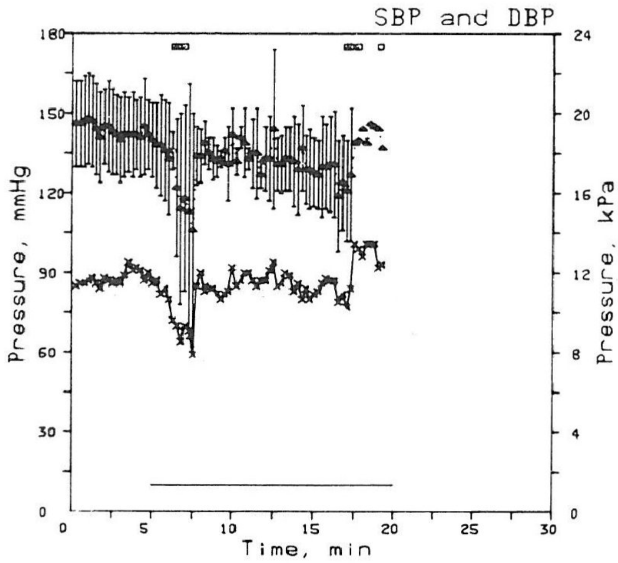

Figure 5. Means and standard deviations of systolic blood pressure (SBP) and diastolic blood pressure (DBP) of swine. Solid line shows when the occlusion was on. Small squares (□) illustrate the occurrence of ventricular fibrillation.

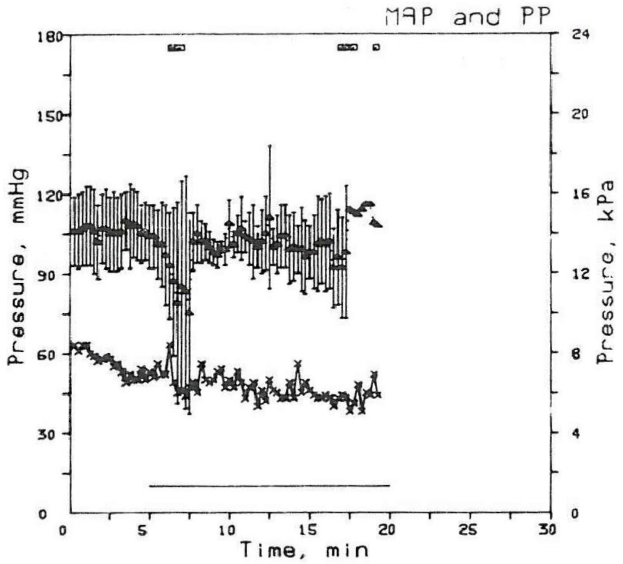

Figure 6. Means and standard deviation of mean arterial pressure (MAP) and pulse pressure (PP) of swine. Solid line shows when the occlusion was on. Small squares (□) illustrate the occurrence of ventricular fibrillation.

of the disease. With the aid of thoracotomy occluding devices can be placed around the coronary artery, and they can be operated either during the surgery or

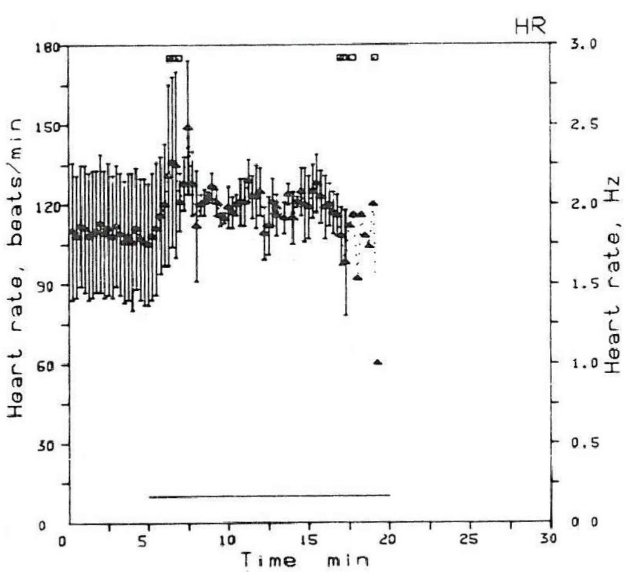

Figure 7. Means and standard deviations of heart rate (HR) of swine. Solid line shows when the occlusion was on. Small squares (□) illustrate the occurrence of ventricular fibrillation.

afterwards. The thoracotomy can be avoided by introducing a catheter into the coronary artery, and producing obstruction with it (*Fozzard* 1975).

When the effects of coronary occlusion are studied, the choice of animal species is of major importance to the relevance of the conclusions made. Although dogs and cats have been the most commonly used species so far, the cardiac anatomy and physiology of the swine seems to resemble most that of man (*Lumb* and *Singletary* 1961, *Schaper* 1971, *Liechti et al.* 1977, *Most, Williams* and *Millard* 1978, *White* and *Bloor* 1981). The presence of major collateral arteries may prevent or modify the production ischemia and there are major differences between different species in this respect. The collateral pattern of swine resembles most closely that of man, while the dog has much more and ungulates practically no collatarals (*Schaper* 1971). Equivalent proximal occlusion of coronary artery in dogs may lead to subendocardial infarction, while it in the swine as well as in man causes transmural infarction (*Fozzard* 1975).

Generally, there are two reasons why the swine has not become a widely used and popular experimental animal in circulatory research. The normal swine grows very fast, and the use of postpubertal animals means handling animals of over 70 kg. The animal's uncooperative attitude and loud voice have repelled many research groups since the days of Pavlov.

The use of miniature swine, an animal originally developed for studies of atherosclerosis, makes it possible to use sexually mature, but reasonably small animals. The Göttingen miniature swine, which was used in this study, can be successfully bred as early as at the age of 200 days, when its weight is still below 20 kg. No obvious pain sensation comparable to anginal pain in man could be detected in conscious animals during the occlusion. Not even any clear behavioural change was seen during the occlusion, and the animals were relatively calm until ventricular fibrillation.

The animals accepted well the immobilization used in this study. There were no problems during the familiarization and the experiments when wires and tubings were connected to the corresponding outlets on the protective box or when handling the box. No recording was commenced before the swines had been in the box for at least 15 minutes, and by this time most of them were sitting or had lain down.

The place of the exteriorization of instrumentation is critical. Three locations for outlets are suggested for the swine. In addition to the location used in this study, the back of the neck and dorsal midline above the scapulae have been used (*Mount* and *Ingram* 1971). Both locations on the neck are liable to an in-out movement of wires and catheters. Consequently all wires and catheters leaving the body must be long enough to allow the animal to move. For instance a catheter exteriorized through the back of the neck is drawn three or four cm into the body when the animal puts its head down (*Mount* and *Ingram* 1971). The area over the scapulae is less liable to movement, but the protection of delicate instrumentation outlets here may be somewhat more difficult.

The movement of the wires and catheters did not cause irritation to our animals, but prevented healing around the wound and kept it moist. Moreover, the PVC- and silicone rubber tubings used in this study decreased the amount of in and out movement through the wound when compared to stiffer polyethylene-tubings.

Contrary to the study by *Skinner, Lie* and *Entman* (1975) a hydraulic occluder around the anterior descending branch of the left coronary artery was used in this study. Their conclusion that hydraulic occluders are impractical is based on the fact that the artery is embedded in a 3–5 mm depth of myocardial fat. In the dog the artery is superficial and consequently hydraulic occluders are easy to use. However, the hydraulic occluder was chosen in this study, because the type used made it possible to detect intraoccluder pressure and thus exclude possible failures due to leaking devices.

Undoubtedly the hydraulic occluder, which was used here (*Dallmer et al.* 1979) necessitated careful preparation of the artery and required a much larger tunnel below the artery than the mechanical occluder of Skinner's group. This requirement of a large tunnel increased the risk of cutting branches, especially intramural ones, of the left coronary artery. In this experimental series only one of the successfully operated animals proved to have a nonfunctioning occluder. Evidently the occluder movement, kinking or rotation, totally occluded the artery before the experiment.

Skinner, *Lie* and *Entman* (1975) reported a dramatic decrease in ventricular fibrillation latency and the number of consecutive 20-minute occlusions with ventricular fibrillation, which was obvious after four adaptation experiments. In this study the number of adaptation experiments for every animal was only two, but the numbers as such are not comparable.

The plywood box, where the animals were kept during the actual experiment, proved to be suitable for the purpose. The animals did not react adversely to this rather loose and flexible immobilisation, and thus allowed all the necessary handling of instrumentation outlets, nor did they move excessively for recording purposes. *Skinner*, *Lie* and *Entman* (1975) immobilized their animals by tying the feet together and keeping the animals on one side, which is undoubtedly more stressful to the animal than the relative freedom of the box used in this study. To overcome the extra stress caused by their immobilisation several adaptation occasions may have been required even to reach the normal baseline.

In preliminary trials for a suitable immobilization method, tying the feet was one of the alternatives, but it was abandoned because of a noisy protest from some of the pigs. The difference in adaptability to immobilisation may be due to the behavioural differences of the pigs used. Göttingen miniature swine are less docile and somewhat more difficult to handle than farm pigs like the ones used by *Skinner*, *Lie* and *Entman* (1975).

The excitement of the swine has been considered one of the major problems when recording cardiac parameters. The heart rate has been suggested to be an indicator of excitement (*Smith et al.* 1964). In this study the heart rate values of conscious animals before any manipulation compare favourably with the data of other studies with farm swine (*Smith et al.* 1964, *Engelhardt* 1966) as well as with those with the miniature swine (*Stone* and *Sawyer* 1966, *Beglinger* and *Becker* 1981). On this basis the pigs of this study cannot be considered excited during the recordings.

Two distinct periods with ventricular fibrillation and ventricular extrasystoles seem to be typical of conscious swine during a 20-minute occlusion. The difference between this finding and the findings obtained in carnivore studies may reflect differences in the collateral circulation. Canine collaterals seem to have a system with 'memory', which is evidenced by an inability to gain a decreased ventricular fibrillation threshold after a second consecutive occlusion (*Gülker et al.* 1977). The activation of these collaterals is believed to occur within minutes at least in conscious dogs (*Elliot* 1973), and this may explain the apparent lack of a second vulnerability period in the dog.

In this study reperfusion ventricular fibrillation could not be studied in conscious animals, because all the animals experienced ventricular fibrillation during occlusion. Another study with conscious swine by *Skinner*, *Lie* and *Entman* (1975) does not report a single reperfusion ventricular fibrillation, although there have been several releases of the occluder subsequent to a 20-minute ventricular fibrillation-free occlusion. This is in great contrast to carnivore studies made with conscious animals (*Yenikomshian et al.*, unpublished observation, loc. cit. *Axelrod*, *Verrier* and *Lown* 1975). It can be suggested that either the adaptation gained through several ventricular fibrillations during the occlusion or the difference in the porcine and canine collateral circulation led to this phenomenon.

A recent article showed that in the conscious Göttingen miniature swine sex, line and age of the individual are significant determinants of arterial pressures and the heart rate (*Nevalainen et al.* 1983). The statistical bias were in this study eliminated with the use of the analysis of covariance.

In haemodynamic parameters of this study the most striking observation is that the heart rate increases in conscious animals during the occlusion. The response of the heart rate to coronary occlusion found in this study agrees well with the findings of studies on conscious dogs (*Bishop* and *Peterson* 1978, *Rutherford*, *Vatner* and *Braunwald* 1981). The increase of the heart rate and a concominant decrease of arterial pressure are likely to be caused by activation of the sympathetic nervous system, and this change lowers the swines' already low diastolic/systolic quotient (*Spörri* 1954). This change tends to further compromise the blood supply of the myocardium.

The finding of *Skinner*, *Lie* and *Entman* (1975) of a decreased heart rate during the occlusion typical to the swine, which did not later develop ventricular fibrillation, could not be verified in this study, because all the conscious animals had

fibrillation during the occlusion. In conscious swine the pressure change was relatively small. This finding supports the conclusion of *Peterson* and *Bishop* (1974) that during coronary occlusion pressure is well maintained in conscious animals.
In conclusion the conscious porcine model described proved to be an operant preparation, with which further information on basic mechanisms of ventricular fibrillation could be achieved.

Sammandrag

Ändamålet med denna forskning var att utveckla en kroniskt instrumenterad, medveten svinmodell för plötslig hjärtdöd förorsakad med koronarocklusion och bedöma modellens utförande och lämplighet. Sju Göttingen minisvin var kroniskt instrumenterade med arteriella katetrar, perikardial EKG-ledning och hydraulisk ockluder med vilken en reversibel ocklusion av koronarärtärer kan åstadkommas. Alla katetrar och ledningar kom ut till en skyddsask bakom vänstra örat. Efter fem dagars konvalescens och två adaptationsprov gjordes det egentliga experimentet. Under resulteringen blev djuren utsatta för tjugo minuters ocklusion i en rörbar fanerlåda. Resultaten av EKG- och artärtryck upptogs på band.
Vänstra koronarocklusionen provocerade ventrikular fibrillation under ocklusionen i alla experiment. Blodtrycket sjönk och hjärtfrekvensen steg under ocklusionen.
Då spontana modeller för plötslig hjärtdöd inte finns tillgängliga, har en inducerad modell utvecklats och använts i denna forskning. Avsikten var att använda kroniskt instrumenterade djur och att använda en djurart, vars koronaranatomi och -fysiologi är lik människans. Svinmodellen skildrad och använd i detta experiment kan jämföras med koronarspasm som födekommer med och utan koronarartärsjukdom hos människan.
Det finns behov av vidare forskning för att undersöka möjligheten att använda modellen när man forskar reperfusionarytmia förorsakad med en inducerad iskemia i en liten del av myokardiet.

Yhteenveto

Tutkimuksen tarkoituksena oli kehittää tajuinen indusoitu sikamalli äkilliselle sydänkuolemalle, ja arvioida mallin sopivuutta. Seitsemän Göttingen-minisikaa instrumentoitiin kroonisesti valtimokatetrilla, perikardiaalisilla EKG-johdoilla ja hydraulisella okluuderilla, jonka avulla aiheutettiin palautuva sepelvaltimon okluusio. Katetrien ja johtojen ulostulo oli suoja-kotelossa vasemman korvan takana. Viiden päivän toipumisajan ja kahden totuttamiskokeen jälkeen tehtiin varsinainen koe. Rekisteröinti suoritettiin eläimen ollessa liikuteltavassa vanerilaatikossa. Eläimet altistettiin 20 minuutin okluusiolle. EKG- ja arteriapainesignaalit taltioitiin nauhalle.
Vasemman sepelvaltimon okluusio aiheutti kammiovärinän kaikissa kokeissa sekä verenpaineen laskun ja sydänfrekvenssin nousun okluusion alkana.
Koska spontaaneja eläinmalleja äkilliselle sydänkuolemalle ei ole, tässä tutkimuksessa on kehitetty ja käytetty indusoitua mallia. Tavoitteena oli käyttää tajuisia eläimiä sekä eläinlajia, jonka koronaarianatomia ja -fysiologia ovat lähellä ihmistä. Tutkimuksessa kuvattua ja käytettyä sikamallia voidaan verrata sepelvaltimospasmiin, jota esiintyy ihmisellä sepelvaltimosairauksien yhteydessä kuin myös muuten.
Indusoimalla iskemia pienenpään osaan sydänlihasta kuvatun mallin avulla avautuu uusia mahdollisuuksia tutkia myös reperfuusion jälkeistä arytmiaa.

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