THE EFFECT OF ALCOHOL INTOXICATION ON HAEMODYNAMIC PHYSIOLOGY OF ACUTE CARDIAC TAMPONADE

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I, Peter MacDonald Hewitt, hereby declare that all the work on which this thesis is based is original (except where acknowledgements indicate otherwise) and that neither the whole work nor any part thereof has been, is being, or is to be submitted for another degree in this or any other university.

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5. SUMMARY

It is generally accepted that alcohol impairs haemodynamic physiology in normal subjects. Alcohol is also thought to have a detrimental effect in shock states. However, most research has concentrated on haemorrhagic shock, whereas in cardiac tamponade, the pathophysiology of shock is very different. Although some studies have mentioned alcohol as a negative factor in patients with cardiac tamponade, none have adequately assessed its effect.

In a clinical study of 50 patients who presented to Groote Schuur Hospital Trauma Unit with acute cardiac tamponade due to penetrating chest injury, those who were intoxicated fared the same as their sober counterparts. Although more patients in the intoxicated group were "moribund" or "in extremis" on admission, this did not lead to a higher overall mortality. Haemodynamic parameters and results of special investigations in the two groups were also similar. These findings suggested that intoxicated patients with cardiogenic shock, specifically acute cardiac tamponade, behaved differently from intoxicated patients with haemorrhagic shock. However, the multitude of variables and the stress involved in treating patients with life-threatening acute conditions, makes studies such as this difficult. Because of these limitations, an animal model of acute cardiac tamponade was developed, so that actions of alcohol on haemodynamic physiology could be studied in a controlled environment.

Fourteen young pigs were randomly assigned to receive either 30% alcohol or tap-water via a gastrostomy. The former resulted in blood alcohol levels which were compatible with moderate to severe intoxication.

Cardiac tamponade was then induced by instilling warmed plasmalyte-B into the pericardial sac using a pressure-cycled system. Despite the fact that animals in the tamponade/alcohol group were more hypotensive, and reflex increase in heart rate was inhibited, cardiac output was similar in the two groups. The actions of alcohol in isolation were also studied in eight sham-operated pigs. The only noticeable effect in this instance were higher pulmonary artery wedge pressures in the sham/non-alcohol group. In other words, cardiac performance in both the tamponade/alcohol and sham/alcohol groups was at least equal to, or even better than that in animals that did not receive alcohol.

It would seem therefore, that alcohol does not have a *negative* effect on haemodynamic physiology of acute cardiac tamponade. Theoretically, alcohol may "protect" patients with acute cardiac tamponade by decreasing peripheral vascular resistance and "afterload". It is also possible that inhibitory actions on the respiratory centre may prevent hyperpnoea or tachypnoea, and thereby diminish competitive filling of the right and left ventricles. However, further studies of cardiac function in intoxicated subjects with tamponade using more sophisticated techniques are necessary, before mechanisms will become apparent.

In practice, an aggressive approach should be adopted towards moribund patients with penetrating chest injuries; if they have acute cardiac tamponade and are intoxicated, their prognosis is not necessarily dismal. This is of particular relevance in Cape Town, where both alcohol abuse and assault are endemic. As for a therapeutic effect of alcohol, these studies do not support its use for pharmacological manipulation of cardiac tamponade.

6. HISTORICAL REVIEW

6.1 INTRODUCTION

Alcohol has been imbibed, abused, admired and deplored since the dawn of history (Clinical Pharmacology 7th ed, 1992; Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990; Horwitz 1974). For centuries it was believed that alcohol was the elixir of life; no other substance has been used so widely to treat so many different ailments (Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990; Regan 1966), however, it is now recognized that the therapeutic value of alcohol is extremely limited and that most of its effects are deleterious (Clinical Pharmacology 7th ed, 1992; Knochel 1983; Rubin 1979).

In the Trauma Unit at Groote Schuur Hospital, where sobriety of patients is the exception rather than the rule, there is little doubt that alcohol contributes to the majority of motor vehicle accidents and assault cases, but its effect on degree of injury and clinical parameters is less certain. This is because so many different variables are involved in the trauma equation. Controversy also exists in the literature (Jehle 1988; Jurkovich 1992; Pories 1992; Waller 1986), although there is a general perception that alcohol has a deleterious effect on shock states (Bottoms 1990; Chandler 1991; Horton 1992; Zink 1988). Furthermore, clinical experience at Groote Schuur Hospital suggests that intoxicated patients with exanguination *are* disadvantaged, but interestingly, if they have penetrating cardiac injuries and resultant tamponade, they behave differently. The latter subset of patients are usually admitted to the Trauma Unit in a moribund state, yet they respond well to treatment and invariably

recover uneventfully. It has also been our impression that they often fare better than their sober counterparts with cardiac tamponade. This is contrary to experience with other forms of shock (Desiderio 1987; Horton 1986; Liedtke 1975; Rappaport 1990). Could alcohol in some way "protect" patients with cardiac tamponade, where the pathophysiology is so different from those with major blood loss?

To our knowledge, nobody has adequately addressed this question. Moreover, if the hypothesis proved to be correct, it would alter clinical practice and could conceivably pave the way for pharmacological manipulation of tamponade, particularly when it is associated with chronic conditions such as malignancy or tuberculosis. In Cape Town, the prevalence of penetrating cardiac injuries is also high and cardiac tamponade is a well defined clinical condition. We therefore decided to study the effect of acute alcohol intoxication on cardiac tamponade.

6.2 PHARMACOLOGY OF ALCOHOL

The term "alcohol" when used without qualification denotes ethyl alcohol or ethanol (Butterworths Medical Dictionary 2nd ed, 1978; Churchill's Medical Dictionary 1989; US Pharmacopeia National Formulary 1995). This word is derived from ancient Assyrian "guhlu" or Arabic "al-kuhl", terms that were applied to fine powders obtained by sublimation. Paracelsus was the first to use the term to describe volatile spirit of wine which was manufactured by a similar process, namely distillation. This method of making pure alcohol was discovered by the alchemist Lully (1235-1315) who wrote in his enthusiasm: "The taste of it exceedeth all other tastes, and the smell of it all other smells". He imagined that the production of so potent an essence heralded the approaching end of the world (Alcohol, Drugs and Road Traffic 1979).

6.2a Pharmacokinetics

I. Absorption of alcohol.

Alcohol is produced in minute quantities in humans and in some animals. This has been ascribed to the ability of micro-organisms in the gut to manufacture alcohol from glucose. The amount of alcohol produced in this way is, however, negligible (Alcohol, Drugs and Road Traffic 1979), so that for practical purposes, alcohol detectable in body fluids comes from an exogenous source.

Unlike other nutrients, ingested alcohol is absorbed from the gastrointestinal tract without undergoing any chemical changes. This occurs by a process of simple diffusion, mainly from the stomach and the

first part of the small intestine, and will continue as long as a concentration gradient exists between the gut lumen and the blood perfusing the submucosal capillary network. Very little absorption of alcohol, if any, occurs in the large intestine or rectum after ingestion. Because alcohol is lipid soluble, absorption occurs virtually as soon as it is ingested. It can be detected in the blood 5 minutes after ingestion and the concentration usually reaches a maximum after about an hour (Applied Pharmacology 12th ed, 1980). The rate of absorption is dependent on factors such as alcohol concentration, diet, regional blood flow, nature of the absorbing surface and sex of the individual (Clinical Pharmacology 7th ed, 1992; Alcohol, Drugs and Road Traffic 1979). Another site of absorption is the lungs. Although only a small amount of alcohol is usually absorbed via this route, fatal toxicity has been reported following inhalation of vapourized alcohol (Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990). Alcohol may also be administered via the rectum (Nadjem 1990), or may be injected intravenously or intraperitoneally. The latter routes of administration can result in rapid attainment of toxic blood levels. In addition, because alcohol is a common solvent used in skin preparation, there is some debate as to whether this could influence concentration in body fluids, but actual absorption is probably negligible (Alcohol, Drugs and Road Traffic 1979).

After absorption, alcohol is distributed rapidly throughout the body water compartments (Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990). The fat and bones contain little alcohol, but the concentration in the rest of the body is fairly uniform. This allows correlation between blood concentration and concentration in other body fluids (Alcohol, Drugs and Road Traffic 1979).

II. Elimination of alcohol.

More than 90% of absorbed alcohol is eliminated from the body by metabolism. This involves the breaking down of alcohol in various stages to substances which are included in the common metabolic pathways. The metabolism of alcohol differs from that of most substances in that the rate of oxidation is relatively constant, in spite of changes that may occur in blood levels (zero-order kinetics). The amount of alcohol oxidized per unit of time is roughly proportional to body weight; in adults the average rate at which alcohol can be metabolized is 120mg/kg/hour, or 30ml (1oz) in 3 hours (Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990). Metabolism of alcohol is confined to organs containing specific enzymes, the liver being the most important. The first step is the removal of two hydrogen ions (oxidation) which are accepted by the coenzyme NAD. This reaction, which is catalysed by the zinc-containing enzyme alcohol dehydrogenase, results in the formation of acetaldehyde and is the rate-limiting step in the metabolism of alcohol. The second step is the oxidation of acetaldehyde to acetic acid (acetate), catalysed by NAD-dependent dehydrogenase (fig 6.1). The latter reaction is so rapid, that the level of acetaldehyde normally does not become appreciably elevated during the oxidation of alcohol. Acetate, or its activated form acetyl-coenzyme A, is a central metabolite of intermediary metabolism. It can undergo a number of different reactions such as oxidation to carbon dioxide and water, fatty acid and steroid synthesis, condensation to ketone bodies and others (Alcohol, Drugs and Road Traffic 1979; Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990).

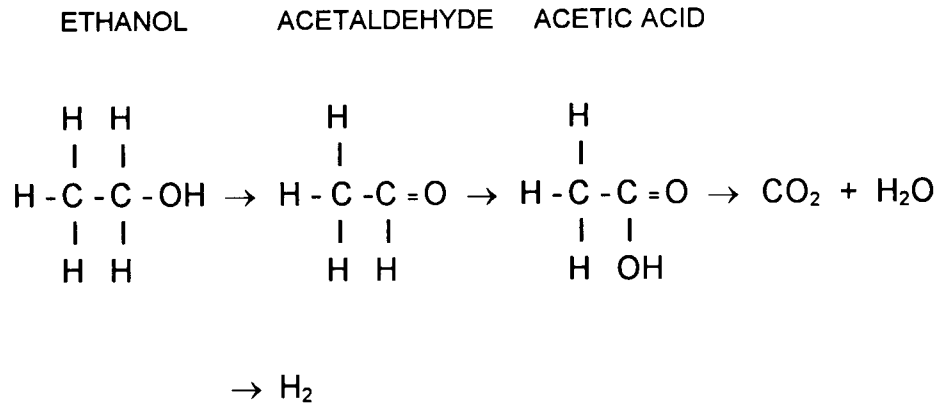


Figure 6.1: The primary steps in the metabolism of alcohol
(Taken from Alcohol, Drugs and Road Traffic 1979)

Enzymes that occur in the smooth endoplasmic reticulum of cells (microsomal ethanol oxidising systems) have also been reported to oxidise alcohol (Badawy 1978). These systems are fully active at a physiological pH and resemble the microsomal drug detoxifying enzyme systems. The extent to which these systems metabolize alcohol in man is probably small, but their contribution increases as the concentration of alcohol rises, particularly in individuals who consume alcohol regularly.

Excretion of alcohol occurs mainly in urine and expired air. Insignificant amounts are excreted in sweat, saliva, semen and milk of nursing mothers. The concentration in urine is usually slightly higher than the blood level, whereas the concentration in alveolar air is only 0.05% that of blood (Alcohol, Drugs and Road Traffic 1979).

6.2b. Pharmacodynamics

Alcohol is allied to the group of drugs known as sedative-hypnotics. Except for the benzodiazepines, this group of agents depresses the central nervous system (CNS) in a relatively nonselective, dose-dependent

fashion, producing progressive calming and drowsiness (sedation), sleep (pharmacological hypnosis), unconsciousness and finally coma with fatal depression of respiration and cardiovascular regulation (Table 6.1). This action of alcohol on the brain is at variance with the popular idea that alcohol is a stimulant to mental processes (Applied Pharmacology 12th ed, 1980; Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990). The reason for this misconception is that the highest and most easily deranged functions are chiefly inhibitory, and hence the first action of alcohol is to diminish such characteristics as hesitation, caution and self-criticism (Applied Pharmacology 12th ed, 1980; Clinical Pharmacology 7th ed, 1992).

In the past, alcohol was used as an intravenous anaesthetic agent, particularly where cardiovascular stability was desired. Solutions of 7-7.5%, when administered rapidly, can produce anaesthesia with blood alcohol levels of 180 to 200 mg/dl. This effect is potentiated by premedication with pentobarbitone (Textbook of Pharmacology 2nd ed, 1980) and is largely due to inhibition of the midbrain reticular activating system. Anaesthetic and analgesic properties of alcohol may also be attributed to a direct action on nerves and nerve synapses. Alcohol concentrations of 5-10% block conduction in isolated peripheral nerves and skeletal and cardiac muscle, by depolarizing cell membranes. Lower levels can modulate simple spinal reflexes by presynaptic inhibition. This involves partial depolarization so that the height of the action potential reaching the synapse is reduced and less acetylcholine is released. Alcohol also reduces ventral root responses to dorsal root stimulation, probably because of postsynaptic inhibition (Kalant 1975). This explains why alcohol impairs muscular coordination and prolongs reaction time.

Table 6.1: Stages of acute alcoholic influence/intoxication
(Adapted from Dubowski 1980)

Blood alcohol level (% w/v) and stage of alcohol influence	Clinical signs/symptoms
0.01-0.05/Sobriety	No apparent influence; Slight changes detectable by special tests.
0.03-0.12/Euphoria	Mild euphoria, talkativeness; Increased self-confidence; Decreased inhibitions; Diminution of attention, judgement and control; Loss of efficiency in finer performance tests.
0.09-0.25/Excitement	Emotional instability; Decreased inhibitions; Loss of critical judgement; Impaired memory and comprehension; Decreased sensory response and increased reaction time; Some muscular incoordination.
0.18-0.30/Confusion	Disorientation, mental confusion, dizziness; Exaggerated emotions; Disturbance of sensation and of perception of color, form, motion, dimensions; Decreased pain sense; Impaired balance, muscular incoordination, staggering gait, slurred speach.
0.27-0.40/Stupor	Apathy; General inertia approaching paralysis; Markedly decreased response to stimuli; Marked muscular incoordination: inability to stand or walk; Vomiting; Incontinence; Impaired consciousness: sleep or stupor.
0.35-0.50/Coma	Complete unconsciousness, coma, anaesthesia; Depressed or abolished reflexes; Subnormal temperature; Incontinence; Embarrassment of circulation and respiration; Possible death.
0.45+/Death	Death from respiratory paralysis.

Although alcohol exerts its effect at every level and on every organ-system, this review will concentrate mainly on the cardiovascular actions of alcohol. The literature abounds with contradictions regarding haemodynamic effects of alcohol (Abel 1980; Altura and Altura 1982; Friedman 1981; Horwitz 1974; Thomas 1994). This is mainly due to variations in study design as well as problems related to extrapolation of animal data to clinical practice (Zweifach 1961). In addition, the actions of alcohol on cardiovascular performance are not only dependent on dose, route and duration of administration, but multiple individual variations including prior alcohol usage and physiological condition, also have a profound influence (Ahmed 1973; Desiderio 1987; Gould 1971; Thomas 1994). Furthermore, it is uncertain how much the congeners normally present in alcoholic beverages, contribute to the haemodynamic effects (Altura BM 1982; Nakano1972).

Alcohol could affect the cardiovascular system at at least two distinct sites: either by alteration of the central control of the cardiovascular system, as has already been alluded to, or by directly influencing the sympathetic nerve terminals or the end organs themselves (Pohorecky 1982).

I. Effect on the circulation.

It is generally accepted that acute administration of alcohol produces vasodilatation and lowers blood pressure in a dose-related manner (Altura and Altura 1982). For example, Battey et al reported that 50% of a group of patients with severe alcohol intoxication had systolic blood pressures below 90mm Hg (Battey 1953). Low levels of alcohol have also been reported to decrease blood pressure, particularly where autonomic reflexes are impaired. Chaudhuri et al showed that blood levels of 50-60

mg/dL, lowered supine blood pressure and worsened postural, hypotension in patients with primary autonomic failure (Chaudhuri 1994). Furthermore, in vivo studies have shown that vasodilatation occurs regardless of the route of alcohol administration (Altura and Altura 1982).

For years, vasodilatation was thought to be due to actions of alcohol on the heart and central nervous system (Bing 1978; Moss 1959; Rubin 1979; Thomas 1980; Timmis 1975), but recent studies have suggested that this phenomenon may result from a direct action of alcohol on vascular smooth muscle cells, at both macro- and microcirculatory levels. At least two mechanisms appear to be responsible for this: 1) - inhibition of normal rhythm or vasomotion (spontaneous mechanical activity) of vascular smooth muscle and 2) - depression of the contractile responses to endogenous neurohumoral substances (Knochel 1983).

Low to intermediate concentrations of alcohol (1-50 mmol/L) in vitro, cause a dose-dependent inhibition of spontaneous mechanical activity in arteries and veins. In most cases, the greater the concentration of alcohol, the more rapid the inhibition, and the more the resting tension is lowered. These changes in mechanical activity are not tachyphylactic and are not all-or-none responses. Neither are these actions of alcohol due to release of any known endogenous vasodilators and they cannot be prevented with pharmacological antagonists (Altura and Altura 1982; Howes 1986).

Evidence to date suggests that alcohol mediated vasodilatation is related to decreased availability of activator Ca++ for the contractile process (Altura and Altura 1982; Knochel 1983). Alcohol could interfere with mobility of Ca++ both at the vascular membrane and intracellularly, similar to that observed for volatile anaesthetic agents, because it penetrates

membranes and cells rapidly. Direct experiments have also shown that alcohol decreases total exchangeable Ca++ and significantly inhibits membrane-bound Ca++ by 30-40% (Altura and Altura 1982).

Another important effect of alcohol is its interaction with neurohumoral substances. These substances are differentially affected by the concentration of alcohol. For example, low concentrations potentiate the actions of vasopressin, catecholamines and prostaglandins A_1 and B_1, whereas higher concentrations (greater than 100 mmol/L) attenuate contractions induced by these hormones. Prostaglandin E_1 behaves differently; its contractile action is markedly inhibited even by very low concentrations of alcohol (1 mmol/L) (Altura and Altura 1982). However, for practical purposes, responses to all endogenous vasopressors are impaired at levels such as would be seen with mild intoxication (Howes 1986).

Chronic alcohol administration may produce tolerance and hypersensitivity in vascular smooth muscle resulting in hypertension (Altura and Altura 1982; Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990). This has been born out by epidemiological studies showing that alcoholics have a higher incidence of hypertensive vascular disease (Beevers 1977; Klatsky 1981; Mathews 1979). In addition, there are reports which indicate that acute alcohol administration may have biphasic effects on peripheral blood flow (Nakano 1972; Pohorecky 1982), or may even cause vasoconstriction (Altura and Altura 1982; Altura and Altura 1984; Gould 1971). In vitro, this is normally seen with higher concentrations of alcohol (greater that 100mmol/L) but interestingly, constriction of some blood vessels (femoral, intrapulmonary, renal, coronary and cerebral arteries) has been noted at levels from 1-200mmolL

(Altura and Altura 1982). These effects are thought to be partly due to alcohol mediated release of catecholamines (Pohorecky 1982). Idiosyncratic hypertension has also been attributed to high levels of free Ca++ ions and differential effects of alcohol on neurohumoral substances, in particular prostaglandins, at different concentrations (Altura and Altura 1982).

The circulatory responses to the metabolites of alcohol are controversial. Most vascular effects have been attributed to acetaldehyde-mediated release of catecholamines from sympathetic nerve endings and the adrenal medulla (Bing 1982). In physiological quantities, acetaldehyde has been shown to increase pulse rate and cause facial flushing (Mizoi 1979), but when it is administered in pharmacological doses, it causes peripheral vasoconstriction and dilatation of coronary and splanchnic vessels (McCloy 1974). Recent studies, however, have shown that these effects are more likely to be due to acetate (Carmichael 1988; Israel 1994). Although the blood levels of acetate that are usually achieved after ingestion of alcohol were not thought to have any significant cardiovascular effects (Kirkendol 1978), it has been proposed that when acetate is metabolized to acetyl coenzyme-A and adenosine mono-phosphate (AMP) in peripheral tissues, the latter is further hydrolysed by 5'-nucleotidase to generate adenosine, which is a powerful physiological vasodilator (Israel 1994).

Besides having a direct and indirect action on blood vessels, alcohol also affects the circulation by causing shifts in the fluid compartments of the body. Knott and co-workers have shown that gastric administration of alcohol in dogs *decreases* circulating blood and plasma volume (Knott 1963), probably as a result of sequestration in a dilated vascular compartment. This differs from the *increase* in blood and plasma volume

reported by Nicholson and Taylor after administration of a similar dose of alcohol (Nicholson 1940). In the latter study, measurement of the plasma volume only occurred 5 hours after administration of alcohol, which might explain the discrepancy in results. However, other factors may be responsible. It is known that splenic contraction can supplement blood volume, particularly in animals (Hannon 1985; Textbook of Medical Physiology 8th ed, 1991). This has been demonstrated in experimental models, where excessive stress causes the release of endogenous catecholamines, as well as after parenteral administration of adrenaline (Hannon 1985; Nelson 1972). Because alcohol causes catecholamine release (Klingman 1958; Perman 1958; Pohorecky 1982), it theoretically may also induce splenic contraction. Furthermore, several studies have shown that alcohol increases haematocrit (Horton 1987; Klingman 1958, Zink 1988), which supports the notion of alcohol-induced splenic supplementation of blood volume. It is unlikely though, that this plays a significant role in humans (Nelson 1972).

Another reason for haemoconcentration may be the diuretic effect of alcohol. Although diuresis is partly related to the large amount of fluid normally ingested with alcoholic beverages, it is well known that alcohol inhibits anti-diuretic hormone (ADH) secretion when blood levels are rising (Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990; Haggard 1941). The rise in haematocrit not only alters intravascular volume, but also results in increased blood viscosity. Moreover, alcohol increases factor VIII complex and reduces fibrinolytic activity (Hillbom 1983). All these effects together may impair blood flow and perhaps even cause thrombosis.

The actions of alcohol on platelet function are less well defined. Some studies have shown that alcohol consumption is inversely related to the incidence of complications from coronary artery disease, probably because moderate amounts of alcohol have been shown to inhibit platelets (Rubin R, 1994). Others have reported that alcohol shortens bleeding time and promotes brain infarction, particularly in young adults (Hillbom 1983). This may be associated with rebound thrombocytosis after alcohol intoxication (Haselager 1977).

In addition to the overall effect of alcohol on the circulation, various regional blood flow responses have been described. Alcohol causes hyperaemia of skin (Smythe 1953; Regan 1982) but reduces muscle perfusion (Fewings 1966). Gastric mucosal blood flow is substantially increased by alcohol (Puurunen 1980), whereas pancreatic blood flow has been found to undergo a dose-dependent reduction (Horwitz 1980). This latter effect of alcohol may result in an increased production of myocardial depressant factor by the pancreas, which has been implicated as a possible cause for decreased myocardial contractility observed after resuscitation in a canine model of haemorrhagic shock (Horton 1986). Hepatic (Mendelhoff 1954; Stein 1963) and renal (Horton 1986) circulation, is also increased by alcohol.

Most controversy, however, surrounds the effect of alcohol on cerebral and coronary perfusion.

Cerebral perfusion: Although ingestion of small amounts of alcohol may increase cerebral blood flow, the bulk of human and animal studies seem to indicate that higher concentrations produce deficits in regional perfusion (Howes 1986). Recent direct in-situ observations of the rat brain have

shown that alcohol produces graded concentration-dependent spasms of arterioles and venules, irrespective of the route of administration (Altura and Altura 1984). This is another reason why heavy use of alcohol or binge-drinking may cause ischaemic brain infarction (Altura and Altura 1984; Gill 1986).

Coronary perfusion: Because alcohol has a complex array of haemodynamic and metabolic effects, it is not surprising that conflicting observations have been made regarding the effects of alcohol on myocardial blood flow (Friedman 1981). Some scientists have shown an increase in coronary artery flow (Ganz 1963; Gould 1972; Horton 1987; Talesnik 1980), which may be a function of increased myocardial work and oxygen consumption (Horton 1986; Talesnik 1980). Abel, using an isolated heart-lung preparation and intra-atrial infusion of alcohol to concentrations of approximately 210 mg/dL, demonstrated increased coronary blood flow with decreased coronary vascular resistance and myocardial performance, but unchanged myocardial oxygen consumption (Abel 1980). Gilmour and Mallov have even reported that alcohol protects against myocardial necrosis produced by large doses of adrenalin in vivo (Gilmour 1977), perhaps on the basis of coronary dilatation. However, some studies have shown no significant change in coronary perfusion at various blood alcohol levels (Schmitthener 1958). Others have found that alcohol not only increases cardiac work-load, but also compromises coronary blood flow (Webb 1965). Friedman demonstrated that at blood alcohol levels around 200mg/dL, alcohol increased overall myocardial blood flow, but it produced an unfavourable redistribution of perfusion so that acutely ischaemic myocardium received less blood, thereby causing a "coronary steal" (Friedman 1981). It has also been shown that the incremental increase in coronary perfusion in response to exercise is significantly reduced by high

doses of alcohol (Stratton 1981). In support of this, Orlando and colleagues showed that less exercise was required to precipitate angina after ingestion of alcohol by nonalcoholic individuals with ischaemic heart disease (Orlando 1976). This is contrary to the notion that alcohol can be used for the treatment of angina pectoris (Heberden 1772 - ref by Friedman 1981).

II. Effect on the heart.

Although chronic ingestion of alcohol is known to cause cardiac dysfunction, most notably in the form of congestive cardiomyopathy (Burch 1969; Perloff 1971), the acute effects are less well defined (Altura 1982; Child 1979). It is generally agreed that acute alcohol consumption decreases cardiac contractility and produces changes in conduction in vitro as well as in vivo (Gimeno 1962; Rubin 1979). For example, Child et al demonstrated echocardiographic depression in velocity of circumferential fiber shortening in subjects with blood alcohol levels around 110mg/dL (Child 1979) and Horwitz showed dose-dependent increases in left ventricular end-diastolic pressure and diameter, and decrease in stroke volume, in conscious dogs with blood alcohol levels of approximately 120-320 mg/dL (Horwitz 1974). However, there are some reports which indicate that modest amounts of alcohol (110-130 mg/dL) have no significant effect on cardiac function (Greenberg 1982) and others that even suggest a stimulatory action (Dixon 1907). It is debatable whether the latter effect is in fact real. Acute alcohol administration increases hypothalamic activity (Masserman 1940) and circulating catecholamines (Klingman 1958; McCloy 1974; Perman 1958; Pohorecky 1982), which may improve haemodynamics and "mask" the myocardial depression (Child 1979). In support of this, several studies have

shown no effect of alcohol alone, or autonomic blockade alone, on myocardial contractility, but a significant negative inotropic effect with the two in combination (Child 1979; Wong 1973).

Alterations in the function of cardiac cellular membranes may contribute to the pathogenesis of abnormal cardiac function after both acute and chronic administration of alcohol (Katz 1982; Rubin 1982; Rubin and Rottenberg 1982). Like anaesthetic agents, alcohol increases the fluidity, or disorders the phospholipids in the hydrophobic core of biological membranes (Knochel 1983; Rubin and Rottenberg 1982). With chronic administration, adaptation occurs which renders the membranes more rigid, thus making them resistant to disordering by alcohol. At the same time, alcohol impairs a number of membrane-bound functions (Rubin and Rottenberg 1982). Contraction of muscle requires a proper ionic milieu which is maintained by the ion pump of the plasma membrane, or sarcolemma (Rubin 1979). Under normal circumstances, the cardiac action potential results from passive diffusion of Na^+, K^+, Ca^{++} and possibly Cl^- ions across the membrane through ion-specific channels. Active transport mechanisms utilizing membrane ion pumps and energy from ATP, are responsible for restoring and maintaining ion gradients (Katz 1982). Alcohol has been reported to interfere with the transport of sodium and potassium ions (Israel 1970; Katz 1982), presumably by inhibiting the activity of the sodium-potassium-activated adenosine triphosphatase (ATPase) in the plasma membrane (Rubin 1979). This enzyme is involved in hydrolysis of ATP which provides energy for maintenance of the ion pump. Experiments on isolated plasma membranes in vitro, have shown that this inhibition occurs in a dose-dependent manner. Removal of alcohol and its metabolites reverses the inhibition. The concentrations of alcohol needed to inhibit sodium-potassium-activated ATPase in the presence of a normal plasma membrane potassium concentration of 20 mmol/L, are

considerably higher than those found in alcoholic patients. However, when this potassium concentration is lowered to serum levels, inhibition occurs with alcohol concentrations similar to those that can be achieved in vivo (Rubin 1979). Conversely, an increase in K^+ has been found to reduce the inhibitory effects of alcohol on cardiac sarcolemmal Na^+K^+-ATPase activity (Katz 1982). These effects of alcohol are remarkably similar to those produced by cardiac glycosides - notably Digoxin (Knochel 1983), but this drug has a positive inotropic action, which makes it difficult to attribute the negative inotropism of alcohol to inhibition of the sodium pump (Langer 1972; Knochel 1983; Rubin 1979). Therefore, other mechanisms must be responsible for alcohol-related impairment of myocardial contractility.

Alcohol has been shown to inhibit Ca^{++} uptake by the sarcoplasmic reticulum of heart and skeletal muscle cells (Bing 1982, Thomas 1980; Thomas 1994). Under normal conditions, this communicating network of membranous tubules in the cell cytoplasm binds Ca^{++} until stimulation by the action potential. When this occurs, the Ca^{++} is released to the contractile elements, namely actin and myosin. Their association causes cardiac muscle contraction, while dissociation causes relaxation. It is thought that because of the inhibition of the sarcoplasmic reticulum by alcohol, decreased Ca^{++} is released to bind to troponin, which results in impairment of this actin-myosin interaction (Rubin 1979). There is also evidence for Ca^{++}- independent inhibition of contractile proteins at low alcohol concentrations, but the mechanism is unknown (Thomas 1994). Furthermore, chronic consumption of alcohol leads to a decreased association of actin and myosin in vitro, even in the absence of alcohol or acetaldehyde (Rubin 1976), suggesting permanent damage to the structure of these proteins.

Energy for heart contraction is ultimately derived from the mitochondria, which synthesise ATP by oxidative phosphorylation. Although the effects of acute alcohol intoxication on mitochondrial function have not been clarified, chronic administration of alcohol has been shown to alter these organelles morphologically (Hibbs 1965; Song 1972; Vasdev 1975), resulting in decreased function (Hibbs 1965). This includes uncoupling of oxidative phosphorylation and altered lipid metabolism (Rubin 1979; Thomas 1994), and is probably the reason for the increased fat content of cardiac and skeletal muscle in alcoholics (Regan 1974; Song 1972; Vasdev 1975). Furthermore, alcohol and acetaldehyde inhibit protein synthesis, which may explain the deficits that occur in membrane-bound enzymes. It is, however, debatable whether decreased protein synthesis affects the contractile elements (Bing 1982). Schreiber and associates demonstrated inhibition of cardiac microsomal protein synthesis by acetaldehyde, but at the same time, they noted a positive inotropic and chronotropic effect (Schreiber 1974), although this may have been due to acetaldehyde mediated release of catecholamines (Bing 1982; McCloy 1974).

An additional consideration in the acute setting, is alcohol-related acidosis, which may have significant negative inotropic effects. This is most likely due to decreased sensitivity of the myocardium to circulating catecholamines. In a haemorrhagic shock model, Horton showed that myocardial contractility was impaired *after* resuscitation in alcoholic dogs, rather than prior to or during the shock phase, probably on the basis of persistent acidosis (Horton 1986). She also demonstrated that correction of acidosis in the resuscitation phase resulted in improved subendocardial blood flow and better cardiac performance (Horton 1987). There are several mechanisms to explain alcohol-related acidosis. The metabolism of alcohol begins by oxidation with NAD in the liver, which results in an

increase in the ratio of NADH to NAD. This shifts the equilibrium for lactate dehydrogenase toward lactate with resultant lactic acidosis (Garrison 1984). Furthermore, alcohol suppresses ventilation and reduces sensitivity of the respiratory centre to accumulating CO_2 (Goodman and Gilman's: The Pharmacological Basis of Therapeutics 8th ed, 1990). For example, Roeggla et al demonstrated reduced ventilatory adaptation in healthy mountaineers after consuming 50g of alcohol (Roeggla 1995). This not only leads to respiratory acidosis, but also prevents respiratory compensation for alcohol-induced metabolic acidosis.

It would seem therefore, that alcohol acts on the cardiovascular system both directly and indirectly. The overall body of information suggests a negative effect of alcohol on haemodynamics in normal subjects. As with the actions of alcohol on the CNS, the initial effect on the heart appears to be stimulatory, with increased pulse rate and cardiac output. In addition, cutaneous vasodilatation accentuates the clinical features of a hyperdynamic circulation. However, these early effects are only masking the decreased functional reserve of the myocardium, which becomes apparent when alcohol levels increase. When this occurs, blood pressure and cardiac output fall with development of bradycardia or arrhythmias, and even cardiac arrest in extreme cases. As for the effect of alcohol on regional circulation, although blood flow to some organs is enhanced, particularly at lower concentrations, it would appear that distribution of perfusion for the most part is less than ideal.

6.3 CARDIAC TAMPONADE

I. Structure and function of the pericardial sac

The heart is enclosed in a double-walled fibroserous sac, known as the pericardium (Gr=around the heart). The outer fibrous pericardium is a relatively in-elastic conical structure with its apex fused to the roots of the great vessels at the base of the heart and its broad base overlying the central tendon of the diaphragm, with which it is inseparably blended (Last's Anatomy Regional and Applied 8th ed, 1990). The serous pericardium is made up of a parietal layer which lines the inner surface of this fibrous sac and a visceral layer, which covers the enclosed heart and adjacent parts of the great vessels (Cunningham's Manual of Practical Anatomy 14th ed, 1977; Last's Anatomy Regional and Applied 8th ed, 1990). Between these two layers is the pericardial space, which contains 20-50ml of serous fluid (Clinical Anatomy for Emergency Medicine 1993; Demetriades 1983, Robbs 1984). This is sufficient to keep the contiguous surfaces slippery, thereby providing a frictionless environment for cardiac function. The pericardium also prevents excessive dilatation of the heart, particularly where the thin-walled low pressure chambers are concerned, and maintains the heart in a relatively fixed position within the thorax. Furthermore, intra-pericardial pressure is normally subatmospheric and essentially equal to the intra-pleural pressure throughout the respiratory cycle. This may play a role in augmenting atrial filling during ventricular systole (Shabetai 1994).

II. Definition

Cardiac tamponade, also known as pericardial tamponade, is a clinical syndrome in which progressive increments in pericardial pressure are associated with signs of a diminishing cardiac output (Wechsler 1974).

III. Etiology

In tamponade, increased pericardial pressure is caused by accumulation of fluid or gas within the pericardial sac (McAndrew 1986, Pories 1975). The etiology of cardiac tamponade varies widely (Table 6.2). Trauma is by far the commonest cause in Cape Town (unpublished data). This is usually due to penetrating cardiac injury, but may also occur following blunt trauma, or after surgery or cardiac catheterization (Pories 1975). Stab wounds caused by knives or other sharp implements are the most common cause of penetrating cardiac trauma, followed by handgun missile wounds. In most published series, sites of penetration in order of frequency are the right ventricle (40-60%), the left ventricle, right atrium, left atrium and the intracardiac portion of the great vessels. Transection of coronary arteries seldom occurs (4-5%); the left anterior descending artery is most frequently damaged, followed by the right coronary. Intracardiac injuries are also uncommon and are most frequently associated with bullet wounds (Robbs 1984). Rarely, injuries of blood vessels outside the pericardium (ie. internal mammary arteries) may cause blood to accumulate within the pericardial sac, with resultant tamponade (unpublished data).

Table 6.2: Etiology of cardiac tamponade

Direct Trauma
penetrating injury
surgery
cardiac catheterization
pacemakers
pericardial aspiration
oesophageal perforation

Indirect Trauma
blunt chest injury
decelleration injury
radiation
postmyocardial injury syndr
mechanical ventilation

Infection
viral
bacterial
fungal
toxoplasmosis
amoebiasis

Primary Neoplasia
mesothelioma

Secondary Neoplasia
lung
breast
melanoma
lymphoma

Drugs
hydralazine
procainamide
anticoagulants

Hypersensitivity states
serum sickness

Metabolic disorders
uraemia
myxedema
haemorrhagic states

Collagen Diseases
rheumatic fever
lupus erythematosis

Adjacent Disease
pancreatitis
chylous effusion
myocardial infarction
- pericardial effusion
- myocardial rupture

Uncertain origin
Behcet's syndrome
Loeffler's syndrome
Reiter's syndrome

IV. Clinical features

Acute tamponade, especially when it is related to trauma, is very dangerous, because the onset is usually sudden and the clinical picture may be confused by other injuries (Demetriades 1983; Naughton 1989; Pories 1975). Hypovolemia may also add to the woes of the tamponade victim (Demetriades 1983) and the acuteness of the condition often limits the role of compensatory mechanisms (Brown 1992).

The typical signs of traumatic cardiac tamponade are shock, often out of proportion to the degree of injury, and raised central venous pressure. Dyspnoea, tachypnoea and restlessness are frequently present (Gascho 1981; Pories 1975) and there may be evidence of haemorrhage into a body cavity or extracorporeally (Demetriades 1983; Pories 1975). The clinical signs of muffled heart sounds and a paradoxical pulse, have been over emphasized in the past and are often absent (Demetriades 1983; Robbs 1984). In the presence of penetrating trauma confined to the chest, shock in the absence of haemo- or pneumothorax on chest radiography, is particularly suggestive of the diagnosis (unpublished data). Chronic cardiac tamponade differs from the acute situation in that blood pressure is usually maintained (Beck 1935; Guberman 1981; Reddy 1978) and the clinical features are more those of cardiac failure, with oedema, hepatomegaly and increasing abdominal girth due to systemic venous engorgement (Beck 1935; Pories 1975).

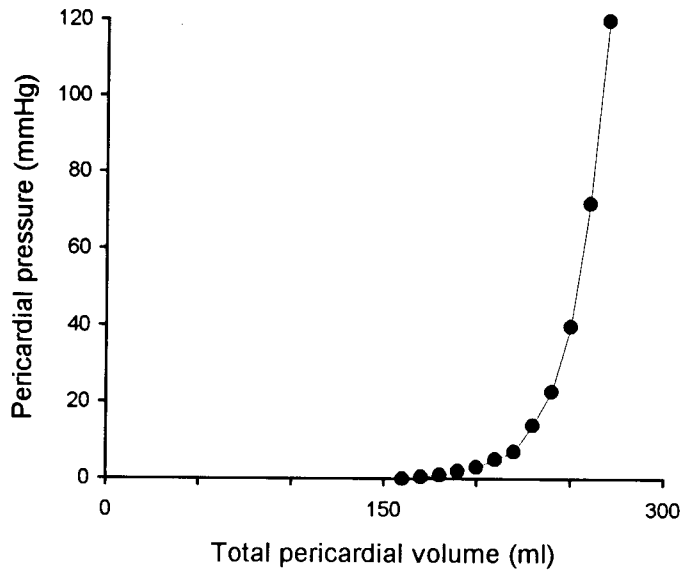
V. Pathophysiology and haemodynamic changes that occur during cardiac tamponade.

Pericardial pressure is determined by the compliance characteristics of the pericardium and the total intrapericardial volume. This volume consists of the heart itself and the pericardial fluid (Reddy 1978). The normal pericardial sac can accommodate 80-120ml before pericardial pressure increases, thereafter the haemodynamic response is related to the rate of fluid or gas accumulation (Pories 1975).

Typically, the pressure-volume curve of the pericardium is characterized by an initial flat portion, during which volume is increased with little or no increase in pressure (Fig 6.2). Thereafter, there is an exponential increase in pressure with minimal changes in volume (Shabetai 1994). Usually venous pressure remains relatively constant until it equilibrates with rising pericardial pressure. Beyond this point, the pericardial pressure-volume curve is equal to or steeper than that of the ventricles (Reddy 1978), venous pressure increases (Shabetai 1970) and cardiac output falls. In advanced tamponade, a critical pericardial pressure is reached where once again equilibration with venous pressure occurs. This is the point at which cardiac filling and heart action ceases (Cooley 1953).

The haemodynamic findings may therefore vary from normal intracardiac pressures and cardiac output in mild cardiac tamponade, to a state characterized by marked elevation of pericardial pressure, intracardiac pressure and systemic vascular resistance, with a substantial decline in cardiac output (Brown 1992; Reddy 1978, Shabetai 1970).

Figure 6.2: Pericardial pressure-volume curve
(Example taken from: Shabetai 1994)



The exact sequence of events following an increase in pericardial pressure, and the mechanisms involved are, however, uncertain. Although experimental work has addressed this issue, these animal studies are fraught with problems such as species variation (Zweifach 1961) and differences in methodology (Brockman 1954; Gascho 1981). Furthermore, human studies are virtually impossible in acute situations, with the result that most of the clinical information available is related to chronic tamponade (Manyari 1983). The latter is often associated with medical conditions (Table 6.2) and pre-existing pathology which may cloud the issue (Brown 1992).

Failure to discriminate between the different etiologies and between tamponade and constrictive pericarditis, also accounts for contradictory findings (Brown 1992; Reddy 1978; Shabetai 1970). Although these two

conditions are similar, there are fundamental differences in their pathophysiology. Normal cardiac filling is bimodal: a surge of venous return to the right atrium occurs at the start of ventricular ejection (coinciding with the x-descent of the venous pressure curve), and again on opening of the tricuspid valve during diastole (coinciding with the y-descent). In constrictive pericarditis, this filling pattern is maintained, but because atrial volume is small, venous pressure drops rapidly resulting in accentuation of the y-descent. Obliteration of the pericardial space and splinting of the heart also prevents respiratory fluctuations in systemic venous return. In tamponade, increased pericardial pressure is exerted on the heart throughout the cardiac cycle, with only momentary relief during ventricular ejection as cardiac volume decreases. This results in unimodal venous return corresponding to the x-descent. In addition, respiration causes significant cyclical changes in intra-pericardial pressure which have a more dramatic influence on venous return than in the normal state (Shabetai 1970; Shabetai 1994).

Historically, decreasing cardiac output due to tamponade was thought to be due to impaired cardiac filling because of an obstructed veno-atrial junction (Cohnheim 1889 - ref by Fowler 1985 and Pories 1975). This theory was supported by the clinical signs of acute tamponade which were highlighted by Beck in 1935, when he described the triad of rising venous pressure, falling arterial pressure and a small, quiet heart (Beck 1935). However, in 1954, Isaacs and co-workers showed that no appreciable pressure gradient occurs at the veno-atrial junction (Isaacs 1954). More importantly, they demonstrated that the pressure-volume relationship of the pericardium, when integrated with Starling's law (Textbook of Medical Physiology 8th ed, 1991; Schlant 1994), explained the decreased cardiac output; ie. limiting the volume of the space availible for diastolic filling of

the ventricles reduces end-diastolic fiber length and therefore, stroke volume and force of contraction fall. Subsequently, gated blood pool scintigraphy (Manyari 1983) and echocardiography (Brown 1992; Martins 1979; Settle 1977), have confirmed that ventricular size is reduced in the presence of tamponade. Other conditions that reduce cardiac filling, such as caval obstruction or positive pressure ventilation, produce the same qualitative effects as tamponade. This supports the concept that function is impaired because the ventricle must operate on the steep portion of the Starling curve at a fiber length too short for the prevailing contractile state (Frank 1971).

Some authors have also emphasized the importance of ventricular interdependence during cardiac tamponade (Ditchey 1981; Nakamoto 1992). Ditchey and co-workers reported that changes in systemic cardiac output are primarily passive, and reflect compression of the right heart with decreased right ventricular stroke volume and pulmonary blood volume, rather than left sided compression. Accordingly, left ventricular stroke volume is maintained until pulmonary blood volume is reduced (Ditchey 1981). Interaction between the left and right heart is also responsible for the clinical phenomenon of a paradoxical pulse. This phenomenon occurs because of exaggerated phasic changes in ventricular dimension associated with respiration (Appleton 1988; Martins 1979, Settle 1977). With inspiration, the negative intrathoracic pressure increases venous return and thereby, right ventricular end-diastolic volume. In tamponade, this impinges on the left ventricle, resulting in a marked decrease in left ventricular filling with subsequent exaggerated reduction in pulse pressure (Dornhorst 1952; Nakamoto 1992). The increased inspiratory augmentation of right ventricular output, is manifest in the systemic

circulation two or three heartbeats later as an expiratory increase in systemic flow and pressure (Shabetai 1970). Additional noticeable changes that occur with respiration are fluctuations in the systemic and pulmonary venous circulations. Reddy found that in human subjects with tamponade, during inspiration pulmonary arterial wedge pressure fell below pericardial pressure while systemic venous pressure was raised, whereas with expiration, the reverse occurred (Reddy 1978). The two most important conditions required for the production of pulsus paradoxus in tamponade are therefore: 1) - competitive filling of both ventricles against a common stiffness and 2) - respiratory changes in venous pressure differential (systemic vs pulmonary), alternately favouring right and left ventricular filling. Other respiration-related factors that may contribute to producing a paradoxical pulse during tamponade include transmission of negative intrathoracic pressure to the heart and aorta (Shabetai 1963), increase in transmural pericardial pressure (Shabetai 1965) and reduction of sinus arrhythmia (DeCristofaro 1969).

Although most studies have highlighted ventricular compression as the reason for reduced cardiac output during tamponade, this has recently been questioned. In 1985, Fowler and Gabel demonstrated that the haemodynamic effects of cardiac tamponade are mainly due to atrial compression, which results in decreased ventricular filling, rather than ventricular compression per se (Fowler 1985). It would appear that the right atrium is more important in this regard (Ditchey 1981). This is also supported by echocardiography, showing that right atrial compression is more consistent than left atrial compression in human cardiac tamponade (Fowler 1985).

In addition to impairing cardiac filling and contractility, tamponade reduces myocardial perfusion (Bernath 1987; Frank 1971; Gascho 1981; Wechsler

1974), which may also contribute to cardiac decompensation. Frank and co-workers demonstrated that coronary flow was decreased during cardiac tamponade, but because aerobic metabolism was maintained in their model, they concluded that the reduction in myocardial blood flow and oxygen delivery was proportionate to the reduction in contractility (Frank 1971). Other studies have also shown that myocardial oxygen consumption is reduced during tamponade (Gascho 1981; O'Rourke 1967), probably on the basis of decreased ventricular wall stress (Johnston 1988). However, Wechsler and co-workers (Wechsler 1974) found that for an apparently similar cardiac oxygen demand, heart rate and afterload, the coronary blood flow was five times greater in dogs subjected to haemorrhagic shock when compared to those who underwent cardiac tamponade. In both these conditions, the left ventricle contracts under the stimulus of a high sympathetic drive at a suboptimal end-diastolic fiber length. This observation suggests that increased pericardial pressure plays a major role in diminishing myocardial perfusion. Furthermore, this study demonstrated that coronary blood flow was significantly decreased even in early tamponade, with reduction in the subendocardial/ subepicardial flow ratio, however, myocardial contractility actually increased and cardiac output was maintained due to an augmented sympathetic state. In more advanced tamponade, the subendocardial/ subepicardial flow ratio stayed the same, but there was a marked decrease in total coronary flow which resulted in myocardial ischaemia and a significant reduction in contractility. In some cases ischaemia was even severe enough to produce subendocardial haemorrhages.

Normally the heart derives its energy by oxidative phosphorylation, in which each mole of glucose yields 36 moles of ATP. However, during hypoxia, or ischaemia such as that induced by cardiac tamponade,

glycolysis supervenes and 2 moles of ATP are provided by each mole of glucose. Beta oxidation of fatty acids is also curtailed. If ischaemia/hypoxia is prolonged, cellular creatine phosphate and eventually ATP are depleted. Eventually, lactic acid accumulates (impaired washout) and causes a decrease in intracellular pH - this inhibits further glycolysis, fatty acid use and protein synthesis, which results in membrane impairment, cellular damage and ultimately necrosis of myocardial cells (Cardiovascular Physiology 1986). Some lactate may also be produced during early cardiac tamponade despite the aerobic conditions that still prevail. This is due to work-load dependent recruitment of glycolytic activity in the myocardium, stimulated by catecholamines (Lewandowski and Ingwall 1994).

The factors that have been implicated in reducing coronary flow during tamponade include extravascular compression of coronary vessels in the face of decreased diastolic perfusion pressure (Downey 1975; Wechsler 1974), high impedance to diastolic flow because of low transarterial pressure gradients (Wechsler 1974), vasoconstrictor reflexes activated by systemic hypotension (Bernath 1987; Mohrman 1978) and tachycardia with reduced diastolic tension time index (Wechsler 1974). McAndrew and Downey though, have shown that tamponade-induced changes in coronary blood flow are primarily due to changes in aortic blood pressure (McAndrew 1986). They demonstrated a linear relationship between aortic blood pressure and myocardial perfusion. They also showed that when aortic blood pressure was maintained by infusion of blood from a pressurized reservoir during cardiac tamponade, coronary blood flow was maintained. Moreover, volume expansion increases cardiac output by increasing ventricular filling pressures and thereby stroke volume (Gascho 1981). Although others have also demonstrated the beneficial effect of volume expansion in acute tamponade (Cooley 1955; Cooper 1944),

Johnston and colleagues (Johnston 1988) have cautioned against overzealous volume expansion, as this may increase coronary sinus pressure. If the rate of increase of the latter exceeds that of the diastolic arterial pressure, coronary perfusion will decrease.

Gascho et al not only confirmed the beneficial effects of volume expansion during tamponade, but a significant additional improvement in myocardial perfusion was noted after the addition of nitroprusside, without a significant change in cardiac output. Although this vasodilator *decreased* blood pressure, it probably improved coronary flow by reducing right atrial pressure, which in turn would have resulted in decreased coronary sinus pressure and a higher coronary perfusion gradient (ie. coronary perfusion pressure is inversely proportional to coronary sinus pressure).

The usual equation for calculating coronary blood flow is as follows:

$$CBF = \frac{CPP}{CVR} = \frac{DP - LVEDP}{CVR}$$

(CBF = coronary blood flow; CPP = coronary perfusion pressure; DP = diastolic blood pressure; LVEDP = left ventricular end-diastolic pressure; CVR = coronary vascular resistance)

Nitroprusside also reduced left ventricular end-diastolic pressure and afterload, which meant that cardiac output could be maintained in spite of the decreased preload (Gascho 1981).

Many of the haemodynamic changes that occur during tamponade are due to compensatory mechanisms. Heart rate increases to maintain cardiac output because stroke volume is limited (Pories 1975). Contractility may even increase in early tamponade. Later, cardiac output falls (Wechsler 1974) and in an advanced stage, bradycardia or arrhythmias may occur as

a pre-terminal event. The initial positive inotropic and chronotropic effects during tamponade are associated with an increase in endogenous catecholamine levels (Bernath 1987, Brown 1992). Administration of inotropes such as adrenaline or isoproterenol (Martins 1980; Pories 1975; Shabetai 1970) have also been reported to increase cardiac output during tamponade, although this effect is greater in animals than in humans and perfusion of critical organs is not improved (Martins 1980). In addition, an increased sympathetic tone is responsible for increasing the total peripheral vascular resistance (Cooley 1953; McAndrew 1986), thus helping to maintain arterial blood pressure until late in tamponade, even in the face of a declining cardiac output (Bernath 1987; Cogswell 1986). At the same time regional perfusion of virtually all organs decreases (Bernath 1987; Gascho 1981). The increased total peripheral resistance during cardiac tamponade is primarily due to alpha-adrenergic mechanisms (Bernath 1987; Cogswell 1986). Cardiac tamponade is also a potent stimulus for the release of renin and the generation of angiotensin-II (Bailey 1987; Bulkley 1986; Cogswell 1986). This causes a profound reduction in splanchnic blood flow which is disproportionate to the reduction in cardiac output and is in accord with the traditional concept that splanchnic perfusion is selectively compromised, while blood flow to more essential organs is maintained during shock states (Bulkley 1983). However, the renin-angiotensin system does not have a dramatic effect on total peripheral resistance (Cogswell 1986).

Cardiac tamponade also results in increased sodium and water retention, which supplements the intravascular volume and delays development of hypotension. Osborn and Lawton (Osborn 1986) showed that moderate elevation of pericardial pressure decreased urinary sodium excretion, in spite of unchanged aortic blood pressure, renal artery flow and glomerular filtration rate. Furthermore, this effect was prevented by renal denervation

and bilateral cervical vagotomy, suggesting that the response was neurally mediated and dependent on afferent sensory information from pericardial, cardiac, and splanchnic receptors. At high levels of pericardial pressure, antinatriuresis was maintained, but vagotomy under these conditions had no effect. The authors postulated that arterial baroreceptor unloading in response to hypotension contributed to sodium and water retention in advanced tamponade. Sodium retention in early tamponade could also be attributed to renin release. This may occur in the absence of hypotension due to: 1) - direct beta-adrenoceptor activation after increased renal nerve activity (Osborn 1982) or 2) - stimulation of the macula densa because of decreased NaCl in the distal tubule (Osborn 1986).

The commonly reported haemodynamic changes that occur during cardiac tamponade can be summarized as follows (Brown 1992; Frank 1971; Gascho 1981: Johnston 1988; McAndrew 1986; Pories 1975; Reddy 1978; Shabetai 1970; Shabetai 1994):

Increased:
- pericardial pressure
- systemic venous pressure
- right and left atrial pressures
- pulmonary artery wedge pressure
- right and left ventricular pressures
- heart rate
- systemic vascular resistance

Decreased:
- aortic pressure/blood pressure
- aortic blood flow
- coronary artery flow
- cardiac output
- left ventricular end-diastolic volume
- stroke volume
- stroke work index
- tension time index

Absent:
- y-descent in the venous pressure cycle with monophasic venous return, forward flow being confined to ventricular systole
- early diastolic dip of right ventricular pressure

In conclusion, acute cardiac tamponade is well defined clinical entity. The underlying mechanism for impaired haemodynamics is increased intra-pericardial pressure which limits heart filling, so that end-diastolic myocardial fiber length is reduced and the ventricles have to operate on the steep portion of the Starling curve. This results in decreased stroke volume and force of contraction. At the same time, coronary perfusion is retarded, resulting in ischaemia and anaerobic metabolism within the myocardium and further impairment of contractility. Multiple compensatory mechanisms which include increase in heart rate and peripheral vascular resistance, selective perfusion of critical organs and antinatriuresis, maintain cardiac output and blood pressure initially. With increasing levels of tamponade, however, these mechanisms fail, until a point is reached where shock is so profound and cardiac filling is so compromised, that heart action ceases.

"Upon the first goblet he read this inscription, monkey wine; upon the second, lion wine; upon the third, sheep wine; upon the fourth, swine wine. These four inscriptions expressed the four descending degrees of drunkenness: the first, that which enlivens; the second, that which irritates; the third, that which stupefies; finally the last, that which brutalizes."

Victor Hugo (1802-1885) Les Miserables

6.4 ALCOHOL AND TRAUMA

Alcohol has been associated with injury since at least the time of the Old Testament (Proverbs 23: 29-30). This relationship has been attributed to alcohol's ability to impair judgement and psychomotor performance (Applied Pharmacology 12th ed, 1980; Clinical Pharmacology 7th ed, 1992; Council on Scientific Affairs of the American Medical Association 1986). Not only is alcohol a major etiological factor in motor vehicle accidents (Huth 1983; Jehle 1988; Thal 1985; Waller 1986), but it is also the commonest contributing factor leading to violent acts. Alcohol has been implicated in 56% of incidents of marital violence, 64% of homicides, 75% of stabbings and 30% of all suicides (Pories 1992). Furthermore, it has been estimated that up to 25% of all persons hospitalized for injury are alcoholics or have an identifiable drinking problem, which is why some authorities view trauma as a marker of alcohol abuse (Holt 1980; Jurkovich 1992).

In spite of all this evidence implicating alcohol as a major cause for trauma, relatively few studies have specifically addressed its effect on injured patients (Hadfield 1983; Jehle 1988; Jurkovich 1992). It is generally accepted that alcohol increases the susceptibility of an individual to injury (Council on Scientific Affairs of the American Medical Association 1986; Irwin 1983, Waller 1986), but the relationship between alcohol and the degree of injury sustained, is less well defined (Pories 1992). A large epidemiological study of five years of automobile crash data from North Carolina, pertaining to more than a million drivers, showed that for similar types and degrees of accident, the drinking driver was more likely to suffer serious injury or death compared to those who were sober (Waller 1986).

Contrary to this finding is the popular notion that the drunk individual can "roll with the punches", and thus escape more serious injury (Huth 1983; Pories 1992; Waller 1986).

The effect of alcohol on hospital course and outcome of patients is even more controversial (Horton 1987; Jehle 1988; Jurkovich 1992). This is partly due to the multiple variables affecting the clinical status of trauma victims (Jehle 1988), as well as the confounding effect of alcohol on injury severity scores (Jagger 1984). In addition, alcohol may result in a higher mortality at the scene of of the accident (Jehle 1988), so that only "selected" intoxicated patients reach hospital alive (Huth 1983). All these variables make it difficult to develop a reliable objective relationship between alcohol intoxication and clinical outcome (Garrison 1984). For this reason, the literature abounds with contradictions. Some studies have concluded that intoxicated trauma patients have a higher mortality and become more hypotensive than sober patients with the same degree of haemorrhage (Elmer 1985; Lee 1967; Rappaport 1990). Others have reported that alcohol has no effect on the hospital course of injured patients (Huth 1983; Thal 1985). Ward and colleagues have even suggested that alcohol may have a protective effect in trauma. They reviewed 1 198 trauma cases with regard to degree of injury and outcome, and found a significantly lower mortality among those who had been drinking (Ward 1982).

Because of the limitations of clinical studies, most work on alcohol and its effect on trauma has been experimental. However, laboratory conditions are far removed from the "real world". Also, it must again be emphasized, that animal studies have to be interpreted in the light of species variation (Moore 1961; Zweifach 1961) and differences in methodology. Different

dosages and routes of administration of alcohol (Horton 1986), and interaction of alcohol with anaesthetic agents (Shatney 1976; Zink 1988), are just some of the factors that confuse the issue. Bronowski though, has pointed out that "the essence of both the scientific and the artistic process is to find unity in the variety of nature" (Moore 1961). To this end, numerous animal models have been developed which allow study of all kinds of injury in a more controlled environment, both in vivo and in vitro, although the bulk of experimental research involving alcohol and trauma appears to be related to its effect on haemorrhagic shock (Bottoms 1990; Chandler 1991; Garrison 1984; Horton 1992; Zink 1988).

It has been consistently reported that alcohol exaggerates hypotension in the setting of haemorrhagic shock (Gettler 1963; Moss 1959; Reves 1972; Zink 1988). It has also been shown that it requires less blood loss to cause a drop in blood pressure in intoxicated animals (Malt 1971; Moss 1959). However, the effect of alcohol on outcome after haemorrhagic shock appears to be less clear. Gettler and Allbritten reported that alcohol increases the mortality of animals subjected to acute haemorrhage (Gettler 1963). Others have shown that alcohol does not have a significant effect on survival (Zink 1988). Knott and co-workers found that although alcohol appeared to decrease circulating blood volume, possibly on the basis of sequestration due to vasodilatation, it in no way caused a greater proportional blood loss and did not have an untoward effect on the response to haemorrhagic stress (Knott 1963). Horton demonstrated that two hours of shock affected cardiac function and regional perfusion to a similar extent in both intoxicated and non-intoxicated dogs, but the response to resuscitation was impaired in the intoxicated group because of persistent metabolic acidosis (Horton 1986; Horton 1987). This was most likely due to increased production of lactate in the intoxicated animals

(Garrison 1984). Even more significant though, was impaired respiratory compensation for the shock-induced metabolic acidosis, because of suppression of ventilation by alcohol (Gettler 1963, Malt 1971). In support of this concept, Malt and Baue have shown that the haemodynamic effects of alcohol include maintenance of, or even an increase in cardiac output, until ventilation fails (Malt 1971). They also highlighted the myocardial irritability which occurs due to the combined effects of alcohol and shock. No study, however, has shown that alcohol is advantageous in hypovolemic shock, although it is conceivable that in the situation of spontaneous haemorrhage, early hypotension caused by alcohol could lead to decreased bleeding and thus have a protective effect (Zink 1988).

In cardiac tamponade the mechanism of hypotension differs from that due to excessive haemorrhage (Textbook of Medical Physiology 8th ed, 1991), yet very few studies have examined the effect of alcohol on this form of shock. Although several clinical studies have speculated on the possible effect of alcohol on assault-related cardiac injuries (Buckman 1993; Demetriades 1983: Naughton 1989), none have specifically addressed the action of alcohol on haemodynamics of tamponade. As for experimental work, there is a host of information on physiology of tamponade per se, but it appears that only Cooley and Brockman in 1953, alluded to the effect of alcohol on this condition in an animal model (Cooley 1953).

In the Cape Metropolitan Area, more than a third of all trauma cases can be attributed to assault (Cape Town Metropolitan Area Trauma Survey). Penetrating chest injuries with associated cardiac involvement are therefore not uncommon. In addition, a large proportion of these cases are alcohol related. A prospective clinical study was therefore mounted to study the effect of alcohol on cardiac tamponade.

6.5 DEMOGRAPHY OF TRAUMA IN THE CAPE TOWN METROPOLITAN AREA

Based on a survey conducted by the National Trauma Research Programme of the Medical Research Council for 1990 (CMTS) (Dr J van der Spuy). This included all levels of State and Private sector services; All Ages; Fatal and Non-fatal trauma. Data was collected on 28 random days during 1990 to obtain a representative 4 week period and then extrapolated for the year.

Information was obtained from the following sources:

3 Teaching hospitals:	Groote Schuur
	Tygerberg
	Red Cross Childrens Hospital
5 Service hospitals:	Conradie
	Victoria
	Woodstock
	Somerset
	False Bay
1 SADF hospital:	No 2 Military hospital
11/13 Private clinics	
27/28 Day hospitals/clinics	
1 Mobile trauma centre	
49/493 General practitioners (10%)	
30/301 Dentists (10%)	
20/206 Surgeons (10%)	
2 State pathology services	
4 District surgeons	

Additional postmortem data was obtained from the Salt River Medicolegal Laboratory (Dr HJ Scholtz, personal communication)

POPULATION:	2.517 MILLION
INJURED PATIENTS:	248 843
RATE OF INJURY:	9 886/100 000

TOTAL NO OF VIOLENCE CASES:

85 159/248 843 = 34.2% of all trauma

Assaults	-	83 157
Rape	-	567
Civil unrest	-	671
Suicides	-	764

PENETRATING CHEST INJURIES:

15 113/248 843 = 6.1% of all trauma

15 113/85 159 = 17.7% of all violence

PENETRATING CARDIAC INJURIES:

830/248 843 = 0.33% of all trauma

830/85 159 = 0.97% of all violence

830/15 113 = 5.5% of all penetrating chest injuries

ASSOCIATED ALCOHOL:

(Clinically judged, therefore an underestimate)

159 508/248 843 = 64.1% of all trauma

10584/15 113 = 70% of penetrating chest injuries

No data for all penetrating cardiac injuries

MORTALITY:

3057/248 843 = 1.2% for all trauma

1084/15 113 = 7.2% for penetrating chest injuries

407/830 = 49% for penetrating cardiac injuries

% of fatal penetrating cardiac wounds where tamponade was the cause of death: 31/323 = 9.6% ie. 90% died as a result of exanguination (figures for 1/1/1990 - 31/12/1991; Salt River Medicolegal Laboratory)

ALCOHOL RELATED MORTALITY:

1508/3057 = 49.3% of all trauma deaths

749/1084 = 69.1% of penetrating chest injury deaths

258/323 = 80% of penetrating cardiac injury deaths had positive blood alcohol (figures for 1/1/1990 - 31/12/1991; Salt River Medicolegal laboratory)

PROVERBS 24

29. Who hath woe? who hath sorrow? who hath contentions? who hath babbling? who hath wounds without cause? who hath redness of eyes?

30. They that tarry long at the wine; they that go to seek mixed wine.

7. THE EFFECT OF ALCOHOL INTOXICATION ON HAEMODYNAMIC PHYSIOLOGY AND HOSPITAL COURSE OF PATIENTS WITH TRAUMATIC CARDIAC TAMPONADE

7.1 INTRODUCTION

There can be no doubt that, for all forms of violent death, alcohol often plays a determining role by encouraging or provoking the behaviour that causes the assault. The effect of alcohol on clinical parameters and outcome after injury is, however, controversial (Horton 1987; Jurkovich 1992). Although several clinical studies have addressed this question, most of them have been retrospective and nonspecific, with little mention of haemodynamic effects (Irwin 1983; Jehle 1988; Pories 1992; Waller 1986), while the majority of clinical reports and reviews of traumatic cardiac tamponade, do not even mention alcohol as a factor (Attar 1991; Feliciano 1984; Moreno 1986; Pories 1975). Others (Buckman 1993; Demetriades 1983; Naughton 1989; Robbs 1984), merely speculate as to the possible role of this agent. The aim of this study was to specifically investigate the effect of alcohol on haemodynamic physiology of acute cardiac tamponade and to determine the influence of intoxication on patient outcome.

7.2 PATIENTS AND METHODS

All patients who were admitted to the Trauma Unit with penetrating chest injuries and suspected cardiac tamponade between August 1991 and April 1992, were prospectively analyzed. Pre-hospital care was uncontrolled as some patients relied on private transport rather than the emergency services. A presumptive diagnosis of the condition was made when the site

of the wound suggested the possibility of heart injury and there was associated shock and/or distended neck veins. The extent of injury, vital signs, Trauma Score (TS) (Champion 1981) and cardiovascular-respiratory component of the Trauma Score (CVRS) (Buckman 1993) were recorded on admission, and patients were stratified according to their clinical status as recommended by Ivatury and associates (Ivatury 1987) (Table 7.2).

Special investigations included on-site supine chest radiographs where possible, as well as the following routine tests: arterial blood gas levels were determined in the Trauma Unit using a Ciba Corning 288 blood gas analyzer (Medfield, USA); serum sodium and potassium levels were measured by ion selective electrode; and glucose was determined by the oxidase method (using an Astra 8 analyzer, Beckman, USA) (Emergency Laboratory, Department of Chemical Pathology). In addition, blood was sampled and stored as serum for later measurement of the following: lactate levels were determined in the Surgical Research Laboratory using enzymatic assay (with lactate dehydrogenase and NAD); catecholamine levels were measured on admission and after release of the tamponade using high flow liquid chromatography with electrochemical detection (Waters system: Millipore, Massachusetts, USA) (Research Laboratory, Department of Anaesthesiology); and alcohol levels were determined by fluorescent polarization immuno-assay (GMBH Diagnostika, Wiesbaden-Delkenheim, W.Germany) (Analytical Laboratory, Department of Pharmacology). Intoxication was defined as a serum alcohol concentration (SAC) greater than 17 mmol/L - those patients with SACs below this, or with negative tests, were defined as non-intoxicated;

Resuscitative measures included volume replacement via large-bore intravenous lines and, where necessary, placement of chest tubes and/or

endotracheal intubation and ventilation. If the patient was "lifeless" or "in extremis" and did not respond rapidly to resuscitation, an anterolateral thoracotomy was performed in the resuscitation area (front-room), cardiac tamponade was relieved by pericardiotomy and cardiac massage was commenced. Bleeding was controlled by finger pressure and the cardiac wound was closed using 3° prolene sutures. Inotropic agents and $NaHCO_3$ were administered if deemed necessary and where no cardiac response was obtained or fibrillation was noted, countershock was employed using internal paddles. If the condition of the patient improved, then he/she was transferred to the operating room for formal repair of the cardiac wound and control of other injuries. Patients who arrived "shocked" or in a "stable" condition were resuscitated, central venous lines were placed and on-site supine chest radiographs were repeated to confirm correct catheter placement. They were then taken to the operating room for relief of tamponade and repair of the cardiac injury under general anaesthesia. Transfusion requirements pre and peri-operatively were recorded and the volume of blood evacuated from the pericardial sac was estimated. Clinical progress of patients was assessed at 24 hours and 72 hours after operation, and APACHE II scores (Knaus 1981) were calculated.

A comparison was made between intoxicated and non-intoxicated patients with acute cardiac tamponade by analyzing their clinical course, as well as haemodynamic and biochemical parameters. Only patients with surgically confirmed acute tamponade were entered into the study. Those who had associated haemorrhagic shock, or an injury older than 24 hours, were excluded. Statistical analysis was done using Fishers exact probability test for nominal data (Epistat computer package) and Wilcoxon rank-sum test for numeric data (Statgraphics computer package), and P-values less than 0.05 were considered significant.

7.3 RESULTS

Sixty two patients fulfilled the criteria for inclusion in the study, but 12 patients with confirmed tamponade, including two who died, had to be excluded because serum alcohol levels were not measured. The median age of the remaining 50 patients was 27 (16-53) years and 47 were men. The most frequent injury was a single stab wound to the left precordium (Table 7.1). No gunshot wounds of the heart were seen during the study period.

Overall mortality was 26%. Mortality for "lifeless" patients was 80%; for patients "in extremis", 50%; and for shocked patients, 13% (Table 7.7). No patient who was admitted in a stable condition died. Seventeen patients underwent front-room thoracotomies, of whom 12 died (71% mortality), while 33 patients had operating-room procedures for relief of tamponade with only one death (3%) ($p<0.0001$). The median delay to surgery in the latter group was 48 (10-660) minutes. The sites of cardiac injury are depicted in Figure 7.1. Four patients with right ventricle penetration died (14%) compared to seven (54%) with wounds of the left ventricle ($p=0.01$). The single patient with a compound injury, survived. One additional patient (intoxicated) had a ventricular septal injury which was detected after emergency surgery. This caused no cardiovascular embarrassment and was managed conservatively. The estimated volume of blood in the pericardial sac of all patients ranged from 100-450 ml (median 250ml). Nine patients had other injuries including six lung lacerations, 2 liver and diaphragm lacerations and one minor skull fracture. One patient was so shocked due to cardiac tamponade that he developed non-occlusive gut ischaemia.

When SACs were analyzed, 35 patients were found to be intoxicated (median 42 mmol/L; range 24-67 mmol/L) and 15 were nonintoxicated (median 0 mmol/L; range 0-17 mmol/L). Because of the unequal size of these two groups, as well as the abnormal distribution of data, nonparametric methods were used for statistical analysis and all values were expressed as the median unless otherwise specified. Besides the fact that intoxicated patients were older than nonintoxicated patients: 28 (17-53) years vs 24 (16-38) years (p=0.02), there were no significant differences between the two groups (Table 7.3). Although intoxicated patients tended to be more shocked on admission (27/35 vs 10/15 had mean BP of 80mm Hg or less), they did not require more fluid for resuscitation (Table 7.4) and had higher initial haemoglobin levels than their nonintoxicated counterparts (Table 7.3). In addition, there were no differences in levels of consciousness or trauma scores in the two groups. The proportion of front-room thoracotomies was also the same (12/35 vs 5/15), however, there was a trend towards earlier surgery in intoxicated patients (median delay; 30 minutes vs 48 minutes). One feature of note, was the higher proportion of non-intoxicated patients who had hyperpnoea or tachypnoea on admission (67% vs 25%) (p=0.006). This was also apparent from the lower pCO_2 values in this group (Table 7.5). It is debatable how much emphasis should be placed on this finding though, as assessment of respiration is frequently subjective and is particularly difficult in patients who require immediate endotracheal intubation and ventilation.

The results of other special investigations are also listed in Table 7.5. Serum glucose was raised in both of the study groups, whereas sodium, potassium, urea and creatinine levels were unaffected by cardiac tamponade. As expected, all patients had a metabolic acidosis, but this

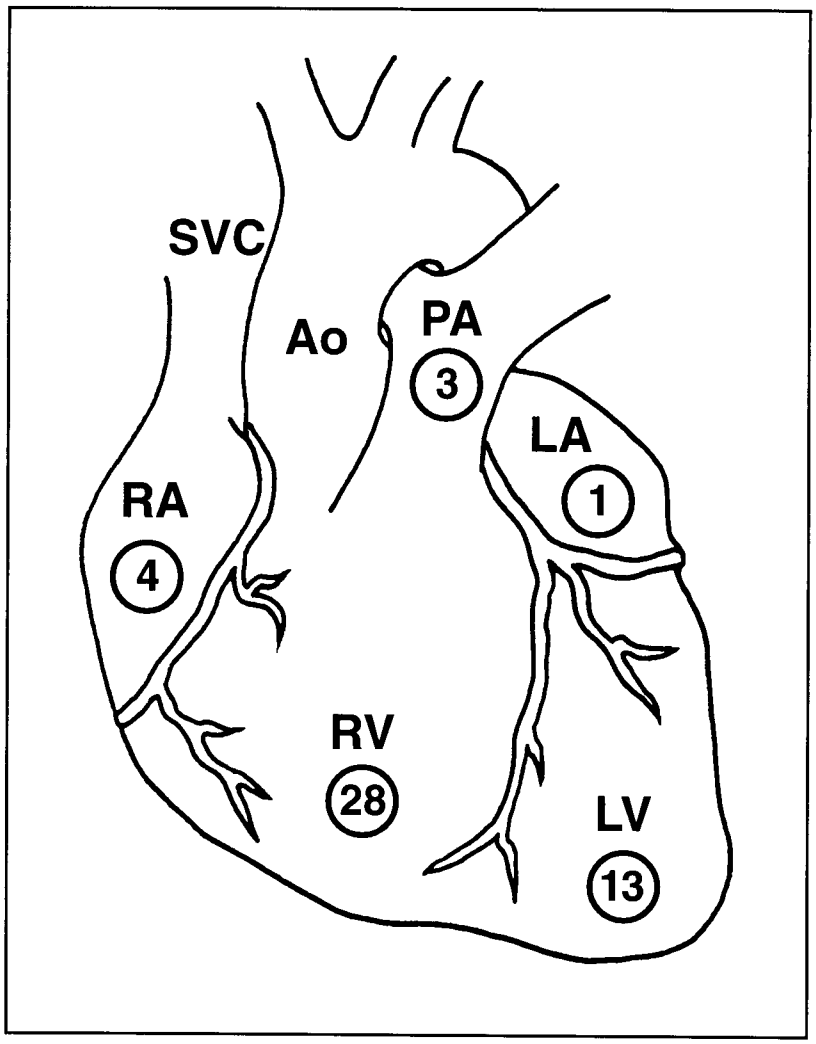
was not aggravated by alcohol and serum lactate levels in both groups were similar. Because of the wide range and abnormal distribution of catecholamine results, these were impossible to interpret. In addition, where adrenaline was used for resuscitation, or ketamine for anaesthesia, results were unreliable and were not included in the analysis.

Patients who survived initial resuscitation and surgery, generally did well, with remarkably low APACHE II scores 24 and 72 hours after operation, and a relatively short hospital stay (Table 7.6). Only two patients in the non-intoxicated group died after 24 hours (one from adult respiratory distress syndrome; one hypoxic brain injury). When mortality of the two groups was compared, overall outcome was similar, although there was a trend towards less mortality in the intoxicated group (22.9% vs 33.3%). This occurred in spite of the fact that a greater proportion of intoxicated patients were "lifeless" or "in extremis" on admission (12/35 vs 2/15 patients) (Table 7.7). When lifeless patients were excluded from the equation, the difference in mortality between intoxicated and non-intoxicated patients was more apparent, although this was not significant ($p=0.14$).

Table 7.1 SITE OF STABWOUND

Left anterior chest	30
Right anterior chest	6
Sternum	5
Left axilla	2
Multiple	7

Figure 7.1 : Cardiac Stabwounds: Site of penetration



* 1 Patient: multiple sites
+ 1 Patient: VSD

Table 7.2 STRATIFICATION OF PATIENTS ACCORDING TO CLINICAL STATE ON ADMISSION

"Lifeless"	10
"In extremis"	4
Shocked	23
Stable	13

Lifeless = unconscious and without vital signs.
In extremis = semiconscious with gasping respiration, thready pulse and no measurable blood pressure.
Shocked = conscious but hypotensive with mean blood pressure of 80mmHg or less.
Stable = conscious with mean blood pressure of more than 80mmHg.

Table 7.3 CLINICAL PARAMETERS ON ADMISSION

	Intoxicated patients	Nonintoxicated patients	p value
	n = 35	n = 15	
Age	28(17-53)yrs	24(16-38)yrs	0.02*
Syst BP	70(0-134)mmHg	84(0-135)mmHg	0.14
Diast BP	40(0-103)mmHg	45(0-80)mmHg	0.36
CVP**	25(10-35)cmH2O	27(6-40)cmH2O	0.78
Hb	11.3(6-16)g%	10.3(4-12.5)g%	0.13
GCS	14 (3-15)	13 (3-15)	0.65
TS	12 (3-16)	12 (3-15)	0.96
CVRS	8 (2-11)	8 (2-10)	0.97

CVP = central venous pressure; Hb = haemoglobin level; GCS = Glasgow Coma Score; Ts = Trauma Score; CVRS = Cardiovascular-respiratory component of the Trauma Score.
**CVP was only recorded in 23 intoxicated and 11 nonintoxicated patients.

Table 7.4 RESUSCITATION REQUIREMENTS

	Intoxicated patients	Nonintoxicated patients	p value
FR crystalloid	2(1-13)L	3(1-7)L	0.62
FR blood	0.5(0-10)U	1.5(0-3)U	0.45
Th crystalloid	1.6(0-6)L	1.5(0-7)L	0.81
Th blood	0.5(0-10.5)U	2(0-7.5)U	0.24
Crystalloid-T	3.5(0.5-13)L	4(1-11)L	0.84
Blood-T	1(0-14.5)U	2(0-10.5)U	0.26
Volume-T	4.5(1-26.5)L	6.5(1-18.5)L	0.61

FR = front room; Th = operating theatre; T = total.

(U = 500ml)

Table 7.5 SPECIAL INVESTIGATIONS

	Intoxicated patients	Nonintoxicated patients	p value
Alcohol mmol/L	42(24-67)	0(0-17)	<0.01
Na^+ mmol/L	141(116-145)	139(133-146)	0.14
K^+ mmol/L	4(2.7-5.4)	4.1(3.4-5.6)	0.22
Urea mmol/L	3.5(1.7-5.2)	4(1.9-7.30)	0.19
Creat mmol/L	89(52-147)	83(57-124)	0.49
Glu mmol/L	8.2(3.2-37.3)	9.2(6.3-16.2)	0.62
pH	7.20(6.7-7.4)	7.22(6.7-7.4)	0.95
pCO_2 - kpa	4.9(2.9-7.1)	4.4(1.9-6.8)	0.14
HCO_3^- mmol/L	14.6(4.6-23)	12.5(6.6-22)	0.44
Base excess	-11.3(-1;-25)	-15.3(-2;-32)	0.22
Lactate mmol/L	5.3(0.5-8.8)	5.4(1.3-6.7)	0.80
Noradrenalin* nmol/L	1357 (550-7258)	5367 (327-17175)	0.20
Adrenalin* nmol/L	1230 (151-24800)	2433 (15-30000)	0.97

Na^+ = Serum sodium; K+ = serum potassium; Creat = serum creatinine; Glu = serum glucose; $HCO3^-$ = standard bicarbonate level.

* Only catecholamine levels on admission are presented - catecholamine levels after release of tamponade were of little value, as too few were taken and ketamine anaesthesia was used in some cases.

Table 7.6 CLINICAL COURSE

patients	Intoxicated patients	Nonintoxicated value	p
APACHE II:24hrs	0 (0-6)	2 (0-10)	0.12
APACHE II:72hrs	0 (0-4)	0 (0-3)	0.86
Hospital stay	6 (4-37)days	7 (4-9)days	0.23

Table 7.7 MORTALITY VS CLINICAL STATE ON ADMISSION

	Intoxicated patients	Nonintoxicated patients	p value
Mortality overall	8/35 (22.9%)	5/15 (33.3%)	0.33
"Lifeless"	6/8 (75%)	2/2 (100%)	0.62
"In extremis"	2/4 (50%)	-	-
Shocked	0/15 (0%)	3/8 (37.5%)	0.03*
Stable	0/8 (0%)	0/5 (0%)	-

7.4 DISCUSSION

There are few clinical conditions that present so acutely and create as much excitement, as penetrating cardiac trauma. Moreover, salvage of the moribund victim with a cardiac wound has become a standard of modern trauma care (Moreno 1986). Despite this interest in the condition, very few prospective studies have been undertaken because of the multitude of factors that affect patients with acute cardiac tamponade. The need for rapid diagnosis and aggressive treatment of tamponade (Marshall 1984; Robbs 1984) also takes precedence over research. In this study, 12 patients had to be excluded because blood alcohol levels were not taken. They did not, however, represent a selected group, as clinical status, treatment and outcome were similar to those of the study patients.

In spite of the fact that cardiac tamponade is a life threatening condition, it is paradoxically protective, for these are patients who have a contained bleed rather than exanguinating haemorrhage (Demetriades 1983; Moreno 1986; Robbs 1984). The majority of patients with the latter scenario never reach hospital alive (Salt River Medicolegal Laboratory data). No doubt, the time taken to reach medical attention is also crucial in most instances (Demetriades 1983; Gervin 1982). We were unable to ascertain if alcohol intoxication influenced pre-hospital treatment, although a large proportion of patients who made use of private transport to reach hospital survived, which vindicates the so-called "scoop and run" policy (Buckman 1993; Naughton 1989).

Any patient with penetrating trauma of the neck, chest or upper abdomen and significant hypotension, must be suspected of having a cardiac injury (Evans 1979; Marshall 1984;.Robbs 1984). Elevation of the central venous

pressure makes the diagnosis even more likely, but falsely high levels can occur if the patient is shivering or straining, or if the catheter tip is positioned incorrectly (Robbs 1984). The presence of a paradoxical pulse or muffled heart sounds are less reliable signs (Demetriades 1983; Robbs 1984; Trinkle 1979). Chest X-ray, which is usually taken on a restless patient in the supine position, is also of limited value in diagnosing tamponade (Demetriades 1983; Trinkle 1979), although we have found it to be very useful in excluding other causes for shock such as haemothorax or tension pneumothorax (unpublished data).

Because victims of assault are frequently under the influence of alcohol, this is an additional variable that needs to be considered. Intoxicated patients may have impaired levels of consciousness and are more likely to be uncooperative (Applied Pharmacology 12th ed, 1980; Clinical Pharmacology 7th ed, 1992), but careful assessment of their haemodynamic and neurological status is essential, before altered mental state can be attributed entirely to inebriation (Evans 1979). Alcohol has also been reported to exaggerate hypovolaemic shock and impair compensatory mechanisms (Elmer 1985; Rappaport 1990; Reves 1972; Zink 1988). However, in this study of patients who had tamponade rather than haemorrhagic shock, alcohol intoxication did not adversely affect clinical parameters. This may be due to the fact that pathophysiology of shock differs in patients with cardiac tamponade (Textbook of Medical Physiology 8th ed, 1991). Hypotension in this instance is due to constriction of the heart, with impaired ventricular filling (Frank 1971), reduced coronary blood flow (Wechsler 1974) and decreased myocardial contractility (Isaacs 1954), rather than exanguination.

Rapid diagnosis, aggressive resuscitation and early operative intervention with relief of tamponade and cardiorraphy, are now established principles of management (Attar 1991; DeGennaro 1980; Demetriades 1983; Feliciano 1984). In spite of the notion that alcohol hampers diagnosis, this was not the case in our study, in fact, there was less delay to definitive treatment in the intoxicated group. Emergency room thoracotomy is indicated for patients with penetrating injuries who are "lifeless" or "in extremis", who do not rapidly respond to basic resuscitative measures (Attar 1991). The proportion of patients who required emergency room thoracotomy was the same in both groups, but this was delayed in three nonintoxicated patients who arrived in a relatively stable condition, only to deteriorate later. We no longer practice pericardial aspiration for diagnosis or therapy, as our experience, as well as that of others (DeGennaro 1980; Demetriades 1983; Ivatury 1981; Marshall 1984; Trinkle 1979), has been disappointing.

Survival of patients with penetrating cardiac injuries is inversely proportional to the degree of shock on arrival (Attar 1991; Naughton 1989). In this series, the highest mortality occured in patients without vital signs. The site of the cardiac injury is also a determining factor. Our experience is the same as that reported in the literature (Attar 1991; Breaux 1979; Elkin 1944; Trinkle 1979), with the right ventricle being most frequently involved. Because of the relative thinness of the right ventricular myocardium which precludes spontaneous arrest of haemorrhage, this is also the most frequent site which leads to tamponade (Robbs 1984). However, in this study, wounds of the left ventricle had a more deleterious effect (mortality 14% and 54% respectively) ($p=0.01$). In 1983, Demetriades and Van der Veen reported similar findings, with a relative mortality of 7.5% for

patients with right ventricular wounds undergoing surgery, compared to 41.9% for those with wounds of the left ventricle (Demetriades 1983). They also emphasized the high mortality associated with wounds of the intra-pericardial aorta as well as those where multiple cardiac sites are involved. The single patient in our series who had wounds of both right-sided heart chambers, survived.

Although clinical (Lee 1967; Rappaport 1990) and experimental (Gettler 1963) studies of hypovolaemic shock have shown that alcohol has a negative effect on prognosis, its effect on cardiac tamponade is unknown. This study has shown no difference in mortality between intoxicated and nonintoxicated patients with cardiac tamponade, in fact there was a trend favouring the former. Buckman et al (Buckman 1993) and Naughton et al (Naughton 1989) have reported similar results.

There are several theoretical reasons why intoxicated patients with tamponade may do better than those with hypovolaemic shock. Alcohol intoxication could "protect" patients with penetrating cardiac cardiac injuries by causing release of endogenous catecholamines (Klingman 1958; McCloy 1974; Perman 1958), which have a stimulatory effect on the heart. Because catecholamine release characterizes the normal response to injury, it has even been suggested that alcohol might "prime" the patient before injury occurs (Ward 1982). However, in this study, median catecholamine levels were actually lower in intoxicated patients. Although the reliability of this result is questionable, it is possible that anaesthetic and analgesic effects of alcohol (Textbook of Pharmacology 2nd ed, 1980) may have resulted in less injury-related stress.

Alcohol may also improve haemodynamics by causing vasodilatation (Altura and Altura 1982). If this action is coupled with the positive inotropic

and chronotropic effects of released catecholamines, the net result is similar to that produced by the drug isoproterenol, which increases myocardial contractility and decreases peripheral vascular resistance. Isoproterenol has been shown to be useful in treating cardiac tamponade (Millard 1983). "Pure" vasodilators such as nitroprusside also improve cardiac output by decreasing afterload (Gascho 1981). In support of a benificial effect of alcohol in cardiogenic shock, Shatney and co-workers demonstrated that it caused significant vasodilatation with improvements in blood pressure and cardiac output, in an experimental model of myocardial infarction. Furthermore, they showed that intra-arterial alcohol resulted in lower creatinine phosphokinase levels, which suggests that it limited infarct size (Shatney 1976). Other studies have also shown that alcohol enhances coronary blood flow (Ganz 1963; Gould 1971; Horton 1986; Talesnik 1980) although it is debatable whether distribution of perfusion is optimal (Friedman 1981). In addition, there is evidence that alcohol increases blood volume (Nicholson 1940) and haematocrit (Horton 1987; Klingman 1958; Zink 1988), which might explain why there was a tendancy towards lower transfusion requirements in intoxicated patients. Moreover, it is now accepted that expansion of intravascular volume has a positive effect on haemodynamics of tamponade (Cooley 1955; Cooper 1944; Gascho 1981).

Another mechanism whereby alcohol may improve the action of the tamponaded heart, is by suppressing respiration (Gettler 1963; Malt 1971). This was a feature of our study, where intoxicated patients with tamponade were less likely to present with associated "air-hunger". There may have been several reasons for this, including the sedative effect of alcohol (Textbook of Pharmacology 2nd ed, 1980), as well as decreased sensitivity of the respiratory centre to accumulating CO2, which occurs even with low

blood alcohol concentrations (Roegla 1995). Although respiratory suppression would normally prevent compensation for shock-associated metabolic acidosis, it could conceivably diminish competitive ventricular filling and the exaggerated phasic changes in ventricular dimension which give rise to a paradoxical pulse.

Clearly, many more patients would be required to show that alcohol actually improved the outcome of patients with cardiac tamponade. Taking mortality as the most important event, if the overall percentage of deaths in this study was maintained, then 387 patients would be needed in each group before the null hypothesis could be reliably accepted or rejected (alpha=0.05; beta=0.10) (Surgical Infections, 1987). However, to undertake a study of this magnitude would be impractical. Although we see approximately 100 patients each year with penetrating cardiac trauma, not all of these have cardiac tamponade alone. In our practice, it would also be a formidable task to recruit enough patients who were nonintoxicated and a multi-centre study would be out of the question. Failure to attain a level of statistical significance though, is not necessarily the "be all and end all" of research. Investigators and clinicians should be more concerned with being able to detect an important clinical difference, rather than placing all their trust in p-values (Freiman 1978). This study has at least shown that alcohol does not have a *negative* effect in patients with acute cardiac tamponade. To a certain extent, it also supports our view that intoxicated patients with cardiac tamponade who reach hospital alive, fare better than their sober counterparts.

8. THE EFFECT OF ALCOHOL INTOXICATION ON HAEMODYNAMIC PHYSIOLOGY IN A PORCINE MODEL OF ACUTE CARDIAC TAMPONADE

8.1 INTRODUCTION

Because alcohol intoxication had no significant effect on patients with traumatic cardiac tamponade, and recognizing the limitations of the clinical study, it was decided to investigate the actions of alcohol on acute cardiac tamponade in an animal model. Although previous experiments have dealt with haemodynamic physiology in cardiac tamponade, very few have examined the effects of alcohol on this condition. Fifty years ago, Denton Cooley and co-workers reported that alcohol exerted a harmful effect in dogs that underwent tamponade (Cooley 1953). However, in their study they used anaesthetic agents that may have affected cardiac performance and administered high doses of alcohol intravenously. Furthermore, pericardial catheterization was done via a thoracotomy and fixed volumes of saline were instilled to induce tamponade. These methods are far removed from the clinical situation.

Our aim was, to develop a more physiological animal model, so that we could evaluate the effect of alcohol on acute cardiac tamponade in a controlled setting. We also hoped that this would complement our clinical study.

8.2 MATERIALS AND METHODS

Our research proposal and methodology were accepted by the Animal Research Committee of the University of Cape Town: Project no 92\024, and all animals received humane care in accordance with South African Medical Research Council guidelines.

Twenty-two young Landrace swine weighing between 23 and 30 kg were randomly assigned to one of four groups:

1. Tamponade/alcohol group: seven pigs received 10ml/kg of 30% alcohol via a gastrostomy, before induction of acute cardiac tamponade by instillation of warmed plasmalyte-B into the pericardial sac.

2. Sham-operated/alcohol group: four pigs received 10ml/kg of 30% alcohol via a gastrostomy, but only underwent acute cardiac tamponade at the end of the experiment for euthanasia.

3. Tamponade/non-alcohol group: seven pigs received 10ml/kg of tap-water via a gastrostomy, before induction of acute cardiac tamponade by instillation of warmed plasmalyte-B into the pericardial sac.

4. Sham-operated/non-alcohol group: four pigs received 10ml/kg of tap-water via a gastrostomy, but only underwent acute cardiac tamponade at the end of the experiment for euthanasia.

Five additional pigs were used initially for development of the cardiac tamponade model and another three were excluded from analysis because of failure to reliably induce tamponade.

All animals were fasted for 24 hours, before being anaesthetized with pentobarbitol sodium (50mg/kg intravenously). They were then intubated with a standard No. 7 cuffed endotracheal tube (Portex Ltd, Hyde, England) and ventilation was commenced using a 70% Nitrous Oxide/Oxygen mixture at a rate of 6L/min through an Ohio anaesthetic ventilator (Airco Inc. Madison, Wisconson, USA) (tidal volume 300-400ml). After induction of anaesthesia, animals were paralyzed with Pancuronium (0.1mg/kg intravenously) and analgesia was provided by a bolus dose of Fentanyl (0.002mg/kg intravenously). Continuous electrocardiographic monitoring was by three standard electrodes connected to a Servomed SMK 154-3 monitor (Hellige GMBH, Freiburg im Brag, West Germany). A right-sided neck incision was made and the internal jugular vein was cannulated using an 8.5F percutaneous sheath introducer (Product no: SI-09800-E; Arrow International Inc. Pennsylvania, USA). Thereafter, paralysis and analgesia were maintained by continuous infusion of Pancuronium (0.32mg/kg/hour) and Fentanyl (0.01mg/kg/hour) respectively. Plasmalyte-B with 25ml 50% Dextrose added to each liter (1.25%) was administered to maintain hydration (10ml/kg/hour intravenously). The carotid artery was cannulated using a 6F infant feeding catheter which was connected to a transducer (1294.105; Hilhorst Instruments cc. RSA) and arterial pressure was recorded on the Servomed monitor. In addition, a flotation pulmonary artery catheter (Swan-Ganz 1.5ml CAP model; American Edwards 93A-131-7F; American Edwards Ltd, Santa Ana, CA) was introduced via the internal jugular vein and its position was confirmed by the characteristic change in trace on the monitor. Central venous pressure was measured manually and pulmonary artery pressure was recorded on the Servomed monitor. Cardiac output was calculated by an American Edwards COM-1 cardiac output computer using 5ml aliquots of iced saline; 3 measurements were taken for each point (at the end of the

respiratory cycle) and the mean was recorded. Body temperature was also monitored continuously and maintained at between 37 and 40^{o}C using a fan-heater.

Following the placement of arterial and central venous lines, animals were positioned supine and the abdomen was opened via a 15cm midline incision. A gastrostomy was constructed using an 18F Foley catheter which was fixed in position using a double purse-string technique. The supraduodenal portal structures were dissected out and a perivascular doppler flow probe (2R 1435; Transonic Systems Inc., Ithaca, NY) was placed around the hepatic artery for continuous monitoring of blood flow using a T201 two-channel ultrasonic blood flowmeter (Transonic Systems Inc., Ithaca, NY). (This instrument is pre-calibrated - only sensitivity needs to be adjusted) (Figs 8.1 - 8.4). The abdominal incision was then closed by an all-layer suture technique.

Finally, the broadest part of the sternum was exposed by a 6cm midline incision and using a no 22 craniotomy burr (Down, England), a hole was drilled through the sternum onto the thick fibrous parietal pericardium (Figs 8.5 and 8.6). This was opened to expose muscle attachments on the underside of the sternum as well as pericardial fat. These structures were gently swept aside and the true pericardial sac was identified (Fig 8.7). A small hole was made in the pericardial sac (Fig 8.8) and an 8F Foley catheter was sited in the pericardial space. The hole around the catheter was sealed using cyanoacrylate glue (Fig 8.9) and correct placement was confirmed by aspirating air that had entered the pericardial sac, followed by serous pericardial fluid (Fig 8.10). This maneouvre was always accompanied by transient cardiac arrhythmias. The pericardial catheter was then connected to a three-way water manometer system which was used for measurement of intra-pericardial pressure, as well as for induction

of acute cardiac tamponade. The degree of tamponade was pressure-regulated by raising or lowering a reservoir of warm plasmalyte-B (Figs 8.11 and 8.12). Changes in intra-pericardial pressure were accompanied by simultaneous changes of fluid volume in the reservoir, which were also measured. The zero level for pericardial and central venous pressure was taken as the point midway between the surface of the operating table and the highest part of the animal's sternum.

After the operative procedures and placement of catheters, 20 minutes was allowed for stabilization before taking baseline haemodynamic measurements and blood samples. Right atrial/central venous pressure (CVP), pulmonary artery pressure (PAP), pulmonary artery wedge pressure (PAWP) and mean systemic arterial/intra-aortic pressure (MAP), were measured. In addition, blood temperature, heart rate (HR), cardiac output (CO) and hepatic artery blood flow, were recorded. Stroke volume (SV), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) were determined indirectly using the following formulas:

$$SV\ (ml) = \frac{CO\ (L/min)}{HR} \times 1000$$

$$SVR\ (dyne \cdot sec \cdot cm^{-5}) = \frac{MAP\ (mmHg) - CVP\ (mmHg)}{CO\ (L/min)} \times 80$$

$$PVR\ (dyne \cdot sec \cdot cm^{-5}) = \frac{PAP\ (mmHg) - PCWP\ (mmHg)}{CO\ (L/min)} \times 80$$

Following measurements of haemodynamic parameters, blood samples were taken and the sampled volume was replaced with normal saline. Serum sodium and potassium levels were measured by ion selective electrode using a KNA-I Analyzer (Radiometer, Copenhagen); serum

glucose was determined by Glucostix (Glucometer II blood glucose meter, Miles Inc, Indiana, USA); arterial blood gases were measured using an AVL 993 Automatic Blood Gas Analyzer (Medizintechnik, Graz, Austria); and full blood count was by Coulter Counter (S^+2, Coulter Electronics, Miami, USA). Serum was also obtained and stored for later measurements of the following: lactate levels were determined using enzymatic assay (with lactate dehydrogenase and NAD); serum catecholamines were measured by High Pressure Liquid Chromatography with electrochemical detection (Waters system - Millipore, Massachusetts, USA); and alcohol levels were measured by Fluorescent Polarization Immuno-assay (GMBH Diagnostika, Wiesbaden-Delkenheim, W.Germany).

The animals then received 10ml/kg of tap-water or 30% ethyl alcohol via the gastrostomy. After one hour, the haemodynamic measurements and blood tests were repeated before induction of acute cardiac tamponade in the two tamponade groups. This was done by gradually elevating a reservoir of warmed plasmalyte-B to increase intrapericardial pressure. (This fluid was pre-heated in an incubator to 37^0C - ie. initial pericardial instillation was approximately at the animal's body temperature - thereafter, the fluid in the reservoir was subject to room temperature). Ten minutes was allowed between each increment of pressure for stabilization, before haemodynamic measurements were recorded. Blood tests were repeated after intrapericardial pressure had risen to 10cm of water, which was also the pressure at which decompensation occurred. This pressure was then kept constant for 1 hour, during which time haemodynamic measurements were made at 15 minute intervals. At the end of this period, blood samples were taken again. Intrapericardial pressure was then raised in increments of 2cm of water and haemodynamic changes were recorded after each increment until death of the animal. In the eight sham-operated animals, haemodynamic measurements were made and blood samples

were taken at the same time intervals as in the tamponade groups. These pigs were then sacrificed by acute high-pressure cardiac tamponade on completion of the experiment. Following death, all animals were subjected to a thoracotomy to ensure proper placement of the intrapericardial catheter and the volume of tamponade fluid was measured.

The four groups were compared with regard to haemodynamic parameters as well as biochemical and haematological results. For aortic blood pressure, heart rate, cardiac output, stroke volume, hepatic artery blood flow, systemic vascular resistance and pulmonary vascular resistance, results were calculated as a percentage of baseline values rather than giving absolute figures. This was a better reflection of haemodynamic trends as there were marked differences in absolute values between some animals. Because pulmonary artery pressure and wedge pressure results were skewed, geometric means were used for statistical analysis rather than true means. BMDP/Dynamic (Release 7, BMDP Statistical Software Inc. LA. California) Program 5V, for unbalanced repeated measures in models with unstructured covariance matrices, was used to compare haemodynamic trends in the tamponade/alcohol and tamponade/non-alcohol groups, and the sham-operated/alcohol and sham-operated/non-alcohol groups. The Wald statistic was used to check the significance of the effects of alcohol on haemodynamic parameters over time. All statistical testing was two-sided and the level of significance was set at 5%.

Biochemical and haematological data were analyzed using the Mann-Whitney test when comparing two groups, and the Kruskal-Wallis test when all four groups were compared (SPSS for Windows release 6.0).

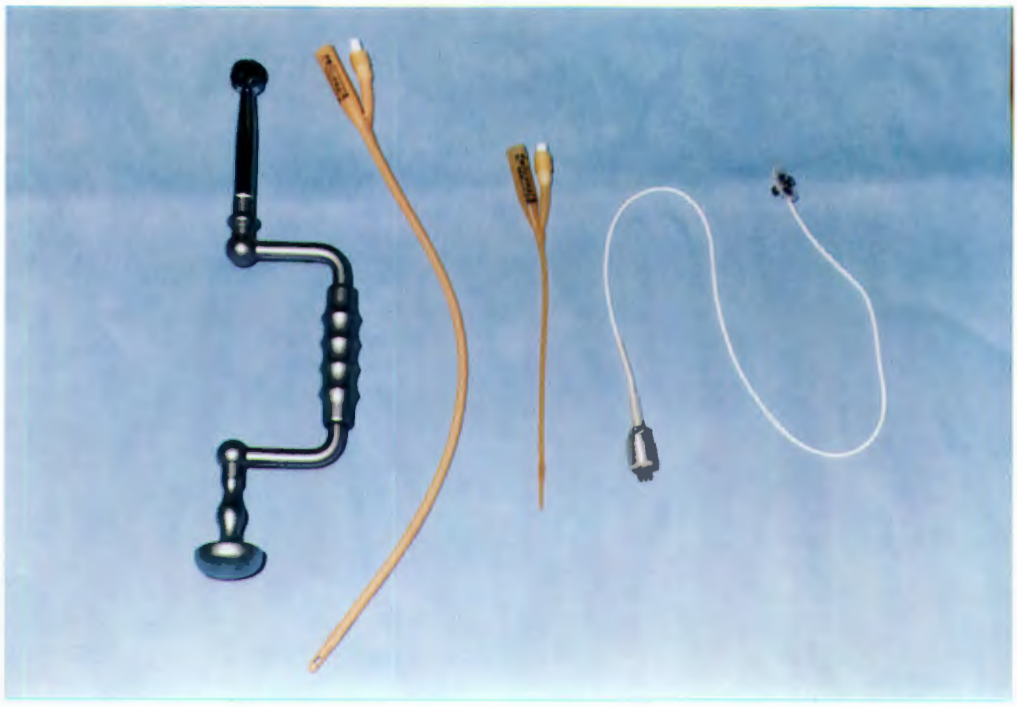


Figure 8.1: Equipment - (from left to right): no 22 craniotomy burr and brace (Down, England); 18F foley catheter; 8F foley catheter; perivascular doppler flow probe and lead (2R 1435, Transonic Systems Inc,Ithaca,N.Y.).

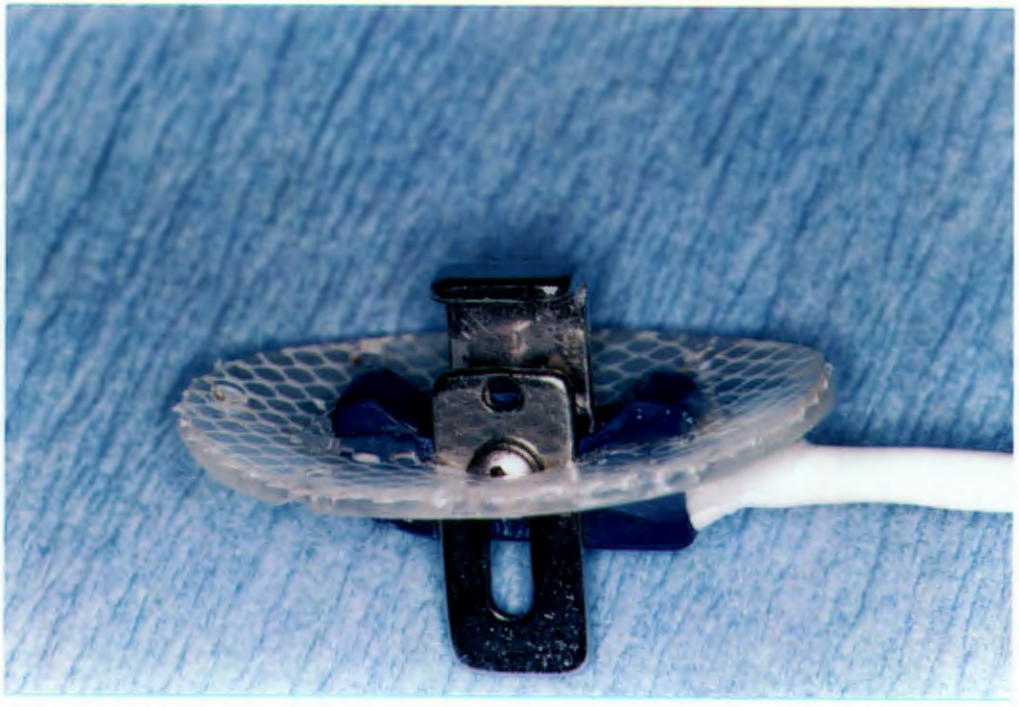


Figure 8.2: Perivascular doppler flow probe (2R 1435, Transonic Systems Inc, Ithaca, N.Y.).

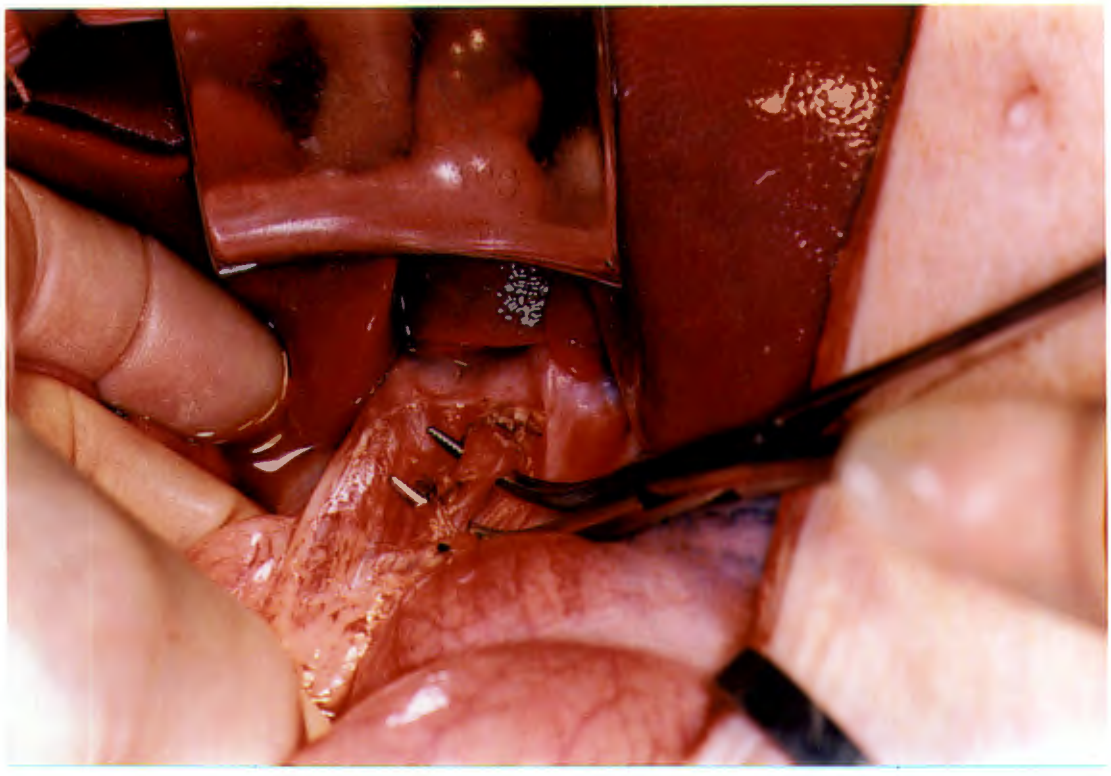


Figure 8.3: The supraduodenal portal structures are exposed and the hepatic artery is demonstrated.

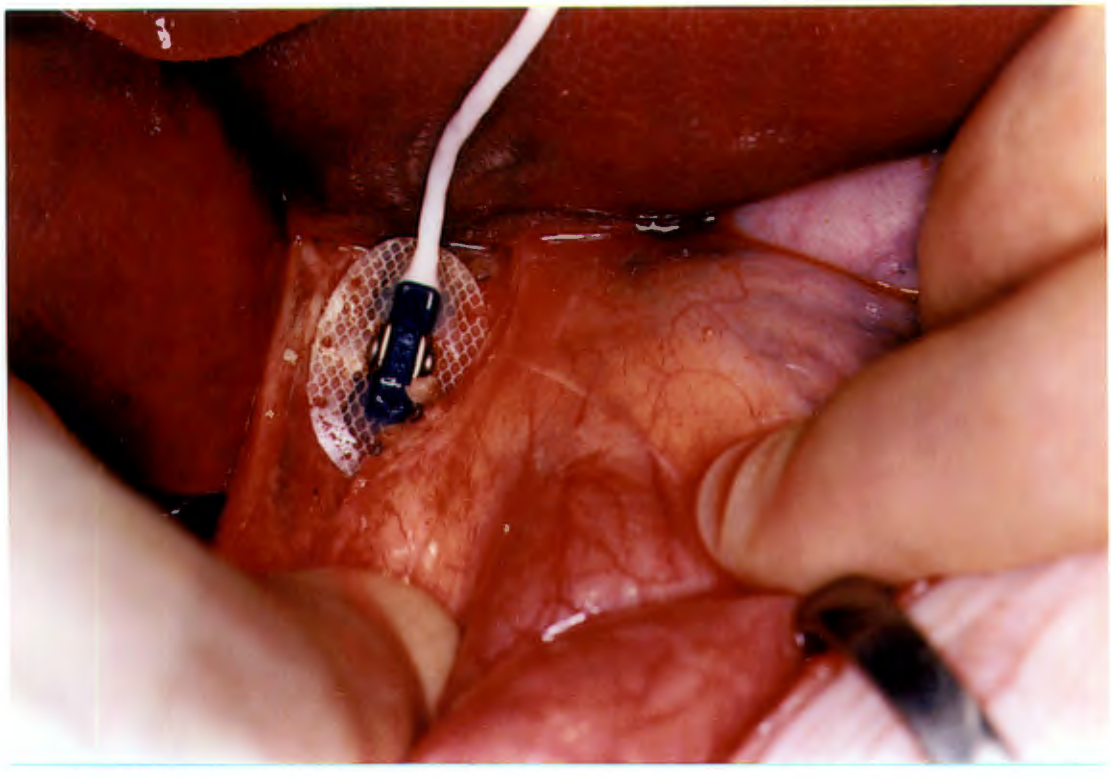


Figure 8.4: The perivascular doppler flow probe is placed around the hepatic artery for continuous monitoring of blood flow.

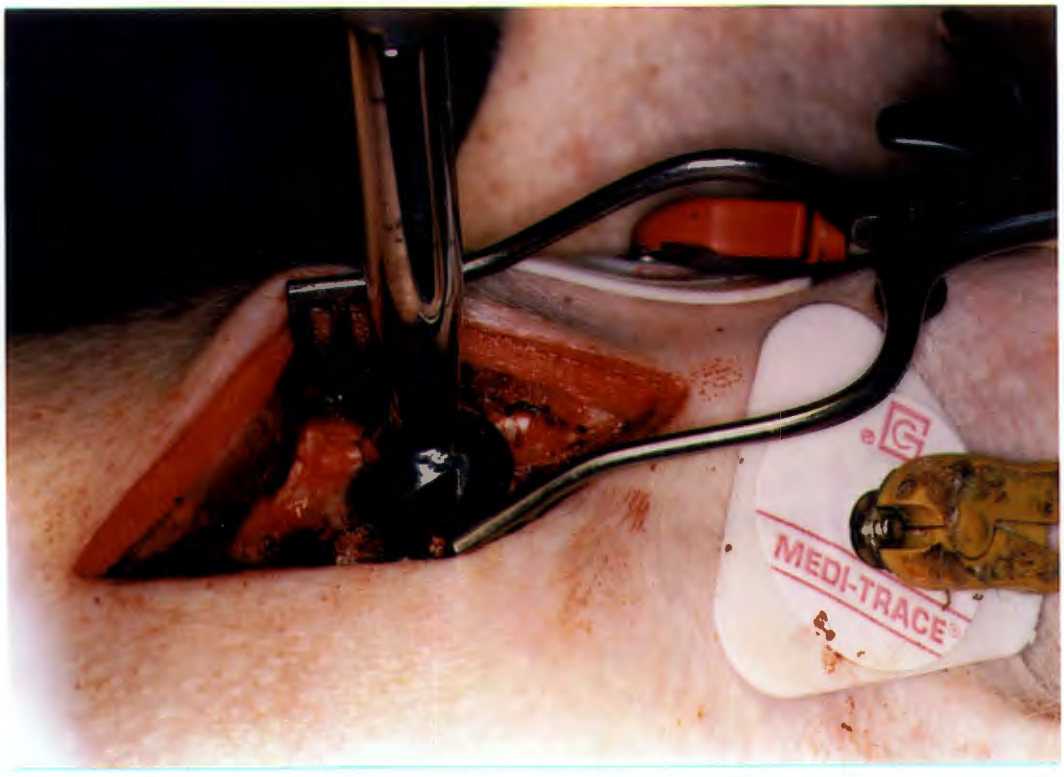


Figure 8.5: Broadest part of the sternum is exposed and a hole is drilled through the sternum to expose the thick fibrous parietal pericardium.

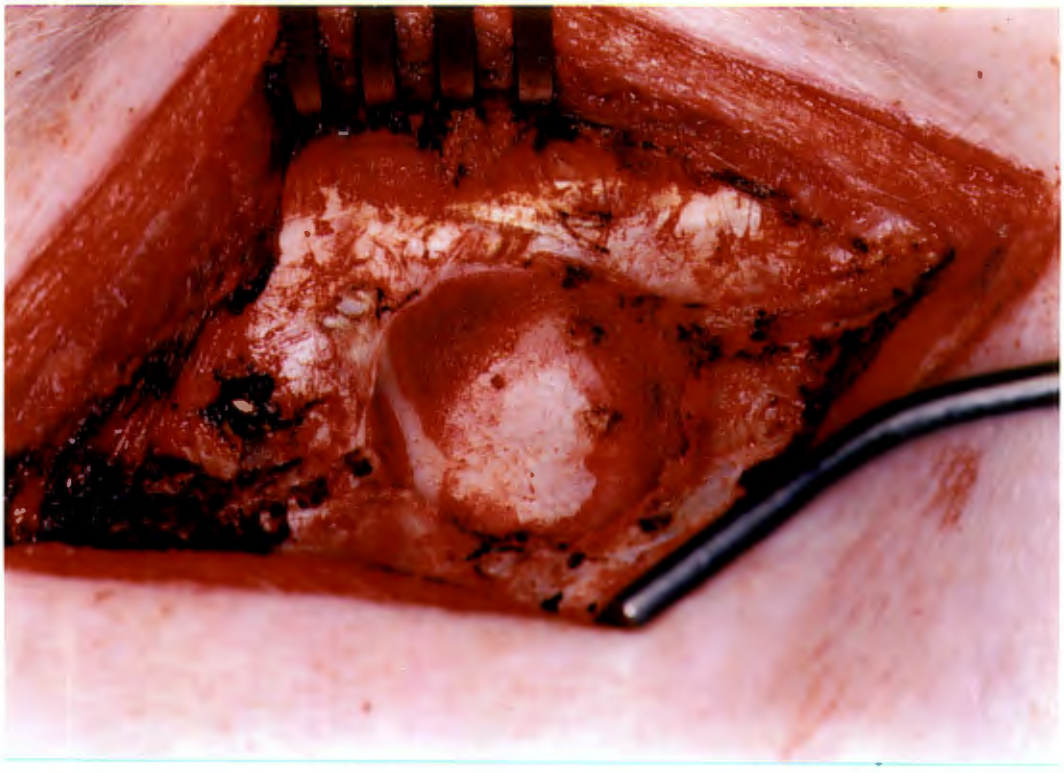


Figure 8.6: The thick fibrous parietal pericardium is demonstrated.

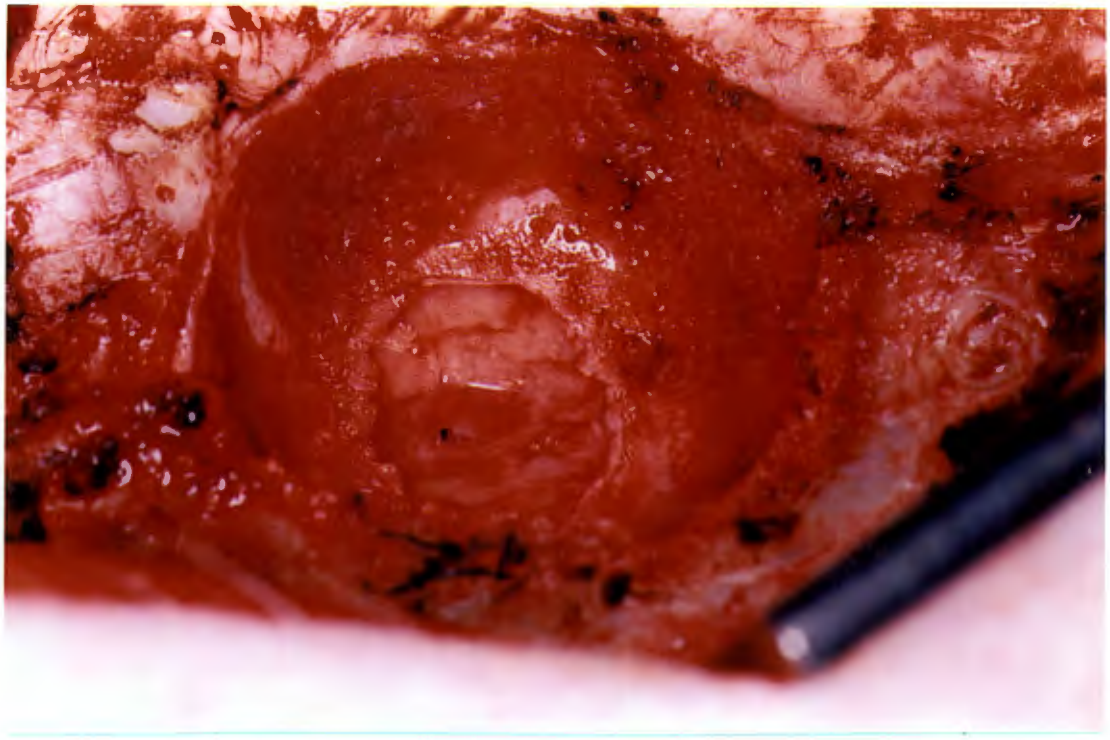


Figure 8.7: The fibrous parietal pericardium is incised, and underlying muscles and pericardial fat are swept aside to reveal the true pericardial sac.

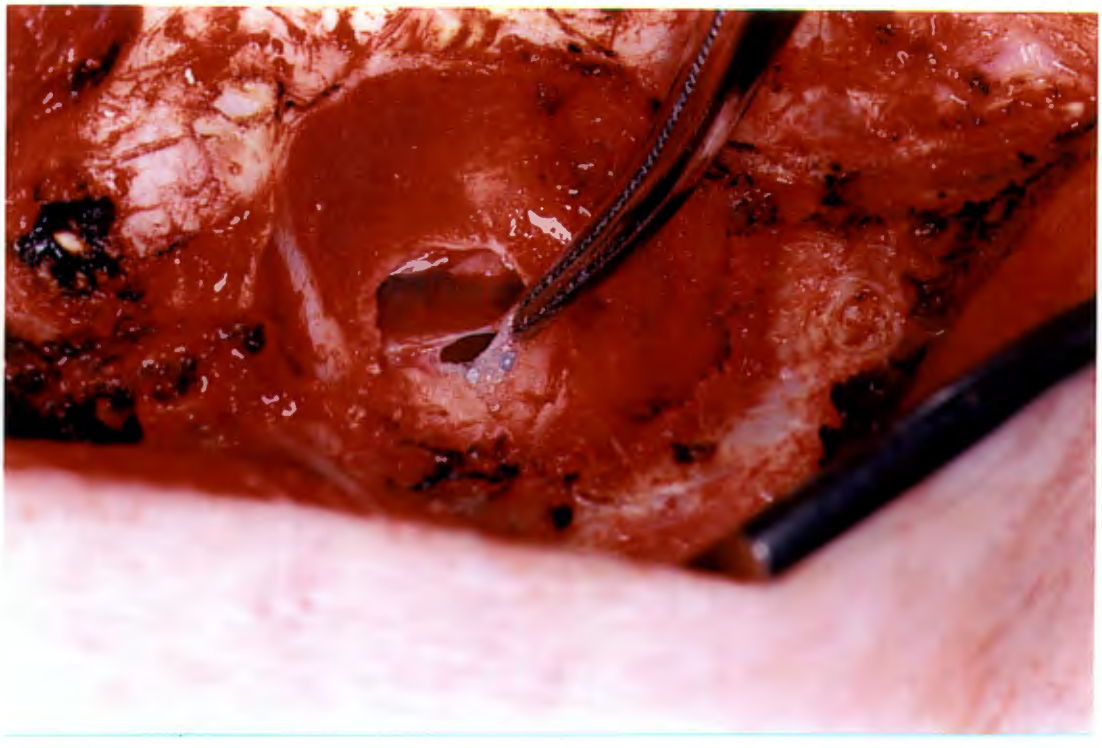


Figure 8.8: Pericardiotomy, with demonstration of the glistening visceral surface of the heart.

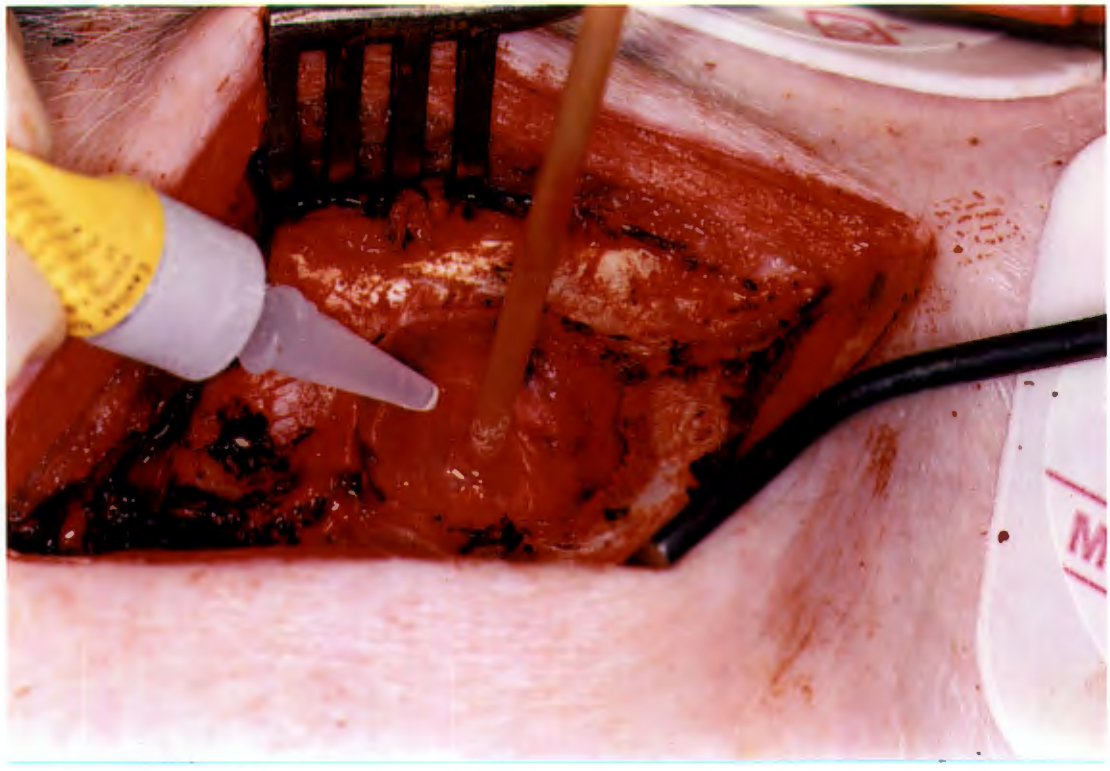


Figure 8.9: An 8F foley catheter is sited in the pericardial sac and the pericardiotomy is sealed using cyanoacrylate glue.

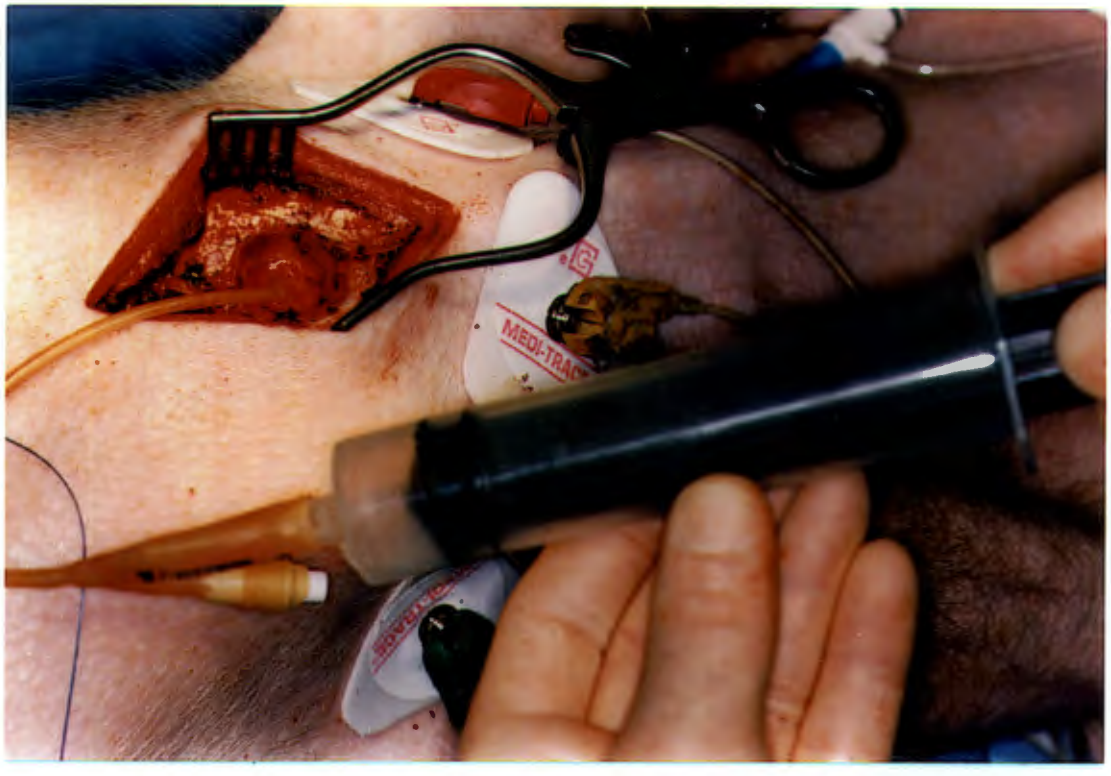
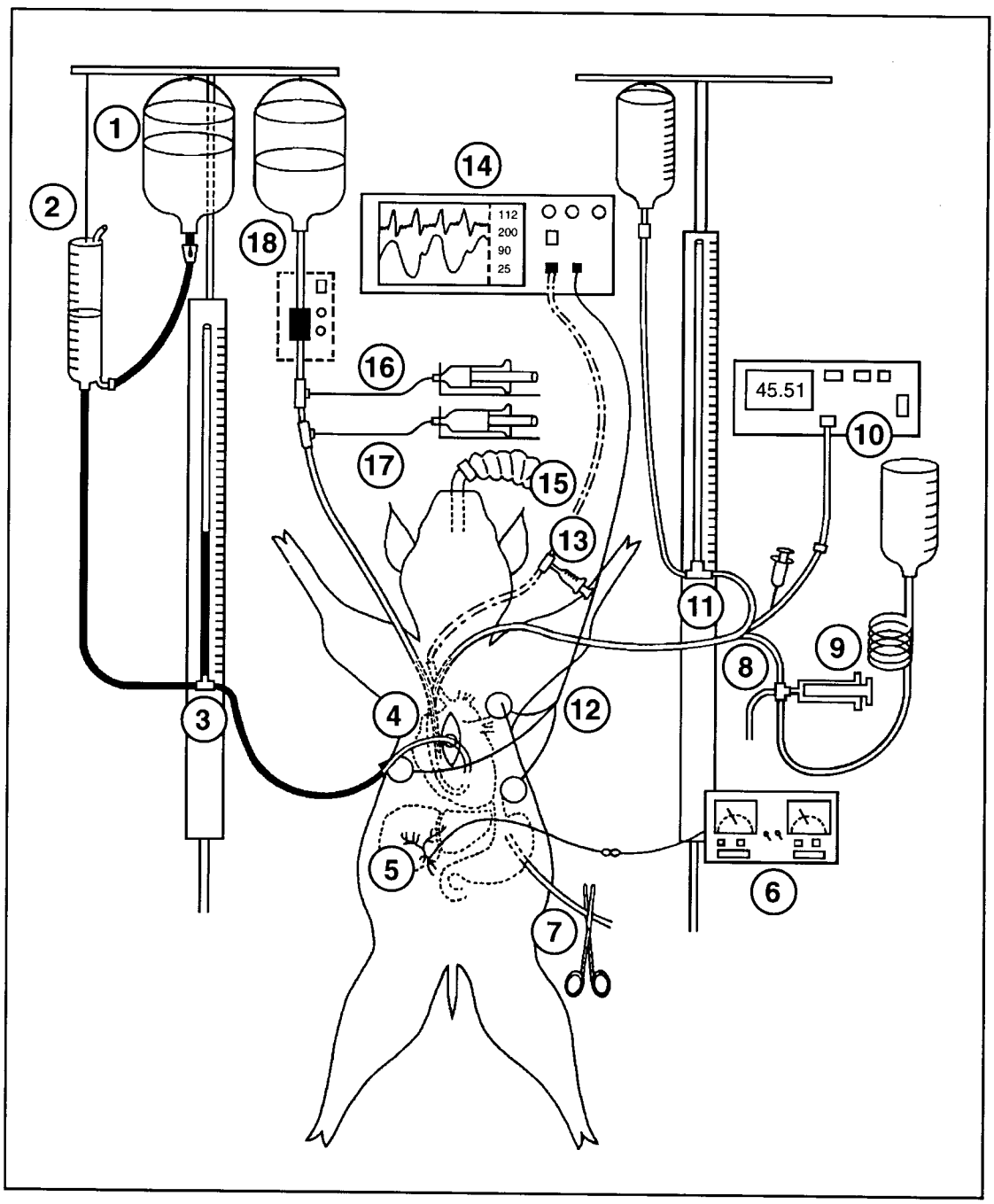


Figure 8.10: Correct placement of the pericardial catheter is confirmed by aspirating air and serous pericardial fluid.

Figure 8.11: The Tamponade Model: a diagramatic representation



Legends to Figure 8.11:

1. Warmed Plasmalyte-B.
2. Reservoir.
3. Three-way water manometer system.
4. Pericardial catheter (8F foley).
5. Perivascular doppler flow probe and lead (2R 1435; Transonic Systems inc.).
6. Two-channel ultrasonic blood flowmeter (T201; Transonic Systems inc.).
7. Gastrostomy tube (18F foley).
8. Flotation pulmonary artery catheter (Swan Ganz 1.5ml CAP; American Edwards 93A-131-7F).
9. Iced saline for measurement of cardiac output.
10. Cardiac output computer (American Edwards COM-1).
11. Central venous pressure system.
12. Three standard ECG leads connected to monitor.
13. Carotid artery catheter (shortened 6F infant feeding catheter) and transducer (1294. 105; Hilhorst Instruments inc.) connected to monitor.
14. Servomed monitor (SMK 154-3).
15. Endotracheal tube (no 7 Portex) with tubing attached to an Ohio anaesthetic ventilator.
16. Syringe-driver and 50cc syringe containing fentanyl for continuous infusion.
17. Syringe-driver and 50cc syringe containing pancuronium for continuous infusion.
18. Maintenance solution of Plasmalyte-B with 25ml 50% dextrose added, for continuous infusion via a rate-minder.

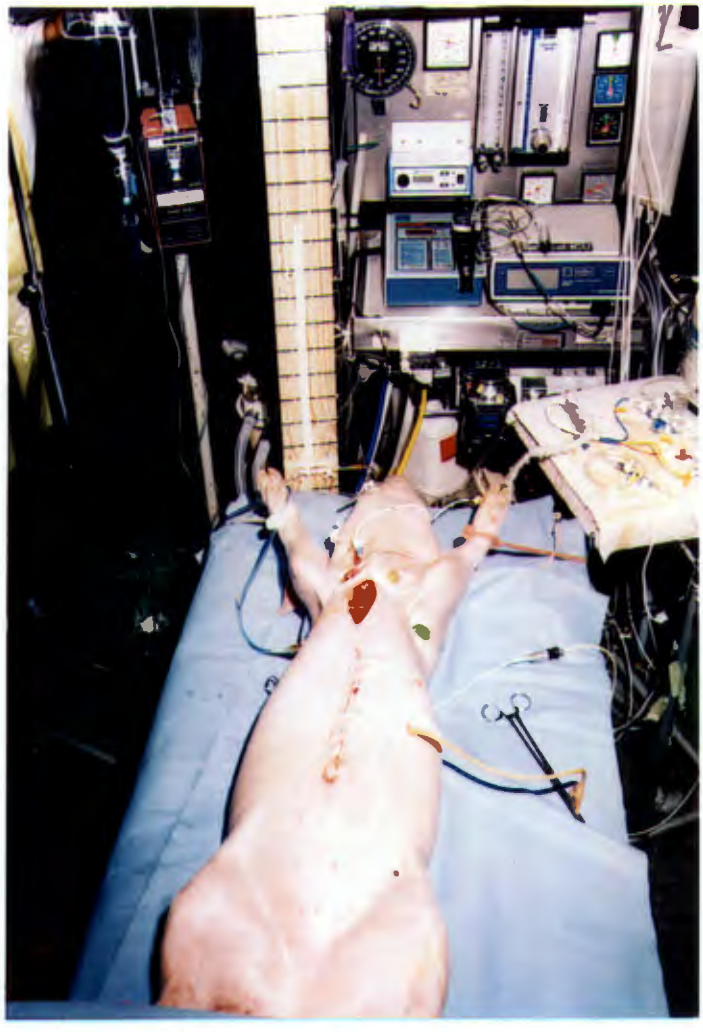


Figure 8.12: On completion of the operative procedures: the pig is supine and is being ventilated; 3 standard ECG leads are attached; the flotation pulmonary artery catheter can be seen exiting via a percutaneous sheath introducer in the right internal jugular vein (carotid arterial line is not well seen); the pericardial catheter is connected to a 3-way manometry system (reservoir of blue-stained plasmalyte-B is noted suspended from a drip-holder on the animal's right side); the perivascular doppler flow probe lead exits through the abdominal wound to connect with the ultrasonic blood flow-meter on the animal's left (out of picture); gastrostomy tube (clamped) exits through the abdominal wall on the left side; anaesthetic ventilator and cardiac output computer are noted in the background.

8.3 RESULTS

Biochemical and haematological results: The 30% alcohol solution which was administered to the tamponade/alcohol and sham-alcohol groups, resulted in similar serum levels, which increased progressively and were compatible with moderate to severe intoxication (range 75-312 mg/dl) (Table 8.1). When compared with the other three groups, serum lactate levels were significantly higher in the tamponade/alcohol group at one ($p=0.0063$) and two hours ($p=0.0284$), and when compared with the tamponade/non-alcohol group, at one ($p=0.035$), one-and-a-half ($p=0.047$) and two ($p=0.047$) hours (Table 8.2). However, this had no effect on pH, in fact all arterial blood measurements remained constant irrespective of whether the animals received alcohol or underwent tamponade (Tables 8.5a-e). Serum sodium and potassium levels were also unchanged over time (Table 8.6a,b), while there was a slight decrease in serum glucose in the tamponade/alcohol group (NS) (Table 8.6c). Unfortunately, some catecholamine levels could not be analyzed due to failure of cold-storage, although these samples would have had little effect on the results which were totally unpredictable with a wide range of values (Table 8.3). (Noradrenalin levels at 1.5 hours were higher in tamponade/non-alcohol and sham/non-alcohol groups; $p=0.028$ and 0.033 respectively).

Changes in the full blood count were limited to the leucocytes (Table 8.4b). These increased over time in both tamponade groups (tamponade/alcohol: $p=0.0269$; tamponade/non-alcohol: $p=0.0386$). Presumably this was due to an increase in the granulocyte fraction, as the % of lymphocytes decreased proportionally (tamponade/alcohol: $p=0.0336$; tamponade/non-alcohol: $p=0.0075$). Although similar trends were noted in the two sham-operated groups, these were not significant.

RESULTS OF SPECIAL INVESTIGATIONS

All values expressed as the median unless stated otherwise

TABLE 8.1. SERUM ALCOHOL: mmol/L
(range)
mg/dl
(range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
0.00 (0-2.0)	0.00 (0-0.4)	0.44 (0-1.9)	0.69 (0-2.1)
0.0 (0-9.0)	0.0 (0-1.7)	2.1 (0-8.6)	3.2 (0-9.0)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
26.28 (16.3-50.8)	0.00 (0-0.5)	42.20 (18.2-67.0)	0.71 (0-2.2)
121 (75-234)	0.0 (0-2.3)	195 (84-308)	3.3 (0-10.2)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
31.80 (27.6-61.9)	0.00 (0-0.4)	44.6 (26.4-59.7)	0.71 (0-1.9)
146 (127-285)	0.0 (0-2.0)	205 (121-275)	3.3 (0-8.6)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
37.01 (30.4-67.8)	0.00 (0-0.3)	48.70 (34.3-58.9)	0.88 (0-2.2)
168 (140-312)	0.0 (0-1.5)	224 (158-271)	4.1 (0-10.1)

TABLE 8.2. SERUM LACTATE: Median mmol/L
Mean mmol/L
(range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
2.80	1.05	0.55	0.43
2.30	1.70	0.54	0.67
(0.19-7.3)	(0.53-3.6)	(0.29-0.76)	(0.14-1.7)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
2.30	1.11	0.87	0.53
3.50	1.90	0.87	0.71
(1.54-6.4)	(0.69-3.4)	(0.31-1.42)	(0.4-1.36)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
2.11	1.04	1.25	0.59
3.60	1.50	1.36	0.99
(1.0-7.2)	(0.37-4.8)	(0.59-2.36)	(0.31-2.5)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
2.20	1.12	1.41	0.61
4.00	1.60	1.53	0.68
(1.44-7.3)	(0.25-4.2)	(0.70-1.87)	(0.11-1.4)

TABLE 8.3. SERUM CATECHOLAMINES (no of pigs/group)*

Noradrenalin: **pg/ml**
(range)
Adrenalin: **pg/ml**
(range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (5)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (3)**
113 (20-375)	175 (26-444)	194 (136-337)	278 (184-474)
183 (54-387)	200 (15-337)	138 (20-228)	78 (20-365)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (5)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (3)**
70 (20-1015)	350 (21-2181)	299 (116-1408)	239 (125-252)
43 (20-918)	20 (20-71)	48 (20-1128)	116 (20-331)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (5)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (3)**
132 (20-171)	222 (57-2433)	192 (102-249)	293 (250-3148)
100 (20-924)	74 (44-888)	42 (12-141)	107 (20-346)
2.5 HOURS			
TAMP/ALC (6)	**TAMP/NON-ALC (5)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (3)**
215 (15-556)	279 (14-4820)	200 (120-522)	236 (123-238)
123 (33-1300)	219 (28-1950)	49 (20-141)	169 (20-347)

* In some cases catecholamine levels were not calculated as serum was unsuitable due to failure of refrigeration

TABLE 8.4a. FULL BLOOD COUNT: **Haematocrit (%) (range) RBC (million/cu mm) (range)**

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
40.5 (37.1-45.3)	34.9 (32.0-44.8)	36.3 (30.5-44.4)	37.1 (33.3-40.1)
7.18 (6.38-7.85)	6.20 (5.55-7.74)	6.50 (5.50-7.89)	6.55 (5.98-7.29)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
43.1 (39.0-50.0)	37.9 (32.7-46.8)	37.2 (34.1-46.0)	37.1 (33.1-42.1)
7.68 (7.25-8.39)	6.70 (5.66-8.05)	6.60 (6.22-8.07)	6.55 (5.94-7.52)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
43.2 (37.8-51.4)	37.8 (32.0-48.8)	37.1 (32.9-45.9)	37.4 (31.7-41.7)
7.70 (7.12-8.66)	6.69 (5.62-8.21)	6.60 (6.08-8.08)	6.54 (5.69-7.54)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
42.8 (37.2-49.0)	37.7 (31.6-47.7)	38.2 (35.5-45.4)	37.2 (32.0-41.3)
7.61 (7.02-8.39)	6.49 (5.57-8.18)	6.77 (6.39-8.07)	6.59 (5.77-7.53)

TABLE 8.4b. FULL BLOOD COUNT: **WBC (thousand/cu mm) (range)**
% Lymphocytes (%) (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
23.7 (14.7-31.2)	13.2 (10.4-19.3)	28.9 (18.8-39.1)	23.5 (9.70-45.3)
36.7 (22.7-63.3)	56.8 (30.5-60.4)	34.9 (17.0-39.2)	27.7 (17.3-46.6)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
35.5 (26.6-39.0)	24.4 (11.1-29.8)	41.1 (28.3-52.0)	39.1 (16.1-53.3
23.3 (14.3-38.5)	32.2 (16.0-51.2)	18.9 (9.6-27.3)	14.4 (9.1-18.2)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
37.8 (24.2-49.0)	25.4 (12.4-37.0)	41.8 (26.4-53.7)	36.9 (16.2-53.2)
19.5 (12.1-26.9)	20.7 (12.6-44.2)	16.6 (7.8-20.8)	12.3 (7.8-18.6)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
43.1 (22.6-51.0)	26.9 (14.7-38.4)	38.0 (23.9-48.4)	36.4 (19.9-52.3)
18.1 (10.0-23.3)	18.2 (11.5-36.7)	15.7 (8.7-20.1)	11.0 (7.4-16.7)

TABLE 8.4c. FULL BLOOD COUNT: Platelets (thousand/cu mm) (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
483 (339-722)	479 (418-989)	512 (220-526)	469 (367-553)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
506 (343-760)	478 (403-1077)	545 (409-608)	495 (369-573)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
477 (341-765)	465 (355-1083)	547 (439-578)	493 (398-541)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
478 (347-786)	454 (393-1276)	591 (513-614)	507 (406-576)

TABLE 8.5a. ARTERIAL BLOOD pH: **Units (range)**

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
7.44 (7.28-7.49)	7.42 (7.31-7.51)	7.47 (7.41-7.48)	7.39 (7.33-7.49)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
7.43 (7.41-7.47)	7.43 (7.31-7.53)	7.42 (7.31-7.47)	7.44 (7.40-7.49)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
7.40 (7.36-7.48)	7.41 (7.36-7.52)	7.42 (7.32-7.47)	7.43 (7.40-7.48)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
7.37 (7.28-7.44)	7.38 (7.32-7.47)	7.43 (7.37-7.45)	7.40 (7.37-7.49)

TABLE 8.5b. ARTERIAL BLOOD pCO_2: mmHg (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
45 (35-65)	45 (34-59)	39 (37-45)	47 (38-50)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
41 (32-51)	44 (34-60)	43 (33-52)	43 (36-49)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
44 (30-51)	39 (33-48)	40 (34-48)	42 (38-49)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
52 (31-56)	42 (37-51)	41 (34-45)	46 (37-51)

TABLE 8.5c. ARTERIAL BLOOD pO_2: mmHg (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
102 (79-149)	97 (90-185)	108 (101-113)	116 (81-149)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
96 (92-148)	103 (94-181)	100 (96-109)	106 (89-165)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
92 (77-151)	99 (92-202)	106 (100-119)	106 (83-158)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
89 (67-151)	92 (89-200)	103 (98-106)	106 (83-158)

TABLE 8.5d. ARTERIAL BLOOD BASE EXCESS: mmHg (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
+4 (+3-+6)	+4 (+2-+7)	+4 (+3-+5)	+4 (+3-+5)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
+2 (+1-+3)	+4 (+2-+7)	+2 (0-+4)	+5 (+4-+5)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
+1 (0-+5)	+3 (0-+6)	+1 (-1-+2)	+4 (+3-+5)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
+1 (-2-+5)	+2 (-4-+6)	+2 (+1-+3)	+5 (+2-+5)

TABLE 8.5e. ARTERIAL BLOOD HCO_3^-: mmol/L (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
29 (26-31)	28 (26-33)	27 (27-28)	29 (27-30)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
26 (23-28)	28 (25-30)	26 (23-28)	29 (26-29)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
26 (21-30)	26 (23-29)	25 (24-25)	28 (26-29)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
25 (20-32)	25 (20-30)	25 (24-27)	29 (27-29)

TABLE 8.6a. SERUM POTASSIUM: mmol/L (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
3.8 (3.1-5.7)	3.4 (3.1-3.7)	3.7 (3.3-3.8)	3.7 (3.4-3.7)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
3.7 (3.1-5.4)	3.5 (3.0-4.5)	3.8 (3.6-4.4)	3.5 (3.5-3.7)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
3.9 (3.6-5.9)	3.9 (3.1-3.9)	3.9 (3.5-4.9)	3.6 (3.3-3.9)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
4.7 (3.5-5.3)	3.7 (3.5-4.3)	4.2 (4.0-5.5)	3.8 (3.7-3.9)

TABLE 8.6b. SERUM SODIUM: mmol/L (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
135 (130-153)	132 (129-138)	135 (132-136)	131 (128-139)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
134 (128-154)	133 (129-136)	134 (130-137)	134 (130-135)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
133 (128-135)	133 (129-136)	133 (132-134)	131 (128-134)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
132 (130-133)	133 (129-135)	132 (129-137)	135 (134-137)

TABLE 8.6c. SERUM GLUCOSE: mmol/L (range)

BASELINE			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
6.8 (5.0-13.5)	6.8 (5.5-9.9)	5.7 (4.8-7.8)	6.9 (5.8-7.6)
1 HOUR			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
5.7 (4.4-6.6)	6.6 (4.6-8.1)	6.8 (6.5-7.7)	6.7 (6.0-7.1)
1.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
5.9 (3.0-7.2)	7.0 (4.3-8.3)	7.4 (6.1-8.0)	6.3 (5.8-6.8)
2.5 HOURS			
TAMP/ALC (7)	**TAMP/NON-ALC (7)**	**SHAM/ALC (4)**	**SHAM/NON-ALC (4)**
4.8 (2.4-9.3)	7.1 (3.8-8.4)	6.7 (6.2-7.3)	6.5 (5.1-6.5)

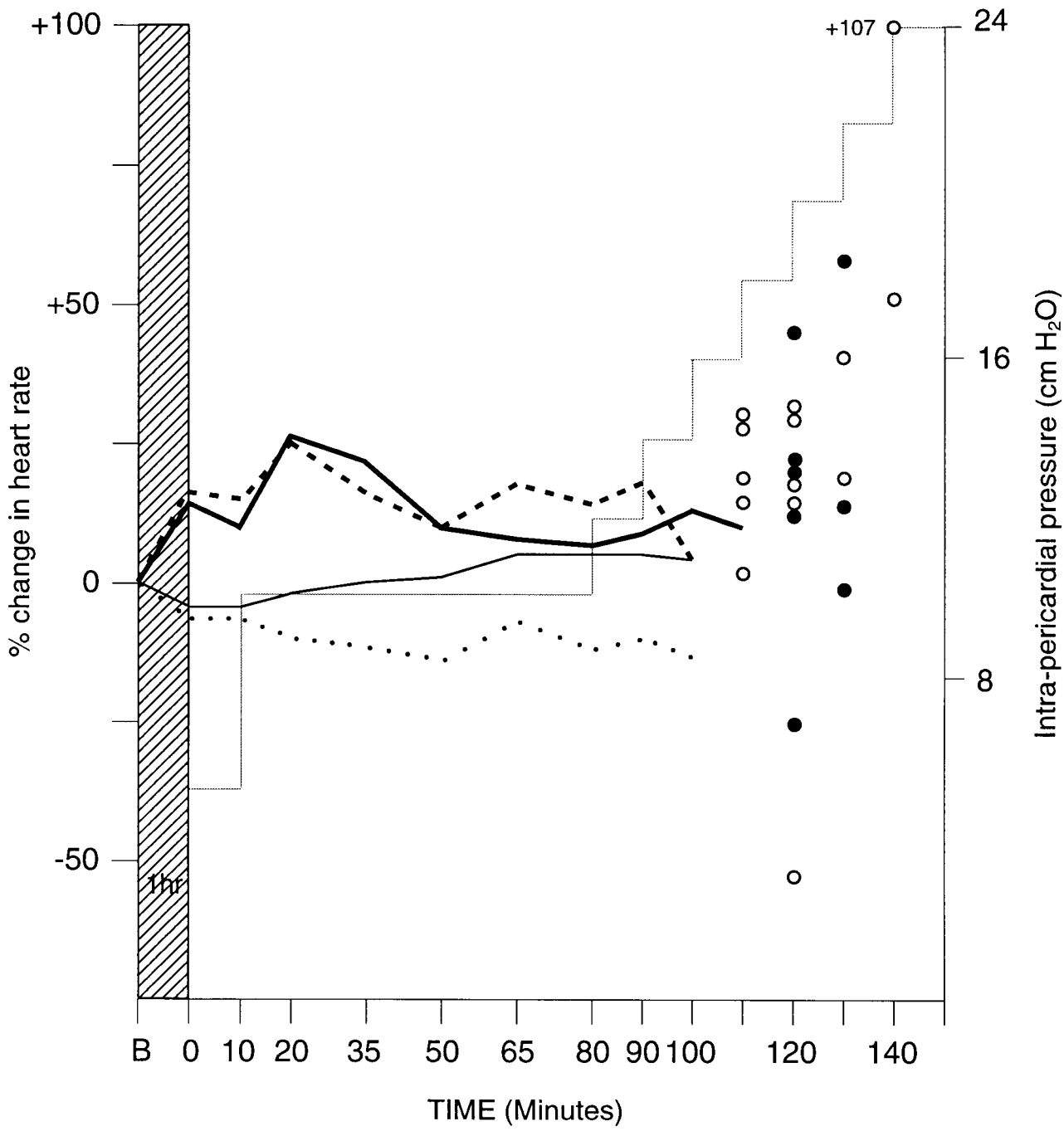
Haemodynamic results: Fourteen pigs were successfully subjected to acute cardiac tamponade. Three animals were excluded from analysis because of failure to successfully induce "pure" tamponade. All these technical failures occurred early in the study. In one pig, the pericardial catheter was placed in the mediastinum rather than in the pericardial sac, while inadvertent creation of pneumothorax in another animal resulted in accentuation of haemodynamic instability and an earlier demise. A third pig had incidental pericarditis, with obliteration of the pericardial space which prevented catheter insertion.

Initially, relatively large volumes of fluid were required to affect changes in intra-pericardial pressure, whereas later in the experiment, small volumes caused dramatic increases. Cardiovascular decompensation, which was defined as a decrease in cardiac output to 70% of baseline values, occurred in all tamponaded animals at an intra-pericardial pressure of 10cm of water (Figs 8.13-22). When the pressure was maintained at this level for one hour, some recovery of haemodynamic function occurred. Thereafter, with increasing increments of intra-pericardial pressure, haemodynamic parameters deteriorated proportionately until death of the animal. Heart rate increased ($p=0.0193$:linear; $p=0.0004$:linear, 0.0025:quadratic) to compensate for decreasing blood pressure ($p=0.012$:quadratic; $p=0.0045$:quadratic) and cardiac output ($p=0.0159$:quadratic; $p=0.0078$:quadratic) in the tamponade/alcohol and tamponade/non-alcohol groups respectively (Figs 8.13, 8.14 and 8.18). Initial decrease in hepatic artery blood flow (Fig 8.20) appeared to be the most sensitive indicator of cardiac compromise, although this trend was not maintained ($p>0.05$ both groups). Central venous pressure remained unchanged initially, but was an accurate reflection of intra-pericardial pressure once decompensation had occurred (Fig 8.15). Pulmonary artery wedge pressure also increased with increasing tamponade (the trend was

only significant in the tamponade/non-alcohol group - p=0.0059:linear, p=0.0007:quadratic) (Fig 8.17), while pulmonary artery pressure was relatively constant throughout (p>0.35 - both groups) (Although Fig 8.16 suggests otherwise, in the presence of such a wide range of values and skewed data, medians may not show the true trend. In addition, the zero on the y-axis is suppressed and the scale is inflated, so that a false impression of increasing pulmonary artery pressure is given. Fig 8.16a depicting the geometric mean is probably a more accurate reflection of the trend).

When comparing the two sham operated groups, pulmonary artery wedge pressure increased in those animals that had *not* received alcohol (p=0.0052:linear) (figs 8.17 and 8.17a). Other haemodynamic parameters were similar (figs 8.13-8.16 and 8.18-8.22). Cardiac output was lower in both groups at one hour, but was maintained thereafter. In the animals that underwent tamponade, alcohol resulted in significantly lower aortic pressures (p<0.0001:linear, p=0.0003:quadratic). This may have been a function of the lower systemic vascular resistance in the tamponade/alcohol group (p<0.0001:linear). Furthermore, pulmonary artery wedge pressures were lower in animals that received alcohol, which is a reflection of these haemodynamic trends (p=0.0177:quadratic). Vasodilatatory effects were also not confined to the systemic circulation - alcohol decreased pulmonary vascular resistance as well (p=0.0179:linear, p=0.0057:quadratic). Interestingly, tachycardia was more pronounced in the tamponade/non-alcohol group (p=0.0296:linear, p=0.0152:quadratic). Other haemodynamic parameters were not affected by alcohol. The volumes of intra-pericardial fluid at the end of each experiment were also similar in the two groups (tamponade/alcohol:- mean 230ml; tamponade/non-alcohol - mean 232ml).

Figure 8.13 : Heart Rate

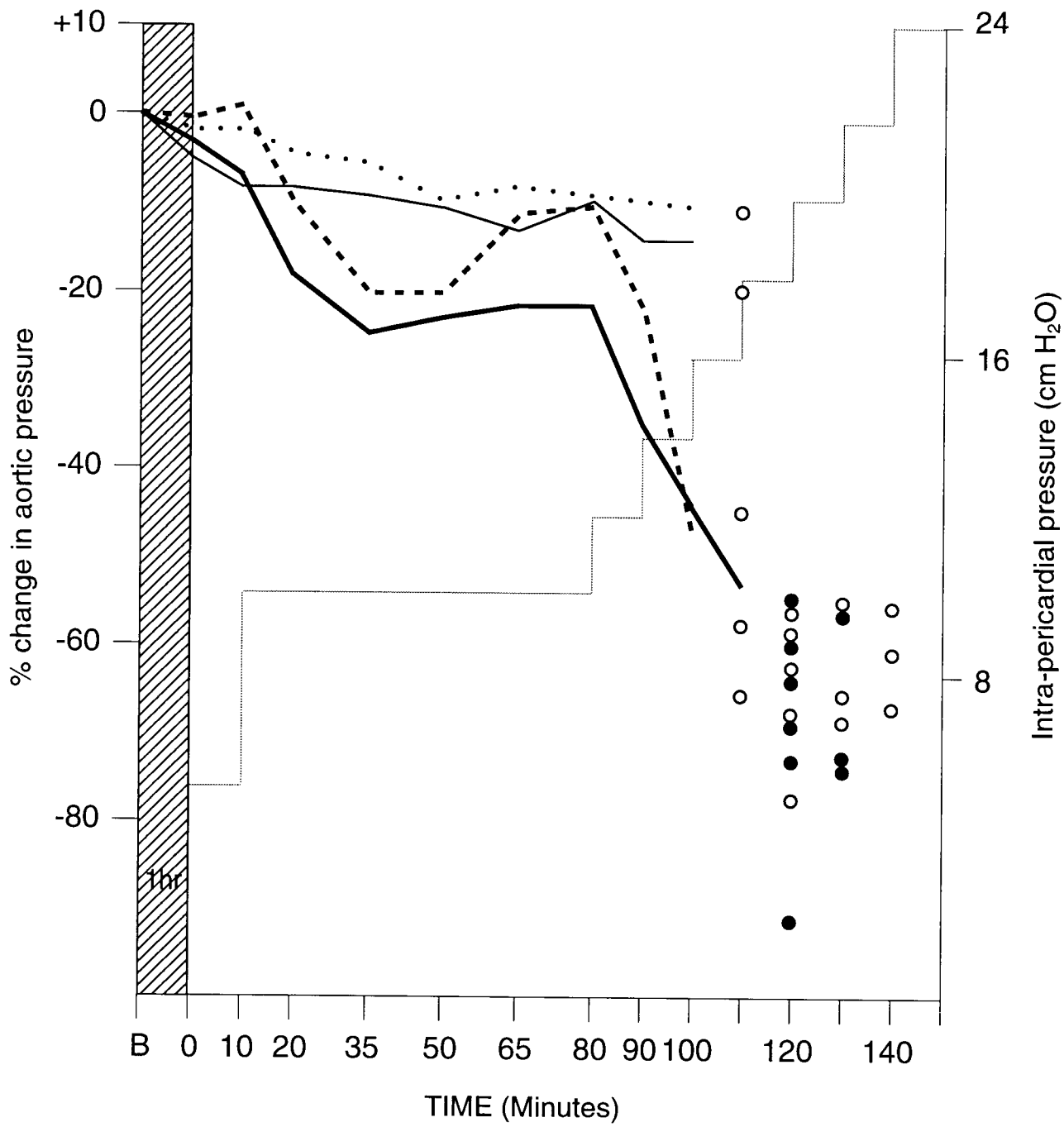


Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE HEART RATE

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	100	114	110	126	122	110	108	107	109	113	110
Median	100	112	111	128	123	106	106	102	99	104	111
Standard deviation		*14.7*	*13.4*	*17.9*	*35.2*	*28.5*	*34.5*	*34.9*	*36.1*	*35.4*	*19.2*
TAMP/NON-ALC											
Mean	100	116	115	125	116	110	117	114	118	104	
Median	100	116	115	122	123	121	119	113	118	120	
Standard deviation		*12.9*	*11.8*	*12.7*	*19.1*	*22.3*	*17.9*	*16.4*	*17.7*	*25.9*	
SHAM/ALC											
Mean	100	96	96	98	100	101	105	105	105	104	
Median	100	93	92	97	99	100	105	101	100	99	
Standard deviation		*14.5*	*13.4*	*13.4*	*16.1*	*17.2*	*19.6*	*16.9*	*18.5*	*18.8*	
SHAM/NON-ALC											
Mean	100	94	94	90	88	86	93	88	90	87	
Median	100	95	94	88	87	85	87	83	90	87	
Standard deviation		*6.4*	*9.4*	*10.1*	*8.9*	*7.3*	*20.1*	*15.6*	*17.4*	*13.9*	

Figure 8.14 : Aortic Pressure

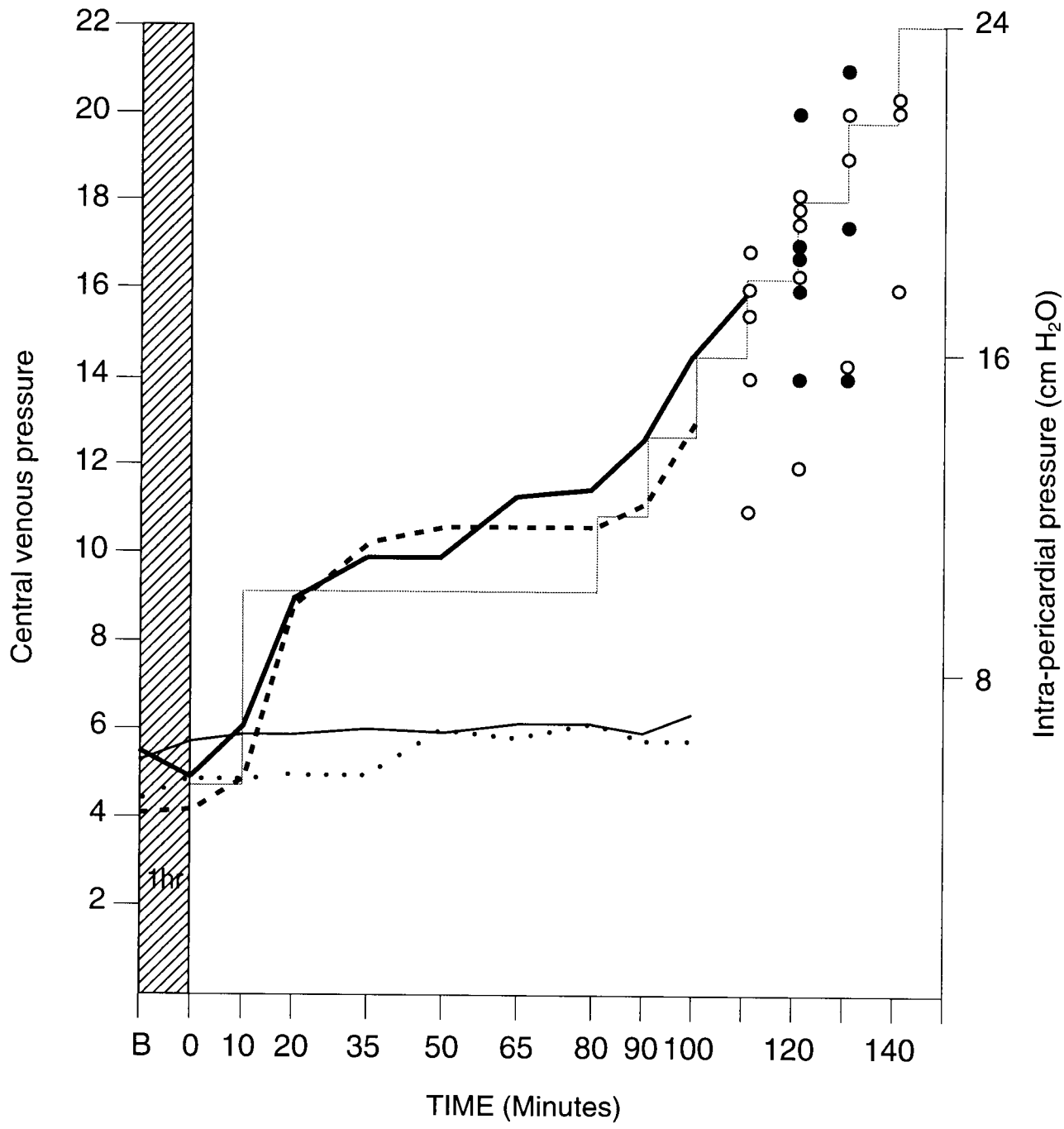


Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE AORTIC PRESSURE

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	100	97	93	82	75	77	78	78	65	56	47
Median	100	95	92	85	70	75	75	77	65	50	41
Standard deviation		*11*	*11.3*	*14.6*	*19.7*	*14.7*	*10.8*	*10.1*	*18.8*	*17.8*	*25.6*
TAMP/NON-ALC											
Mean	100	99	101	90	80	80	88	89	78	53	
Median	100	97	100	95	86	88	90	88	80	57	
Standard deviation		*8.9*	*8*	*16.1*	*21.9*	*29*	*15.3*	*13.2*	*18*	*23.9*	
SHAM/ALC											
Mean	100	95	92	92	91	89	87	90	86	86	
Median	100	96	95	95	93	89	88	90	87	86	
Standard deviation		*6.8*	*8.8*	*8.8*	*9*	*8.8*	*7.5*	*9.8*	*10.3*	*10.3*	
SHAM/NON-ALC											
Mean	100	98	98	96	94	90	92	91	90	89	
Median	100	99	99	96	96	91	95	95	91	89	
Standard deviation		*7*	*7.3*	*9*	*8.5*	*12.3*	*11.3*	*12.6*	*12.7*	*12.1*	

Figure 8.15 : Central Venous Pressure

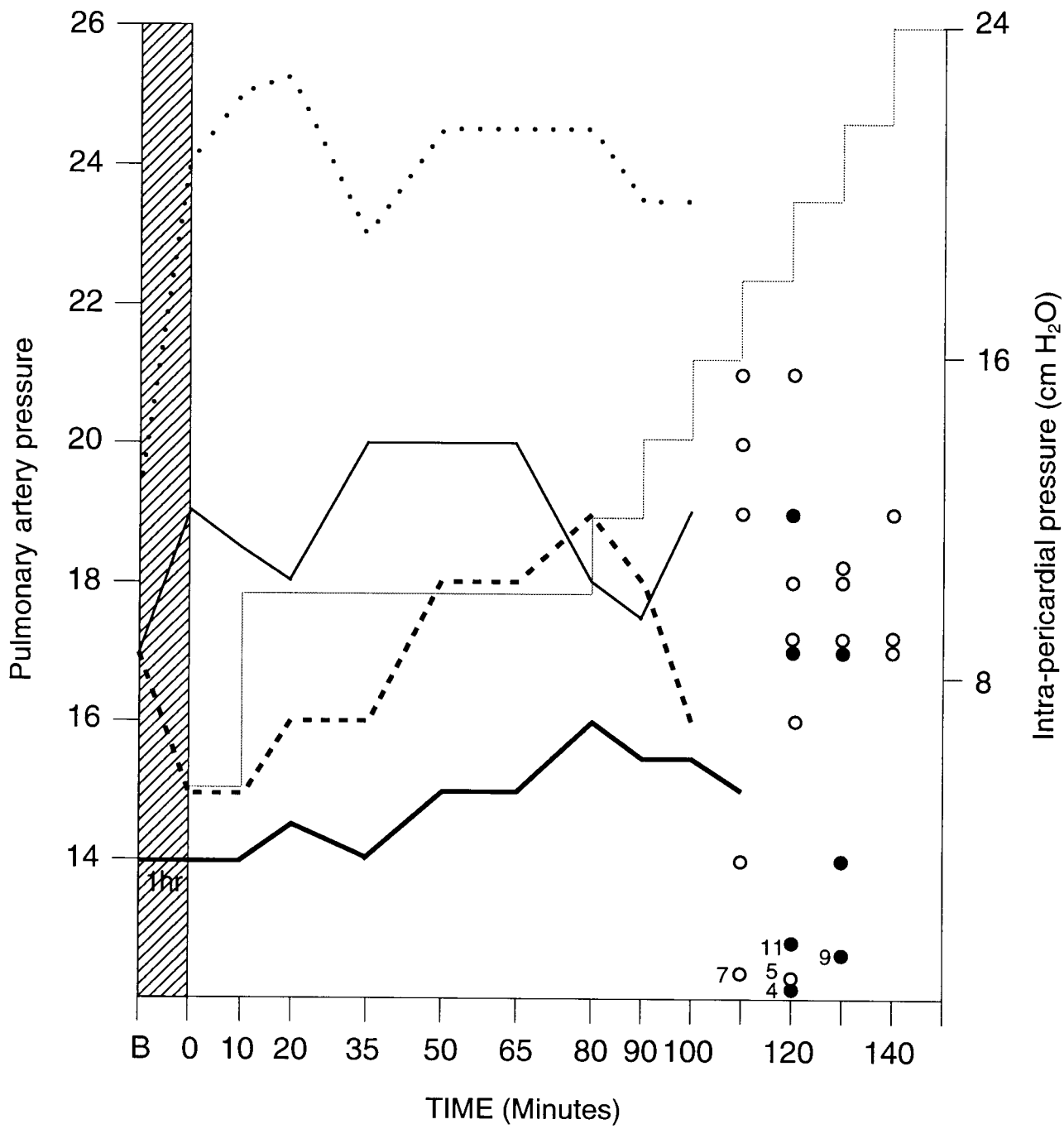


Lines join mean values for groups. Scattergram denotes only survivors.

CENTRAL VENOUS PRESSURE

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	5.6	4.9	6	9	9.9	9.9	11.3	11.4	12.6	14.6	15.8
Median	5	4.5	5	9.5	10.5	11	11	11.5	12.5	15	16
Standard deviation	*2.98*	*1.97*	*2*	*2.74*	*2.67*	*2.59*	*0.99*	*1.13*	*0.8*	*1.1*	*1.07*
TAMP/NON-ALC											
Mean	4.1	4.2	4.9	8.7	10.2	10.5	10.5	10.5	11.1	13	
Median	5	4	5	8	10.5	11	11	11	11.5	13.5	
Standard deviation	*1.93*	*1.41*	*1.18*	*1.38*	*0.95*	*1.15*	*0.87*	*0.91*	*1.38*	*1.61*	
SHAM/ALC											
Mean	5.3	5.8	5.9	5.9	6	5.9	6.1	6.1	5.9	6.4	
Median	4.8	5.8	5.8	5.8	5.8	5.8	6.5	6.3	6.3	6.8	
Standard deviation	*1.19*	*1.19*	*1.75*	*1.75*	*1.58*	*1.03*	*1.18*	*1.75*	*1.31*	*0.95*	
SHAM/NON-ALC											
Mean	4.4	4.9	4.9	5	5	6	5.8	6.1	5.8	5.8	
Median	5	4.5	4.5	4.8	5	6.3	5.5	6.3	6	6	
Standard deviation	*2.36*	*1.18*	*1.18*	*1.08*	*0.87*	*1.08*	*0.96*	*0.85*	*0.5*	*0.5*	

Figure 8.16 : Pulmonary Artery Pressure



· · · · Sham non-alcohol (n = 4)

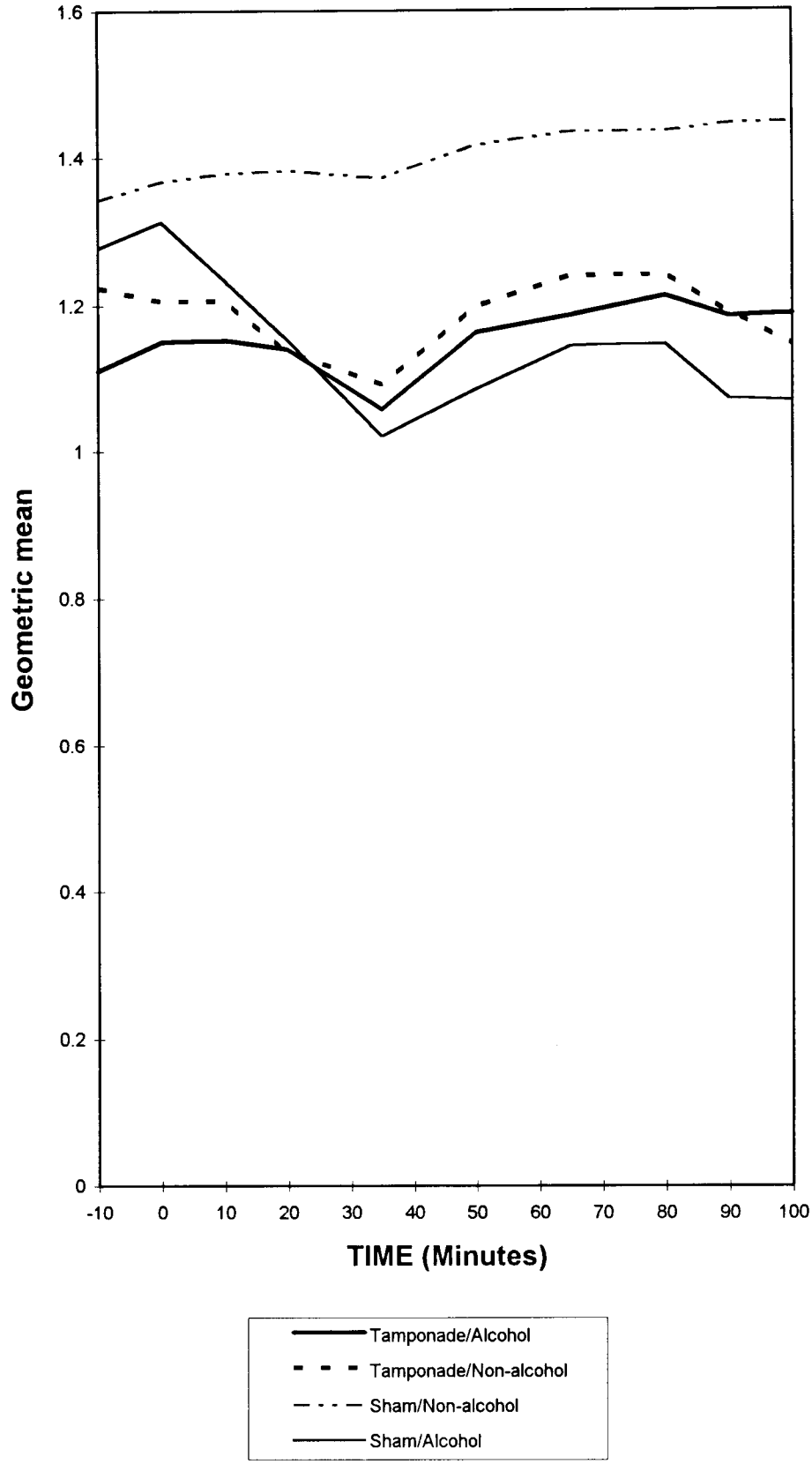
o - - - - Tamponade non-alcohol (n = 7)

——— Sham alcohol (n = 4)

● ——— Tamponade alcohol (n = 7)

Lines join median values for groups. Scattergram denotes only survivors.

Figure 8.16a: Pulmonary Artery Pressure (Geometric Mean)



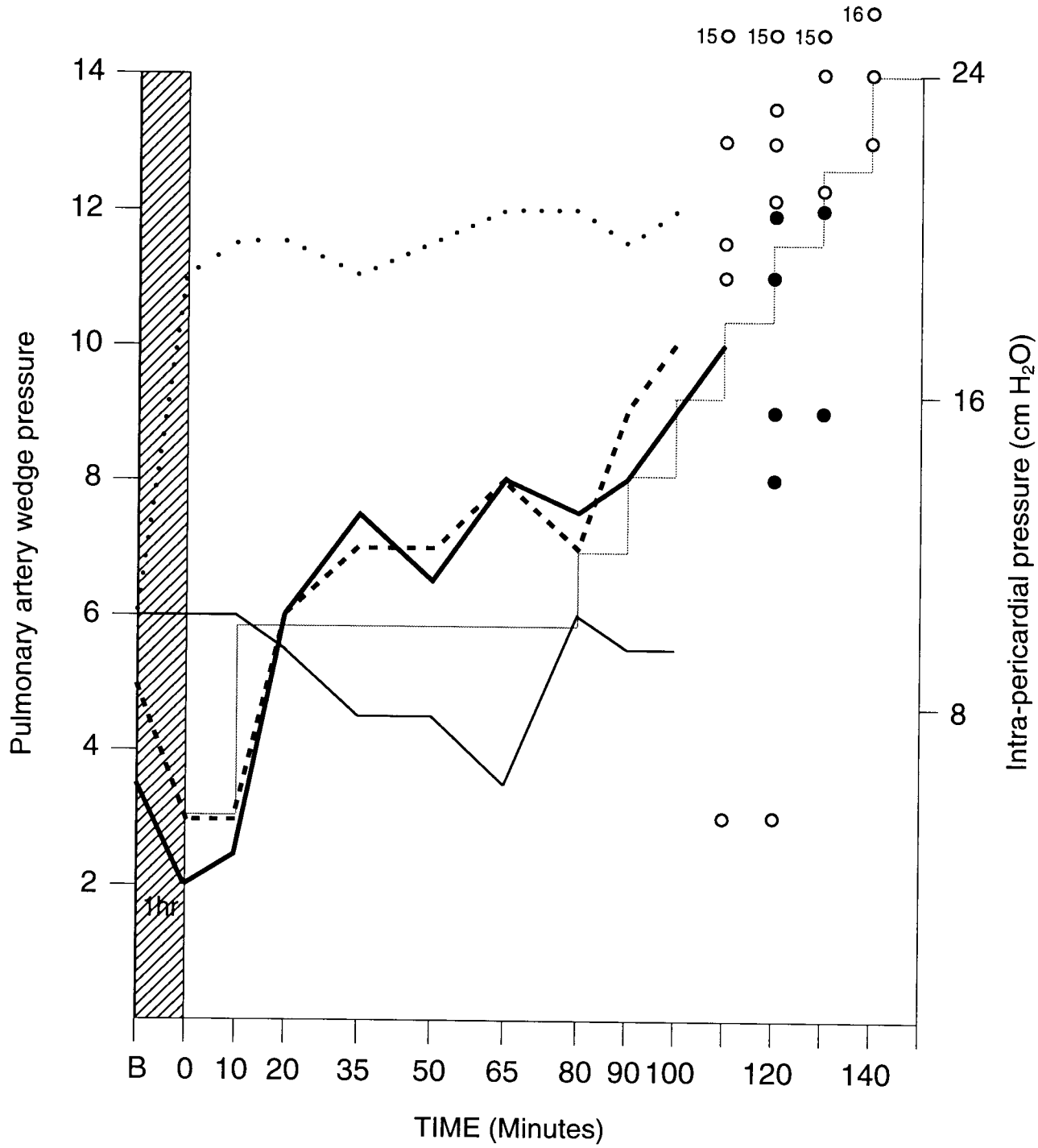
PULMONARY ARTERY PRESSURE

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	13.5	15	15.2	15.2	14.7	16.3	16.5	17.3	16.8	17.7	18.8
Median	14	14	14	14.5	14	15	15	16	15.5	15.5	15
Standard deviation	*4.3*	*5.6*	*6*	*6.9*	*7.5*	*8.1*	*6.8*	*6.6*	*7.7*	*9.5*	*14.3*
TAMP/NON-ALC											
Mean	17.6	17.6	17.7	16.1	15.4	17	18.6	18.7	16.7	15	
Median	17	15	15	16	16	18	18	19	18	16	
Standard deviation	*6*	*8*	*9.1*	*8.9*	*9.6*	*6.8*	*7.4*	*6.8*	*6.5*	*5.1*	
SHAM/ALC											
Mean	19.8	20.7	17.8	15.8	14.3	15.3	16.7	15.5	14.8	14.7	
Median	17	19	18.5	18	20	20	20	18	17.5	19	
Standard deviation	*8.4*	*2.9*	*5.1*	*6.7*	*9.8*	*8.1*	*6.7*	*6.6*	*8.1*	*9.3*	
SHAM/NON-ALC											
Mean	23	24.3	25	25.3	25	28	29.5	29.8	30.5	30.8	
Median	19.5	24	25	25.5	23	24.5	24.5	24.5	23.5	23.5	
Standard deviation	*8.8*	*7.8*	*8.3*	*8.4*	*10.2*	*12.8*	*14.8*	*15.4*	*16.5*	*17*	

PULMONARY ARTERY PRESSURE
(GEOMETRIC MEANS)

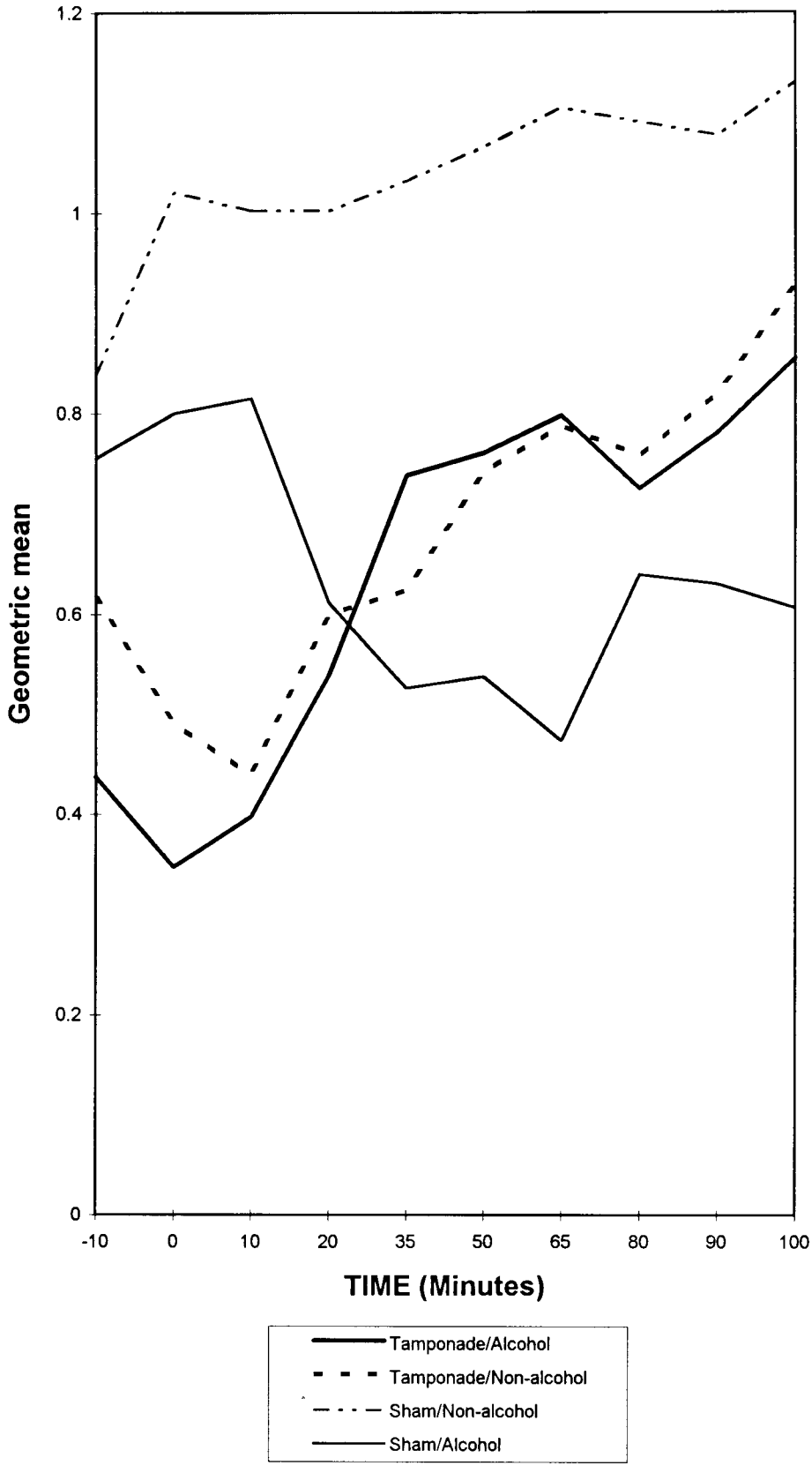
Pericardial pressure	Baseline	0 cm	5cm	10cm	10cm	10cm	10cm	10cm	12cm	14cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min
TAMP/ALC	1.11	1.15	1.152	1.14	1.057	1.162	1.186	1.212	1.184	1.188
TAMP/NON-ALC	1.224	1.206	1.206	1.137	1.091	1.198	1.239	1.241	1.19	1.146
SHAM/ALC	1.278	1.313	1.234	1.152	1.02	1.084	1.144	1.146	1.071	1.068
SHAM/NON-ALC	1.342	1.367	1.378	1.382	1.372	1.416	1.434	1.435	1.445	1.447

Figure 8.17 : Pulmonary Artery Wedge Pressure



Lines join median values for groups. Scattergram denotes only survivors.

Figure 8.17a: Pulmonary Artery Wedge Pressure (Geometric Mean)



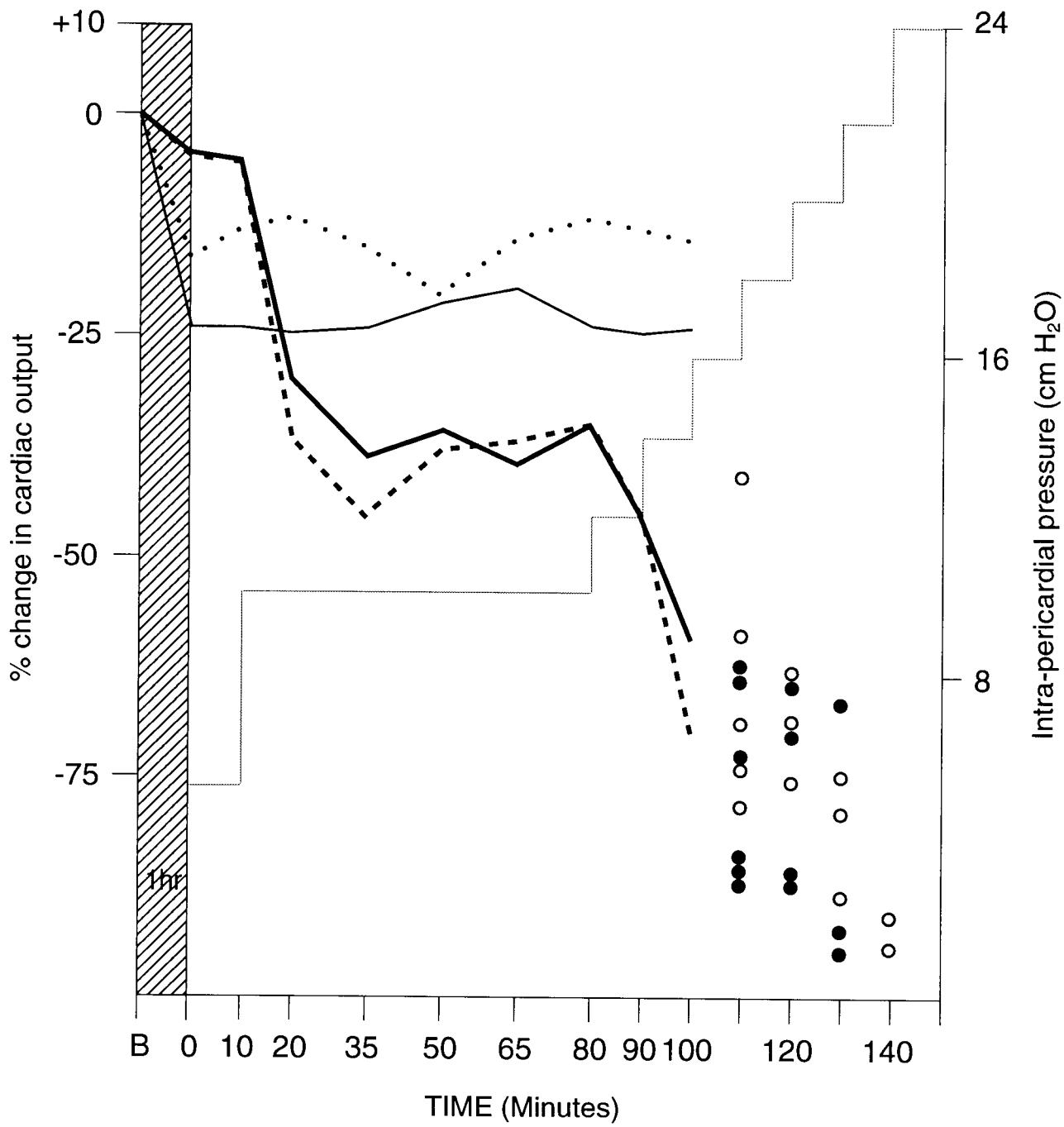
PULMONARY ARTERY WEDGE PRESSURE

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	1.7	1.8	2.3	5	6.7	6.3	7	6.3	7.5	8.2	9.7
Median	3.5	2	2.5	6	7.5	6.5	8	7.5	8	9	10
Standard deviation	*5.5*	*3.6*	*2.4*	*1.3*	*3.1*	*2.4*	*2.8*	*3.5*	*3.7*	*3.5*	*4.3*
TAMP/NON-ALC											
Mean	4.6	3.3	2.9	4.4	5.1	6.4	7.3	6.7	8	9.1	
Median	5	3	3	6	7	7	8	7	9	10	
Standard deviation	*2.1*	*3.6*	*3.6*	*4.8*	*4.5*	*3.2*	*2.9*	*3.4*	*3.5*	*2.9*	
SHAM/ALC											
Mean	6.3	6.8	7.3	5.5	4.8	4.8	4.5	5.5	5.5	5.5	
Median	6	6	6	5.5	4.5	4.5	3.5	6	5.5	5.5	
Standard deviation	*3*	*3*	*4*	*3.9*	*3.9*	*4.6*	*5.4*	*4.1*	*4.5*	*4.5*	
SHAM/NON-ALC											
Mean	8	12.3	12	12	13.8	16	16.8	17	17	17.8	
Median	6	11	11.5	11.5	11	11.5	12	12	11.5	12	
Standard deviation	*5.5*	*7.5*	*7.6*	*7.6*	*10.7*	*14.4*	*14.4*	*15.6*	*16.3*	*15.6*	

PULMONARY ARTERY WEDGE PRESSURE
(GEOMETRIC MEANS)

Pericardial pressure	Baseline	0 cm	5cm	10cm	10cm	10cm	10cm	10cm	12cm	14cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min
TAMP/ALC	0.437	0.347	0.397	0.538	0.738	0.76	0.798	0.725	0.78	0.855
TAMP/NON-ALC	0.619	0.49	0.439	0.6	0.624	0.742	0.787	0.758	0.819	0.929
SHAM/ALC	0.755	0.8	0.815	0.612	0.525	0.537	0.472	0.639	0.63	0.606
SHAM/NON-ALC	0.838	1.021	1.002	1.002	1.032	1.066	1.105	1.091	1.077	1.131

Figure 8.18 : Cardiac Output

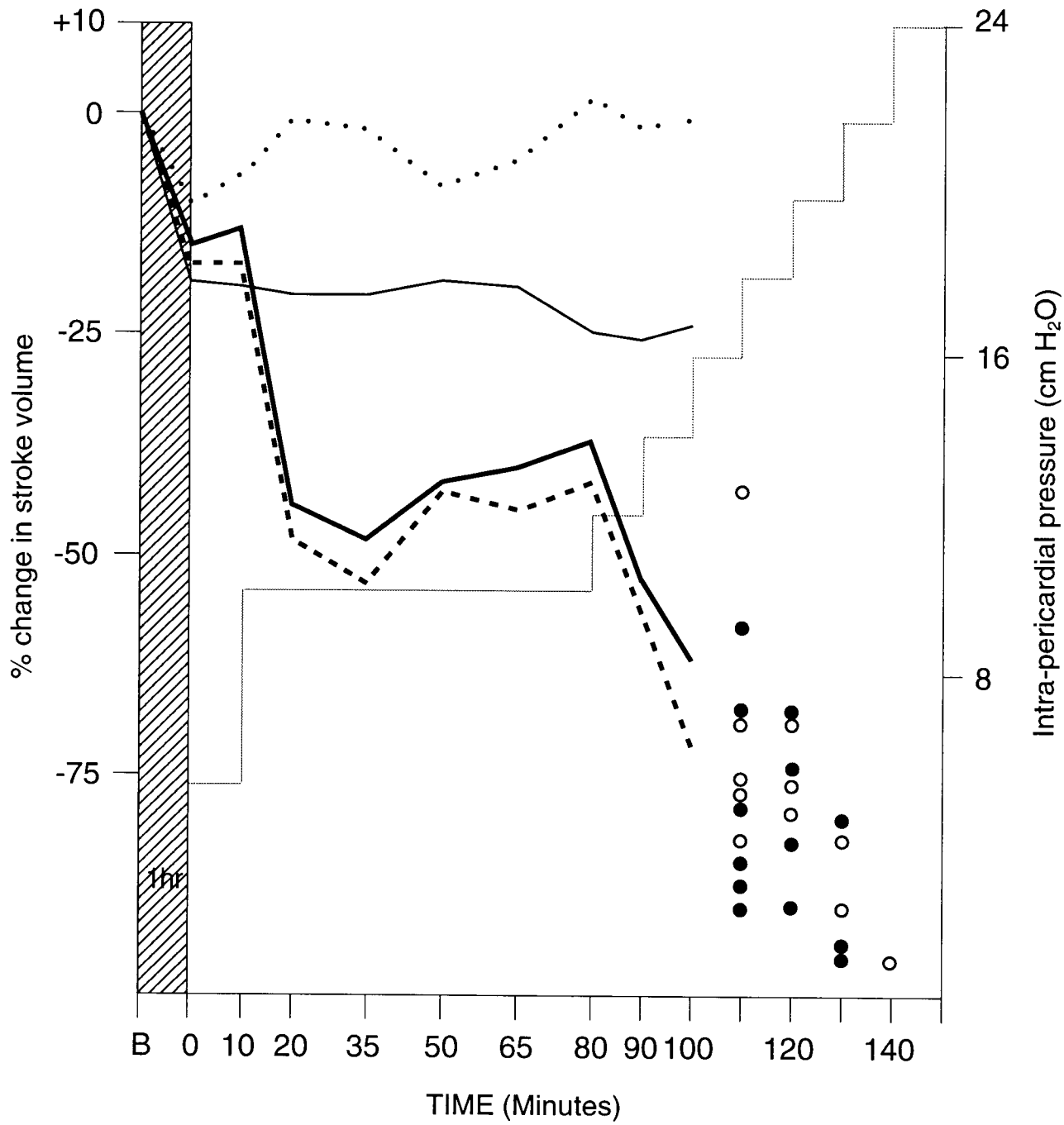


Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE CARDIAC OUTPUT

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMPO/ALC											
Mean	100	96	95	70	62	64	61	65	49	41	
Median	100	86	95	76	63	52	56	61	47	40	
Standard deviation		*17.4*	*18.1*	*19.2*	*18.7*	*23.7*	*15.4*	*15.2*	*14.3*	*15.5*	
TAMP/NON-ALC											
Mean	100	96	95	63	54	62	63	65	49	30	
Median	100	91	92	59	49	59	64	57	48	32	
Standard deviation		*16.4*	*18.2*	*16.8*	*16.9*	*16.4*	*15.4*	*17.9*	*12*	*20.4*	
SHAM/ALC											
Mean	100	76	76	75	76	78	80	76	75	76	
Median	100	72	73	72	73	77	82	75	73	75	
Standard deviation		*14.2*	*12.4*	*12.6*	*11.6*	*11.4*	*12*	*13.4*	*13.6*	*14.5*	
SHAM/NON-ALC											
Mean	100	83	87	88	85	79	86	88	87	86	
Median	100	83	89	88	86	80	86	87	90	87	
Standard deviation		*3.1*	*3.4*	*2.8*	*1*	*7.7*	*9.5*	*7.8*	*16.2*	*12.7*	

Figure 8.19 : Stroke Volume

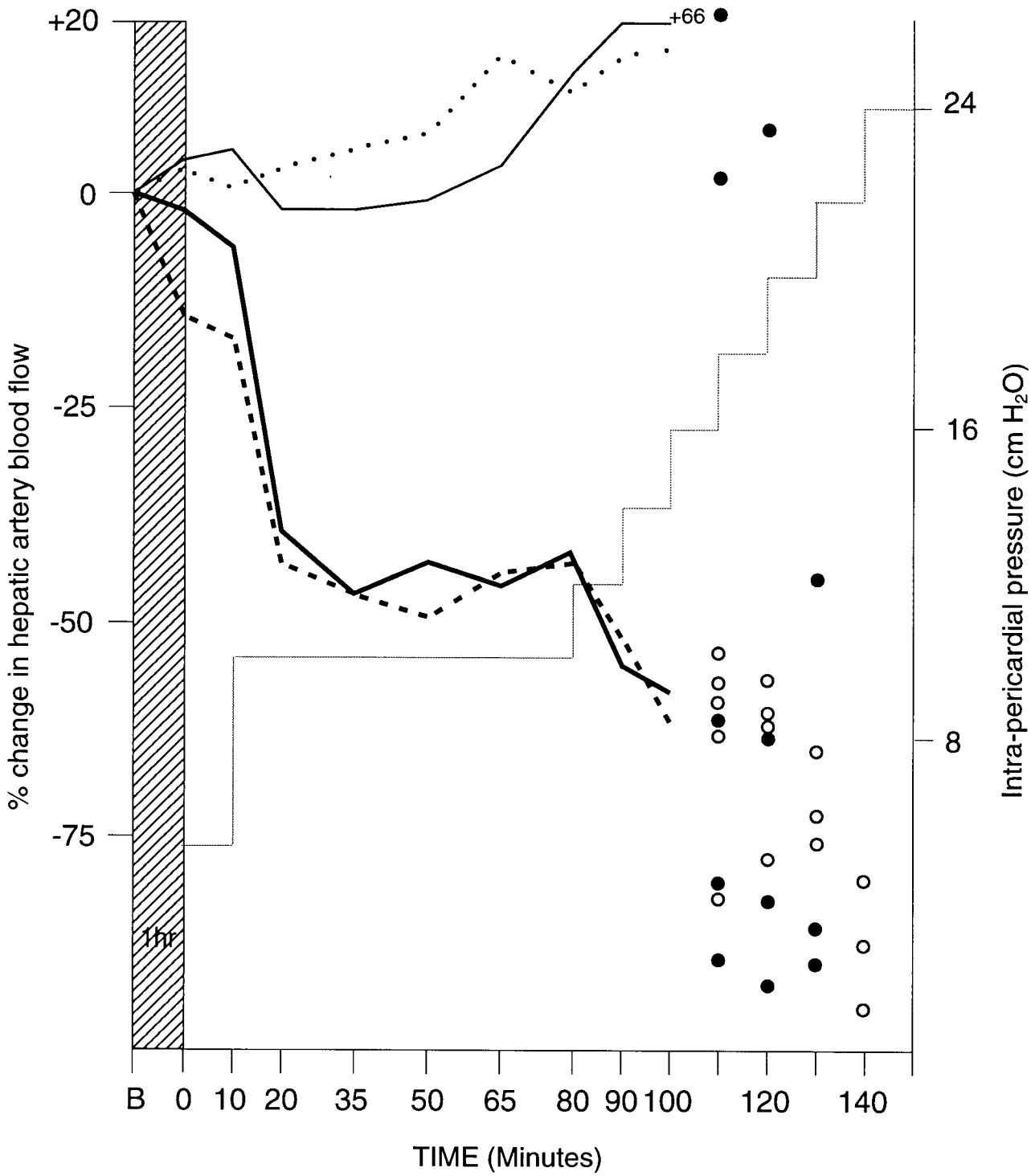


Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE STROKE VOLUME

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	100	85	87	56	52	58	60	63	47	38	
Median	100	81	88	63	43	50	60	72	42	37	
Standard deviation		*15.3*	*17.3*	*14.9*	*14.5*	*16.8*	*16.7*	*14.8*	*17*	*14.9*	
TAMP/NON-ALC											
Mean	100	83	83	52	47	57	55	58	43	28	
Median	100	79	79	47	45	50	49	51	38	25	
Standard deviation		*13.3*	*14.1*	*17.5*	*15.4*	*14.8*	*17.9*	*18*	*17.1*	*20.7*	
SHAM/ALC											
Mean	100	81	80	79	79	81	80	75	74	76	
Median	100	79	79	75	75	77	78	72	71	74	
Standard deviation		*22.2*	*21*	*23.4*	*24.5*	*24.8*	*26.5*	*22.9*	*24.1*	*25.1*	
SHAM/NON-ALC											
Mean	100	89	93	99	98	92	95	103	98	99	
Median	100	89	94	98	98	89	95	106	96	99	
Standard deviation		*8.6*	*11*	*12.4*	*9.4*	*9.5*	*10.9*	*8.7*	*6.2*	*1.7*	

Figure 8.20 : Hepatic Artery Blood Flow

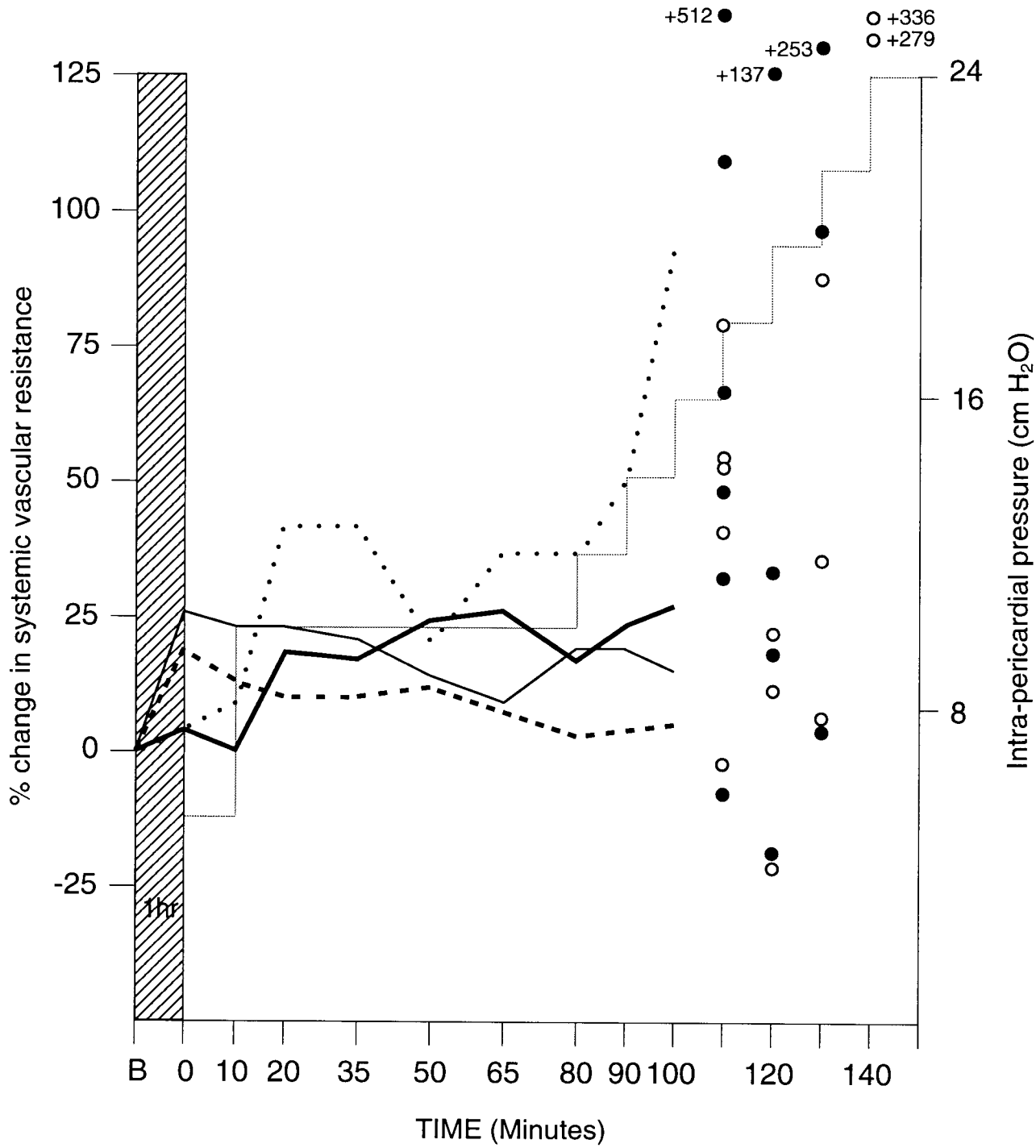


Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE HEPATIC-A FLOW

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	100	98	94	61	53	57	56	58	45	42	
Median	100	88	89	51	45	50	55	53	34	40	
Standard deviation		*20.9*	*23.4*	*24.4*	*24.5*	*28*	*23.8*	*27.9*	*25.6*	*23.2*	
TAMP/NON-ALC											
Mean	100	86	83	57	53	51	56	57	48	35	
Median	100	79	69	52	55	50	56	54	51	31	
Standard deviation		*20.1*	*23.8*	*22.6*	*18.5*	*19.7*	*21.1*	*21.7*	*18.6*	*15.8*	
SHAM/ALC											
Mean	100	104	105	98	98	99	103	114	120	120	
Median	100	103	109	92	92	98	103	104	104	108	
Standard deviation		*23.7*	*24.7*	*30*	*37.8*	*37*	*33.9*	*42.7*	*40.6*	*36.9*	
SHAM/NON-ALC											
Mean	100	103	101	103	105	107	116	112	116	117	
Median	100	106	106	107	107	104	114	110	110	108	
Standard deviation		*18.6*	*12.3*	*8.9*	*9*	*11.4*	*12.7*	*13.5*	*18*	*23.4*	

Figure 8.21 : Systemic Vascular Resistance



· · · · Sham non-alcohol (n = 4)

o - - - - Tamponade non-alcohol (n = 7)

——— Sham alcohol (n = 4)

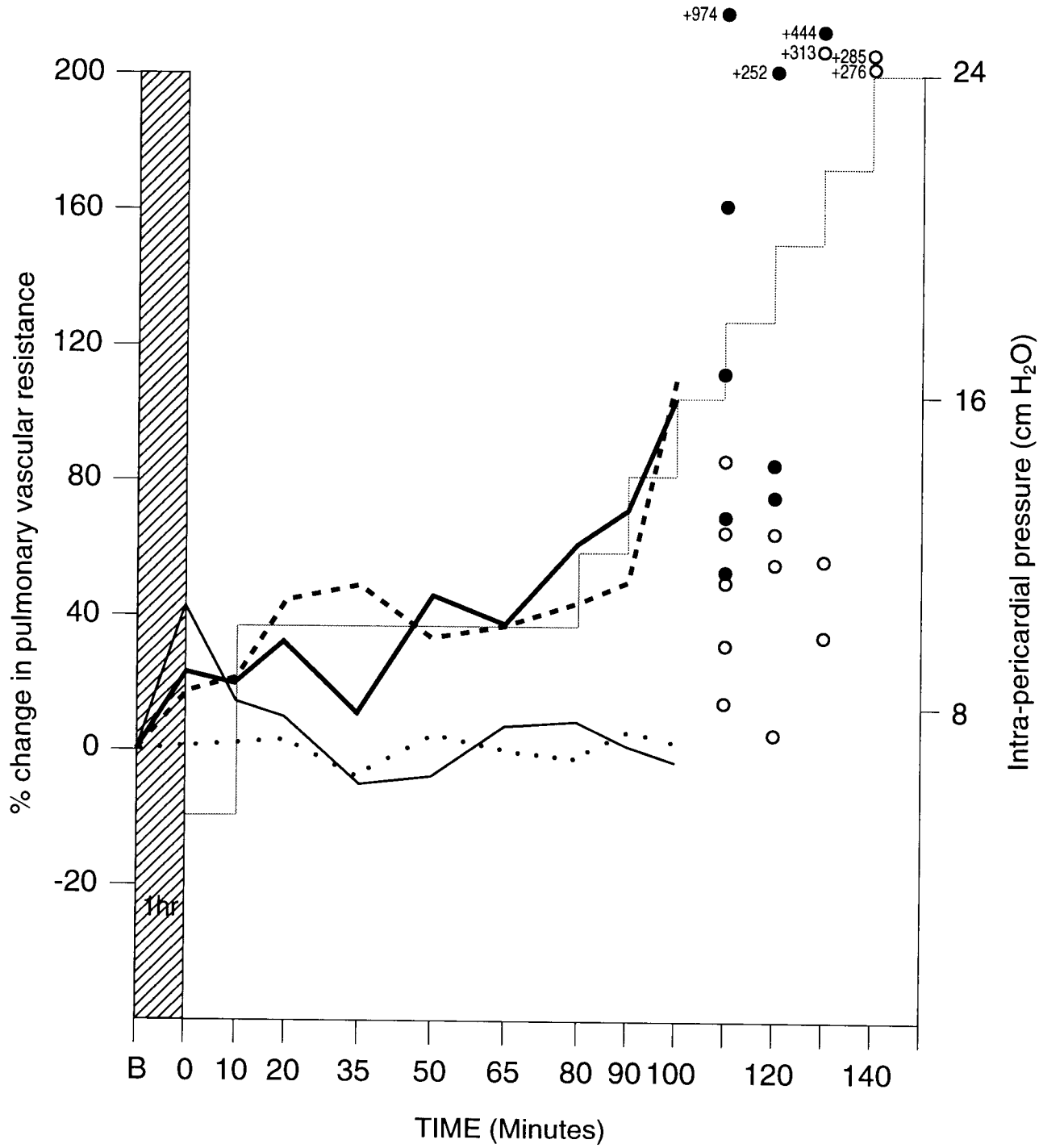
● ——— Tamponade alcohol (n = 7)

Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE SVR

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	100	104	100	118	117	124	126	117	123	127	
Median	100	111	107	109	112	127	133	126	125	129	
Standard deviation		*18.8*	*19.9*	*28.8*	*20.5*	*28.3*	*24.5*	*21.9*	*26.1*	*33.6*	
TAMP/NON-ALC											
Mean	100	105	109	142	142	120	137	137	150	193	
Median	100	105	109	149	139	124	127	129	133	158	
Standard deviation		*15.3*	*19.3*	*25.5*	*16.5*	*37.8*	*29*	*35.2*	*37.3*	*82.7*	
SHAM/ALC											
Mean	100	126	123	123	121	114	109	119	119	115	
Median	100	125	118	120	116	111	111	117	112	114	
Standard deviation		*17.7*	*17.7*	*16.4*	*16.8*	*13.5*	*9.9*	*11.2*	*17.9*	*15.1*	
SHAM/NON-ALC											
Mean	100	119	113	110	110	112	107	103	104	105	
Median	100	123	117	111	112	111	101	100	99	98	
Standard deviation		*10.8*	*9.5*	*9.4*	*10.3*	*10.2*	*11.7*	*16.7*	*17.7*	*20*	

Figure 8.22 : Pulmonary Vascular Resistance



· · · · Sham non-alcohol (n = 4)

o - - - - Tamponade non-alcohol (n = 7)

——— Sham alcohol (n = 4)

● ——— Tamponade alcohol (n = 7)

Lines join mean values for groups. Scattergram denotes only survivors.

% OF BASELINE PVR

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm
Time	0 min	1 hour	1hr 10min	1hr 20min	1hr 35min	1hr 50min	1hr 65min	1hr 80min	1hr 90min	1hr 100min	1hr 110min
TAMP/ALC											
Mean	100	124	121	132	111	146	139	161	173	205	
Median	100	123	120	147	107	134	145	160	172	214	
Standard deviation		*15.2*	*10.6*	*52.5*	*51.3*	*63.1*	*37.2*	*61.8*	*23.3*	*38*	
TAMP/NON-ALC											
Mean	100	117	123	143	149	134	138	144	150	211	
Median	100	107	116	140	127	137	146	132	140	145	
Standard deviation		*28.2*	*32.1*	*42.4*	*69*	*41.9*	*52.2*	*32.1*	*76.6*	*166*	
SHAM/ALC											
Mean	100	142	115	111	90	94	107	109	101	97	
Median	100	177	113	108	78	76	109	97	91	55	
Standard deviation		*64.4*	*60.2*	*56.7*	*67.7*	*50.7*	*41.9*	*58.1*	*66.2*	*73.6*	
SHAM/NON-ALC											
Mean	100	100.8	101.5	103.3	91.8	104.5	100.3	98	105.8	102.5	
Median	100	83	85	87	78.5	102.5	99	94	111.5	108	
Standard deviation		*41.2*	*36.4*	*35.9*	*35.4*	*29.3*	*14.4*	*19.4*	*19.3*	*13.9*	

8.4 DISCUSSION

Anaesthetic technique: Although other experimental studies have provided valuable information about cardiac tamponade, there have been many discrepancies because of species variations and differences in methodology. Of particular note, has been the widespread and inappropriate use of barbiturates and other cardiac-depressant drugs (Shatney 1976). In our study, anaesthetic technique was standardized in all animals and was selected to minimize cardiac effects. Although pentobarbitol sodium was used for induction, this would not have had an appreciable effect because of redistribution. It could also be argued that continuous infusion of pancuronium prevented animals from moving in response to pain, but this was necessary to ensure a stable state so that subtle changes in haemodynamics could be detected. In our experience, the exceptional metabolic capabilities of pigs also makes it impractical to administer bolus doses of muscle relaxant every time the animal moves. Moreover, the combination of 70% Nitrous oxide/oxygen and continuous infusion of Fentanyl (in a dose that exceeds that for humans) appeared to provide adequate analgesia, as evidenced by a stable blood pressure and pulse rate while performing the surgery, as well as during the period prior to instillation of fluid into the pericardial sac. The fact that animals were paralyzed and mechanically ventilated did, however, preclude study of the interactions between alcohol, tamponade and respiration in this model.

Alcohol intoxication: Alcohol was given via a gastrostomy rather than parenterally, because it was felt that this was analogous to the clinical situation - the range of serum levels was similar to that in the previous study. (Only one animal in the tamponade/alcohol group failed to achieve a serum concentration compatible with intoxication after one hour).

Traces of alcohol that were detected in the non-alcohol groups were probably related to the porcine diet (Alcohol, Drugs and Road Traffic 1979) (Table 8.1).

Another reason for administration via the gut is that alcohol is absorbed gradually - parenteral administration may cause sudden changes in haemodynamics. Gut absorbtion is also dependent on perfusion, therefore, serial alcohol measurements would give some indication of the general haemodynamic state. In this study, we were unable to test this because significant cardiac decompensation only occurred after the last alcohol measurement.

Inducing tamponade: The methods used for placement of a pericardial catheter and induction of tamponade proved to be reliable and reproducible. The "burr-hole sternotomy" approach is novel and has several distinct advantages over previously described techniques (Bailey 1986; Brockman 1954; Cooley 1953; Millard 1983; Moller 1979; Sawyer 1952). It is not as invasive as a thoracotomy or full sternotomy, which introduces additional variables such as pneumothorax and chest wall instability. Cyanoacrylate glue also provides a more watertight seal than a purse-string suture, and the entrance of the catheter into the pericardial sac can be visualized at all times during the experiment so that any displacement or leakage is immediately apparent. This is not possible where the catheter is inserted via an intercostal space and traverses the pleural cavity before entering the pericardial sac. However, certain technical points need to be emphasized. After burr-hole sternotomy, which is relatively easy, careful identification of the layers surrounding the heart is necessary so as to avoid misplacement of the catheter. This occurred in one instance early in the study, when the catheter was sited in the mediastinum rather than the pericardial sac. In another animal, incidental

pericarditis with dense adhesions prevented insertion of the pericardial catheter. The best way to ensure correct placement, is to visualize the glistening visceral surface of the beating heart through the pericardiotomy (Fig 8.8) and to aspirate a small amount of serous pericardial fluid after insertion of the catheter (Fig 8.10). The latter maneouvre invariably causes transient cardiac arrhythmias but does not lead to haemodynamic instability. If hypotension does occur, this is usually due to pneumopericardium, as the bellows-like action of the chest may draw in air via the pericardiotomy or catheter during the respiratory cycle. It is therefore imperative to aspirate air from the pericardial sac after catheter insertion and to ensure that connections are air-tight. It is also important to stay as close to the midline as possible, as lateral deviation may result in opening of the pleura with subsequent pneumothorax. In the only animal where this occurred, cardiovascular instability was accentuated and haemodynamic measurements were unreliable.

Previous investigators have described the instillation of fixed volumes (Cooley 1953; Moller 1979), or continuous infusion of fluid into the pericardial sac at a constant rate (Bernath 1987; Cogswell 1986) to induce tamponade. However, it was felt that a pressure-cycled system was more physiological, as volume and compliance of the pericardial sac may differ irrespective of similar animal size and weight. The three-way system also provided a dynamic and easy method of keeping intra-pericardial pressure constant. At the same time, changes in the level of fluid in the reservoir could be measured, which was an indirect reflection of pericardial capacitance.

Effects of alcohol in isolation: There were decreases in cardiac output, stroke volume and systemic vascular resistance in both sham-operated groups ($p<0.05$ in all: linear and quadratic trend). This may have been due to the effect of surgery, as the most dramatic changes occurred early in the experiment. Other haemodynamic parameters were reasonably maintained throughout, except for pulmonary artery wedge pressure (PAWP), which increased in the sham/non-alcohol animals ($p=0.0016$:linear). This was also the only difference between the two groups. PAWP is an indirect reflection of left ventricular end-diastolic pressure and volume. Why these should have been raised in *this* group is uncertain. However, with such small numbers, incorrect positioning of the pulmonary artery catheter in even one animal, could have resulted in a false result. What is more significant though, is the fact that PAWPs were not raised in the sham/alcohol group ($p=0.936$:linear; $p=0.873$:quadratic), which suggests that alcohol did not impair myocardial contractility.

Alcohol alone also made no difference to the results of special investigations, but when intoxication was associated with tamponade, serum lactate levels were higher. Others have reported that alcohol accentuates lactic acidosis (Garrison 1984). However, in this study, pH changes did not occur because the animals were ventilated, which would have compensated for metabolic acidosis. Furthermore, because paralysis was used, we were unable to assess the effect of alcohol on respiratory rate and effort.

Effects of acute cardiac tamponade: The haemodynamic changes that occured during cardiac tamponade were no different from those that have been reported previously (Brown 1992; Pories 1975; Reddy 1978; Shabetai 1994). Cardiac output and blood pressure were initially

maintained by compensatory increases in heart rate and peripheral vascular resistance (although the latter trend was not significant). As the degree of tamponade increased, compensatory mechanisms failed, and cardiac output and blood pressure fell. In some animals, paradoxical increase in hepatic artery blood flow and transient elevation of blood pressure were noted just prior to death. At the same time, their heart rate became very labile with subsequent cardiac arrest by ventricular fibrillation or asystole. These phenomena may have been due to massive outpouring of catecholamines in response to stress (Hannon 1985; Nelson 1972). A catecholamine "surge" has also been associated with splenic contraction and augmentation of blood volume in some animals (Hannon 1985). However, it would be unreasonable to extrapolate this to humans, where splenic contraction in the shock state plays only a minor role (Nelson 1972; Textbook of Medical Physiology 8th ed, 1991). Unfortunately, catecholamine levels were not measured during this stage of the experiment. It was also a mistake to have taken random samples at the outset, because catecholamines have a short life (Ginn 1968). This was evident when analysis of these results proved to be meaningless. Continuous monitoring of catecholamines would be ideal, but this would be extremely difficult.

Initially, relatively large volumes of fluid were instilled to affect increases in pericardial pressure, whereas once decompensation had occurred, only small increments of fluid were required. Others have also demonstrated an exponential effect of volume on intra-pericardial pressure (Morgan 1965; Shabetai 1994). During the period when intra-pericardial pressure was maintained at 10cm of water, the volume in the reservoir remained fairly constant in spite of some improvement in haemodynamic parameters. This implies that other factors, such as increased peripheral vascular resistance or changes in blood volume were responsible for this recovery, rather than

alteration in cardiac volume or contractility. The fluid in the pericardial sac was also not absorbed to any extent, as total tamponade volume at the end of the experiment equaled the volume that had been lost from the reservoir.

Effects of alcohol on haemodynamic physiology of cardiac tamponade: Alcohol accentuated hypotension in the animals that underwent tamponade. This was most likely due to a lower systemic vascular resistance in the tamponade/alcohol group. Gastric administration of alcohol may have also caused splanchnic vasodilatation, with sequestration of blood and decrease in circulating blood volume (Knott 1963). However, despite lower blood pressures, tachycardia was less pronounced. This may have been due to analgesic/sedative effects of alcohol (Textbook of Pharmacology 2nd ed, 1980) which reduced stress and *decreased* catecholamine release. (Although there were no consistent catecholamine results, noradrenalin levels were higher in both non-alcohol groups at one-and-a-half hours). Of particular relevance though, was the fact that cardiac output and hepatic artery blood flow were similar in the two groups. In other words, although alcohol impaired compensatory mechanisms, this did not appear to influence the overall haemodynamic state. Moreover, cardiac performance was probably better in the tamponade/alcohol group. An increase in stroke volume may have been responsible for maintenance of cardiac output in the face of decreasing peripheral vascular resistance, however, we were unable to show a difference between the two groups. Alcohol also had no effect on survival time. Most pigs deteriorated rapidly once pericardial pressure was increased to 16cm of water. Death was either by ventricular fibrillation or asystole.

These results are in conflict with those of other studies (Cooley 1953). One of the reasons for this may be the fact that conditions were more physiological. We did not use cardiac-depressant drugs during experimentation and the "closed chest method" of inducing tamponade avoided pneumothorax and the need for under-water drainage. The one pig that was excluded from the study clearly demonstrated that haemodynamic instability would be compounded by pneumothorax.

Maintenance of cardiac output to some extent, could also be explained by the actions of alcohol per se. Cardiac tamponade is a powerful stimulus for peripheral vasoconstriction. This has been attributed mainly to alpha-effects (Cogswell 1983). However, because of inhibition of vascular smooth muscle (Altura and Altura 1982; Knochel 1983), alcohol caused vasodilatation and decreased afterload, which has been reported to be benificial in tamponade (Gascho 1981). This action of alcohol has also been shown to improve haemodynamics in other models of cardiogenic shock (Shatney 1976). In addition, vasodilatation may have involved the coronary vessels (Ganz 1963; Gould 1971; Horton 1986; Shatney 1976), and the slower heart rate would have allowed more time for cardiac filling and myocardial perfusion. All these effects would enhance cardiac performance.

The failure of alcohol to have a significant effect in this model of acute cardiac tamponade also supports our clinical experience, but further studies are necessary before mechanisms will become apparent. Future work should attempt to define the role of alcohol together with spontaneous respiration in a tamponade model. Assessment of heart action using echocardiography or gated blood pool scintigraphy would also provide valuable additional information.

9. CONCLUSIONS

It is clear from local experience, that alcohol can be implicated in most cases of assault. The Cape Metropolitan Trauma Survey which was conducted in 1990, revealed that at least 70% of patients with penetrating chest injuries had consumed alcohol. This figure is similar to that of the clinical study, where more than two thirds of patients with assault-related acute cardiac tamponade had blood alcohol levels in excess of the "legal limit" of 17 mmol/L.

The relationship between alcohol and the degree of injury sustained, is less well defined. Some authorities are of the opinion that intoxicated individuals are less likely to be affected by trauma because they "roll with the punches". Others have reported that they have a higher chance of sustaining life-threatening injuries. However, studies of this nature are difficult to interpret because they involve so many uncontrolled variables.

The effect of alcohol on clinical parameters and outcome of trauma victims is also controversial. Although relatively few studies have addressed this question, most of them have shown that intoxication has a negative effect. This has been particularly emphasized in research devoted to haemorrhagic shock. There is also ample evidence that the actions of alcohol on the cardiovascular system in normal subjects are deleterious. However, it would be naive to assume that alcohol affects all forms of shock in the same way.

Based on the preceding studies, it can be concluded that alcohol intoxication does not have an adverse affect on haemodynamic physiology of acute cardiac tamponade. In the clinical study, there were no

differences between intoxicated and non-intoxicated patients. Although there was a tendancy for the intoxicated group to be more hypotensive, they responded well to resuscitation and appeared to require less intravenous fluid than their sober counterparts. The exaggerated clinical features may also have led to earlier diagnosis and definitive treatment in this group. Furthermore, hospital course and outcome were not affected by the fact that a greater proportion of the intoxicated patients were "moribund" or "in extremis" on admission.

In the animal study, the model of cardiac tamponade was reliable and reproducable. The method of gaining access to the pericardial sac and inducing tamponade was also more physiological than previously described techniques. The most noticeable effect of alcohol was that it lowered peripheral and pulmonary vascular resistance in animals that underwent tamponade. This meant that these animals were more hypotensive. However, compensatory tachycardia was less pronounced in the tamponade/alcohol group. In haemorrhagic shock, these actions of alcohol would worsen haemodynamics, but in our model, cardiac output was maintained and survival times were similar in the two groups.

This work has generated several theories as to why alcohol affects haemodynamic physiology of cardiac tamponade differently to that of haemorrhagic shock. The most plausible explanation, is that in the absence of major blood loss, systemic vasodilatation improves cardiac function by reducing afterload. (There is no doubt that alcohol was associated with hypotension in both studies). Alcohol also suppresses ventilation and may therefore limit respiratory fluctuations in venous return. (Unfortunately this could not be assessed in our ventilated animal model).

Although alcohol has been reported to release catecholamines, with beneficial inotropic and chronotropic effects, we were unable to demonstrate this. In fact, heart rate was slower in animals that received alcohol, which may have allowed more time for heart filling and myocardial perfusion. However, further studies of cardiac function in intoxicated subjects with tamponade using more sophisticated techniques are necessary, before these mechanisms can be confirmed.

In practice, all patients with suspected cardiac tamponade should be managed aggressively, as they can be salvaged even when they are admitted in a moribund state. Furthermore, alcohol intoxication does not confer a worse prognosis. We would even go so far as to suggest that immediate "front-room" thoracotomy should be considered in patients with penetrating chest wounds who are "dead on arrival", particularly if they have imbibed alcohol and little time has elapsed since cardiac arrest. This is of particular relevance in Cape Town, where both alcohol abuse and assault are endemic. As for a therapeutic effect of alcohol, these studies do not support its use in acute cardiac tamponade. The cornerstones of management in this condition are early diagnosis, aggressive resuscitation and surgical relief of intra-pericardial pressure rather than pharmacological manipulation. In chronic cardiac tamponade, alcohol may have some beneficial effects, but until more evidence becomes available, clinicians should resort to proven medical therapy.

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11. APPENDIX

HAEMODYNAMIC PARAMETERS FOR INDIVIDUAL PIGS

TAMPONADE-ALCOHOL (Pig 7)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.04	39.02	39.11	39.22	39.34	39.38	39.68	39.81	39.73	39.73	39.71	38.81		
Heart rate (beats/min)	179	195	194	203	136	133	131	137	145	149	174	133		
Mean BP (mmHg)	115	109	103	81	51	64	96	88	50	47	36	31		
CVP (cm water)	7.5	3.5	4	4	4.5	4.5	11	12.5	12.5	15.5	16	16		
PAP (mmHg)	8	9	9	8	5	6	9	11	7	6	6	4		
PAWP (mmHg)	-4	-4	-2	-1	1	2	2	0	1	2	3	9		
Cardiac output (L/min)	4.09	3.49	3.08	1.74	1.31	1.74	2.29	2.29	1.13	1.03	0.53	0.98		
	3.64	3.16	2.85	1.49	1.17	1.54	2.08	2.04	1.12	0.89	0.64	0.48		
	3.65	3.1	2.81	1.36	1.2	1.7	2.04	2.04	1.02	0.92	0.5			
Stroke vol (ml)	21.2	16.7	15	7.5	9	12.5	16.3	15.5	7.5	6.4	3.2	3.7		
Hepatic A flow (ml/min)	245	294	267	134	72	75	136	128	82	94	47	16		
SVR (dyne . sec. cm-5)	2309	2618	2749	4078	3095	2922	3280	2967	2982	2979	3429	3102		

TAMPONADE-ALCOHOL (Pig 11)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	36	35.7	36	36	36.14	36.37	36.49	36.88	36.86	36.79	36.83	36.68	36	
Heart rate (beats/min)	110	134	122	172	198	207	182	195	192	196	204	157	161	
Mean BP (mmHg)	124	137	135	112	98	87	94	93	101	81	56	40	38	
CVP (cm water)	11	8	8	9.5	12	12.5	12.5	13	12	12	15	17.5	20	
PAP (mmHg)	47	28	27	32	33	40	43	56	51	52	46	44	45	
PAWP (mmHg)	33	16	16	23	26	34	34	56	36	43	43	45	46	
Cardiac output (L/min)	2.51	2.75	2.62	2.1	1.65	1.65	1.84	1.83	2.01	1.59	1.26	0.45	0	
	2.05	2.37	2.37	2.19	1.57	1.4	1.63	1.76	1.83	1.34	1.26	0.45	0	
	1.89	2.41	2.21	2.02	1.69	1.72	1.67	1.52	1.86	1.24	1.16		0	
Stroke vol (ml)	19.5	18.7	19.7	12.2	8.3	9.4	8.7	9.9	7.1	6	1.9			
Hepatic A flow (ml/min)														
SVR (dyne . sec. cm-5)	4307	4175	4300	3995	3906	3959	3918	3874	4144	2911	7167			

TAMPONADE-ALCOHOL (Pig 13)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.1	38.1	38.1	38.2	38.4	38.4	38.5	38.6	38.6	38.6	38.6	38.6	38.3	
Heart rate (beats/min)	159	215	207	218	209	174	171	162	158	165	198	191	157	
Mean BP (mmHg)	135	105	99	75	89	101	95	99	98	92	87	49	36	
CVP (cm water)	2	3	5	10.5	10.5	11	11.5	11.5	12	13.5	14	14	14	
PAP (mmHg)	9	10	10	10	11	13	13	13	13	13	13	11	9	
PAWP (mmHg)	2	2	2	5	6	6	8	5	7	7	8	8	9	
Cardiac output (L/min)	3.1	3.32	2.99	1.76	1.78	1.38	1.27	1.42	1.36	1.22	0.92	0.49	0.25	
	2.86	2.74	2.82	1.61	1.69	1.22	1.15	1.33	1.18	1.11	0.82	0.34	0.24	
	2.91	2.66	2.68	1.47	1.57	1.19	1.15	1.22	1.17	1.02	0.7	0.26		
Stroke vol (ml)	18.6	13.5	13.7	7.4	8	7.2	7	8.1	7.8	6.8	4.1	1.9	1	
Hepatic A flow (ml/min)	270	220	197	100	98	87	60	65	65	44	29	45	26	
SVR (dyne . sec. cm-5)	3608	2825	2693	3335	3863	5889	5807	5477	5742	5848	7536	8556	12750	

TAMPONADE-ALCOHOL (Pig 14)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	37.4	37.6	37.4	37.2	37.4	37.6	37.5	37.5	37.3	37.2	36.3			
Heart rate (beats/min)	159	164	144	209	207	168	188	200	205	206	153			
Mean BP (mmHg)	115	107	112	95	76	77	79	74	45	43	15			
CVP (cm water)	3	3	4	9.5	10	10	10.5	12	14	16	16			
PAP (mmHg)	17	12	11	9	9	11	11	11	12	12	10			
PAWP (mmHg)	7	2	2	6	7	6	6	7	7	8	9			
Cardiac output (L/min)	1.94	1.63	1.53	1.17	0.99	1.02	1.02	1.12	0.7	0.4				
	1.67	1.57	1.57	1.2	1.03	0.9	1.01	1.16	0.62	0.3				
	1.97	1.48	1.34	1.24	1.01	0.98	1.03	1.12	0.67	0.22				
Stroke vol (ml)	11.7	9.5	10.3	5.7	4.9	5.8	5.4	5.7	3.4	1.5				
Hepatic A flow (ml/min)	280	239	233	124	98	104	105	100	70	49	0.2			
SVR (dyne . sec. cm-5)	4849	5372	5892	5858	5426	5732	5578	4602	4182	8000				

TAMPONADE-ALCOHOL (Pig 17)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	37.2	37.8	39.8	40.1	40.3	40.1	40	39.9	39.9	40.1	40.3	40.1	39.4	
Heart rate (beats/min)	140	157	155	179	172	174	148	145	161	133	122	172	221	
Mean BP (mmHg)	133	134	123	127	131	124	114	115	110	66	55	53	58	
CVP (cm water)	5	4.5	9	13	12	11	12	11.5	13.5	15	15	17	21	
PAP (mmHg)	14	16	17	19	17	17	17	19	18	18	17	17	14	
PAWP (mmHg)	5	5	5	8	8	7	8	8	9	10	11	11		
Cardiac output (L/min)	2.82	3.45	3.55	2.31	2.57	2.96	2.35	2.22	2.13	1.05	0.95	1	0.94	
	2.65	3.21	3.24	2.11	2.36	2.79	2.14	2.19	1.56	1.12	0.92	0.97	0.78	
	2.45		3.09	2.16	2.44	2.71	1.9	1.86	1.44	0.99	1.02	1.02	0.74	
Stroke vol (ml)	18.9	20.6	21.2	12.2	14.3	16.2	14.4	14.4	10.6	7.9	7.9	5.8	3.7	
Hepatic A flow (ml/min)	260	210	189	121	141	165	140	138	88	106	102	95	142	
SVR (dyne . sec. cm-5)	3917	3235	2827	4283	3967	3284	3944	4072	4673	4171	3646	3220	4122	

TAMPONADE-ALCOHOL (Pig 19)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.2	39.1	39.1	39.1	39.3	39.4	39.6	39.7	39.7	39.8	39.9	40	40	
Heart rate (beats/min)	175	160	170	175	169	164	158	156	129	190	197	196	200	
Mean BP (mmHg)	104	112	106	101	104	103	101	98	93	90	60	47	27	
CVP (cm water)	5.5	5	5	8.5	11	11	11	11.5	12.5	14	16	17	17.5	
PAP (mmHg)	19	21	21	22	23	23	23	25	23	25	21	19	17	
PAWP (mmHg)	6	6	4	7	8	8	8	8	9	10	11	12	12	
Cardiac output (L/min)	3.37	2.97	3.28	2.47	2.3	2.51	2.42	2.47	1.93	2	1.31	1.1	0.38	
	3.45	2.82	3.07	2.69	2.1	2.28	2.3	2.37	1.9	1.99	1.23	0.94	0.35	
	3.34	2.64	3.27	2.62	2.11	2.4	2.22	2.3	1.93	1.86	1.15	0.94		
Stroke vol (ml)	19.4	17.6	18.9	14.8	12.8	14.6	14.6	15.4	14.9	10.3	6.2	5.1	1.2	
Hepatic A flow (ml/min)	57	73	76	54	47	45	46	52	49	41	58	61	8	
SVR (dyne . sec. cm-5)	2357	3082	2548	2923	3530	3158	3212	2979	3484	3262	3122	2768	4625	

TAMPONADE-ALCOHOL (Pig 26)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.4	39.9	39.9	40	40	40.2	40.3	40.3	40.2	40.4	40.5			
Heart rate (beats/min)	192	240	235	230	206	193	155	142	166	166	214			
Mean BP (mmHg)	176	160	153	150	143	130	119	123	111	111	159	14		
CVP (cm water)	5	7	7	8	9	9	10	9	12	13	16			
PAP (mmHg)	14	22	23	23		28	26	25	28	32	46			
PAWP (mmHg)	-6	0	3		10	9	10	10	12	12	16			
Cardiac output (L/min)	4.8	4	4	3.9	3	2.6	2.4	2.5	2.3	2.4	1.1			
	4.7	3.5	4.1	3.5	3.2	2.2	2.2	2.6	2.2	2.2	0.9			
	4.9	3.9	3.6	3.6	2.8	2.2	2.4	2.6	2.3	2.5				
Stroke vol (ml)	25	15.8	16.4	16	14.6	12.1	15	18.1	13.7	14.3	3.1			
Hepatic A flow (ml/min)	187	169	176	164	157	181	156	170	126	122	311	0		
SVR (dyne . sec. cm-5)	2870	3258	3070	3130	3633	4232	3828	3619	3595	3418	17552			

TAMPONADE-NONALCOHOL (Pig 9)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.22	39.08	39.04	38.9	39.1	39.1	39.04	39.05	38.99	38.94	38.81	38.28		
Heart rate (beats/min)	160	225	218	234	223	200	190	177	169	192	191	75		
Mean BP (mmHg)	116	108	111	102	81	101	98	88	82	55	49	27		
CVP (cm water)	5.5	4	4	9	10	10	10	9.5	10	13.5	15.5	16.5		
PAP (mmHg)	13	7	9	6	6	8	10	7	8	6	7	5		
PAWP (mmHg)	3	-3	-3	1	1	0	1	0	1	3	3	3		
Cardiac output (L/min)	3.61	3.55	3.75	2.08	1.72	2.06	2.48	2.02	1.82	1.01	0.78			
	3.18	3.37	3.52	1.83	1.53	1.94	2.02	1.85	1.66	0.91	0.71			
	3.35	3.21	3.59	1.89	1.55	1.97	1.98	1.81	1.59	0.94	0.7			
Stroke vol (ml)	21.1	15	16.6	8.2	7.2	10	11.4	10.7	10	4.9	3.8			
Hepatic A flow (ml/min)	265	174	181	106	90	99	103	88	96	79	47	3		
SVR (dyne . sec. cm-5)	2648	2485	2387	3948	3675	3759	3352	3423	3527	3779	4096			

TAMPONADE-NONALCOHOL (Pig 12)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.15	39.26	39.44	39.67	39.8	40.15	40.07	40.03	40.14	40.2	40.33	40.65		
Heart rate (beats/min)	205	214	225	240	219	205	236	232	241	246	271	272		
Mean BP (mmHg)	141	137	141	137	121	130	134	124	116	95	78	44		
CVP (cm water)	6	6	7	11	11.5	11.5	11.5	11.5	11.5	14	17	18		
PAP (mmHg)	18	19	19	19	18	20	21	19	20	20	21	21		
PAWP (mmHg)	5	8	7	9	10	10	10	11	12	12	15	15		
Cardiac output (L/min)	4.33	3.57	3.48	2.25	2.16	2.2	2.29	2.18	1.66	1.58	1.52	0		
	4.17	3.54	3.37	2.19	2.06	2.02	2.17	2.12	1.68	1.45	1.21	0		
	4.21	3.41	3.3	2.23	1.97	2.12	2.32	2	1.63	1.44	1.17	0		
Stroke vol (ml)	20.7	16.4	15	9.3	9.4	10.3	9.6	9.1	6.9	6.1	4.8			
Hepatic A flow (ml/min)	390	466	455	280	239	260	220	210	203	181	180	90		
SVR (dyne . sec. cm-5)	2575	3020	3213	4640	4364	4602	4438	4395	5175	4537	4015			

TAMPONADE-NONALCOHOL (Pig 15)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	37.3	37.9	37.8	37.9	38.1	38	38	38.1	38	37.6				
Heart rate (beats/min)	197	235	228	236	243	239	240	239	235	179				
Mean BP (mmHg)	93	81	84	69	58	50	64	68	40	26				
CVP (cm water)	5.5	2	5	8	10.5	11.5	11	11	12	13.5				
PAP (mmHg)	27	33	36	31	32	28	32	30	27	18				
PAWP (mmHg)	8	7	7	6	8	8	8	7	9	10				
Cardiac output (L/min)	1.85	1.48	1.47	1.08	0.77	0.92	1	1	0.58	0.18				
	1.56	1.37	1.22	0.87	0.69	0.93	0.87	0.95	0.52	0.18				
	1.56	1.4	1.45	0.98	0.63	0.86	1.01	0.91	0.58					
Stroke vol (ml)	8.4	6	6.1	4.2	2.9	3.8	4	4	2.4	0.7				
Hepatic A flow (ml/min)	112	88	71	58	67	79	90	87	57	19				
SVR (dyne . sec. cm-5)	4283	4479	4652	5143	5729	3678	4646	5032	4429	10583				

TAMPONADE-NONALCOHOL (Pig 16)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	36.7	37.2	37.4	37.5	37.9	37.9	38.1	38.4	38.5	38.5				
Heart rate (beats/min)	199	202	192	242	178	154	204	194	231	112				
Mean BP (mmHg)	128	124	128	83	57	36	87	113	102	27				
CVP (cm water)	5	5	5	8	9	9	11	11	10.5					
PAP (mmHg)	24	15	15	16	13	12	11	17	9	10				
PAWP (mmHg)	6	4	3	7	7	8	8	6	7	9				
Cardiac output (L/min)	3.33	2.62	2.4	1.5	0.99	1.1	1.24	1.4	1.57	0.39				
	3.18	2.51	2.39	1.24	0.84	1.18	1.17	1.42	1.34					
	3.11	2.35	2.23	1.23	0.84	1.21	1.14	1.32	1.31					
Stroke vol (ml)	16.1	12.3	12.2	5.5	5	7.5	5.8	7.1	6.1	1.2				
Hepatic A flow (ml/min)	84	69	58	34	45	32	63	61	57	13				
SVR (dyne . sec. cm-5)	3097	3863	4248	4667	4517	2017	5339	6072	5340	11077				

TAMPONADE-NONALCOHOL (Pig 18)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	37	37.5	37.7	37.8	38.2	38.5	38.8	38.9	39.1	39.3	39.4	39.5	39.5	39.3
Heart rate (beats/min)	145	163	169	191	186	192	204	194	194	180	166	170	172	300
Mean BP (mmHg)	112	121	123	116	118	127	123	122	108	64	38	45	38	37
CVP (cm water)	4	4	3.5	8	10.5	11	10.5	10.5	12	12.5	14	17.5	19	20.5
PAP (mmHg)	13	15	15	16	16	18	18	19	17	16	14	16	17	17
PAWP (mmHg)	3	2	2	6	6	7	8	7	8	10	11	12	12	13
Cardiac output (L/min)	3.61	3	3.25	2.25	2.35	2.93	2.55	2.75	1.7	1.19	0.87	0.82	0.58	
	3.23	2.95	3	2.02	2.18	2.65	2.16	2.55	1.58	1.1	0.88	0.85	0.64	
	3.29	3.3	3.05	1.99	2.11	2.57	2.25	2.61	1.61	0.92	0.9	0.8		
Stroke vol (ml)	23.3	18.9	18.3	10.9	11.9	14.2	11.4	13.6	8.4	5.9	5.3	4.8	24	
Hepatic A flow (ml/min)	159	112	126	100	88	80	72	84	64	77	60	62	38	8
SVR (dyne . sec. cm-5)	2580	3065	3106	4211	3986	3493	3983	3458	4859	4084	2500	3146	4829	

TAMPONADE-NONALCOHOL (Pig 20)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	38.6	39	39	39.1	39.4	39.5	39.6	39.5	39.6	39.5	39.6	39.7	39.8	39.9
Heart rate (beats/min)	151	177	173	199	198	196	200	198	214	192	197	200	211	230
Mean BP (mmHg)	138	133	135	131	129	121	124	121	103	85	111	61	62	54
CVP (cm water)	1	5.5	5.5	10	11	11.5	11	11	13	14.5	16	17.5	20	20.5
PAP (mmHg)	17	20	20	20	20	21	21	21	18	16	19	17	18	17
PAWP (mmHg)	5	3	4	7	7	7	7	7	9	9	11	13	14	14
Cardiac output (L/min)	3.65	3.92	3.83	2.81	2.69	2.88	3.08	3.33	2.22	1.49	1.45	1.03	1.02	0.37
	3.38	3.89	3.82	2.68	2.66	2.76	2.76	2.93	1.96	1.41	1.4	1.08	0.84	0.31
	3.6	3.69	3.7	2.72	2.62	2.49	2.61	3.09	1.85	1.36	1.44	1.21	0.79	
Stroke vol (ml)	23.4	21.6	21.8	13.8	13.4	13.8	14.1	15.8	9.4	7.4	7.3	5.6	4.2	1
Hepatic A flow (ml/min)	127	98	85	46	30	29	31	35	21	39	54	55	44	16
SVR (dyne . sec. cm-5)	3102	2692	2770	3606	3632	3317	3284	2819	3711	4176	5538	3477	4273	13522

TAMPONADE-NONALCOHOL (Pig 24)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.6	39.4	39.6	39.8	40	40.2	40.3	40.3	40.3	40.2	40.1	40.1	40.2	40
Heart rate (beats/min)	147	171	164	157	140	127	128	132	130	137	151	166		
Mean BP (mmHg)	112	127	127	123	112	110	110	116	108	102	100	40	35	49
CVP (cm water)	2	3	4	7	9	9	9	9	9	10	11	12	14	16
PAP (mmHg)	11	14	10	5	3	12	17	18	18	19	20	18	18	19
PAWP (mmHg)	2	2	0	-5	-3	5	9	9	10	11	13	13	15	16
Cardiac output (L/min)	4.7	6.2	6.1	4.6	3.7	3.8	4.2	4.2	3.6	3.3	3	1.9	1.5	1.3
	5	6.3	5.8	4.3	3.4	3.6	3.8	4.1	3.4	3	2.8	1.7	1.6	
	4.9	5.8	6.2	4.6	3.2	3.6	3.7	4	3.3	3.1	2.8	1.6		
Stroke vol (ml)	33.1	35.6	36.8	28.7	24.5	28.9	30.5	31.1	26.4	22.8	19	10.4		
Hepatic A flow (ml/min)	294	321	343	291	234	218	215	245	206	164	117	115	80	59
SVR (dyne . sec. cm-5)	1815	1641	1645	2093	2455	2251	2118	2132	2362	2415	2557	1434	1903	6884

SHAM-ALCOHOL (Pig 22)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	37	37.9	38	38.2	38.4	38.5	38.7	39	39.2	39.2	39.3			
Heart rate (beats/min)	148	125	129	147	161	161	173	160	151	150	153			
Mean BP (mmHg)	140	119	110	110	109	109	108	109	102	104	104			
CVP (cm water)	4.5	4.5	4	4	4.5	5	4.5	5.5	6	6.5	6.5			
PAP (mmHg)	15	-	11	6	3	6	9	6	3	4	4			
PAWP (mmHg)	3	6	5	1	1	0	0	0	0	-1	-1			
Cardiac output (L/min)	1.81	1.21	1.23	1.17	1.29	1.2	1.2	1.06	1.08	0.98	1.04			
	1.64	1.17	1.11	1.12	1.08	1.1	1.05	1.05	1.01	1.12	1.1			
	1.72	1.04	1.06	1.06	1.17	1.15	1.14	1.09	1.11	1.04	1.13			
Stroke vol (ml)	11.6	9.1	8.8	7.6	7.3	7.1	6.5	6.7	7.1	7	7.2			
Hepatic A flow (ml/min)	116	146	144	96	69	64	71	86	113	121	138			
SVR (dyne . sec. cm-5)	6355	8114	7575	7643	7161	7322	7407	7841	7290	7552				

SHAM-ALCOHOL (Pig 23)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39	40.5	40.5	40.4	40.3	40.3	40.2	40.3	40.3	40.3	40.2			
Heart rate (beats/min)	171	167	164	160	153	155	158	161	168	165	165			
Mean BP (mmHg)	135	129	126	127	124	115	117	122	116	114	114			
CVP (cm water)	4.5	6.5	6.5	6.5	6.5	6.5	7	7	6.5	7	7			
PAP (mmHg)	16	19	17	17	10	9	10	16	16					
PAWP (mmHg)	5	4	4	4	2	2	-1	6	5					
Cardiac output (L/min)	3.8	2.89	2.95	2.89	2.78	3.13	3.39	3.21	2.95	3.19	3.21			
	3.62	2.91	2.97	2.88	2.76	2.99	3.17	2.78	2.92	3.05	3.06			
	3.62	2.72	2.82	2.87	2.91	3.04	3.14	2.93	2.81	2.96	2.9			
Stroke vol (ml)	21.5	17	17.7	18	18.4	19.7	20.4	18.4	17.2	18.6	18.5			
Hepatic A flow (ml/min)	170	142	158	170	174	170	178	168	158	154	160			
SVR (dyne . sec. cm-5)	2861	3496	3330	3392	3379	2889	2768	3145	3076	2834				

SHAM-ALCOHOL (Pig 28)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.2	39.4	39.4	39.4	39.4	39.4	39.6	39.6	39.6	39.5				
Heart rate (beats/min)	163	142	140	137	136	136	137	148	143	144				
Mean BP (mmHg)	131	132	130	130	130	129	125	133	129	130				
CVP (cm water)	7	7	8	8	8	7	7	8	7	7				
PAP (mmHg)	30	24	23	21	20	20	21	20	21	21				
PAWP (mmHg)	10	11	13	10	9	10	11	10	11	11				
Cardiac output (L/min)	2.5	2.5	2.4	2.6	2.4	2.5	2.4	2.4	2.5	2.4				
	2.5	2.3	2.2	2.2	2.2	2.3	2.2	2.2	2.2	2.3				
	2.6	2.3	2.3	2.2	2.2	2.2	2.4	2.4	2.2	2.2				
Stroke vol (ml)	15.3	16.9	16.4	16.8	16.9	16.9	16.8	15.5	16.1	16				
Hepatic A flow (ml/min)	192	235	243	267	285	279	277	335	345	335				
SVR (dyne . sec. cm-5)	4024	4225	4313	4313	4313	4304	4165	4417	4304	4339				

SHAM-ALCOHOL (Pig 30)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.5	40.6	40.7	40.7	40.6	40.6	40.5	40.4	40.3	40.3				
Heart rate (beats/min)	104	121	120	121	122	126	130	133	136	136				
Mean BP (mmHg)	104	100	100	99	98	97	93	93	91	91				
CVP (cm water)	5	5	5	5	5	5	6	4	4	5				
PAP (mmHg)	18	19	20	19	20	20	20	20	19	19				
PAWP (mmHg)	7	6	7	7	7	7	7	6	6	6				
Cardiac output (L/min)	3.9	2.6	2.5	2.5	2.4	3	2.8	2.6	2.4					
	3.5	2.3	2.3	2.5	2.4	2.5	2.9	2.5	2.5					
	3.7	2.4	2.5	2.4	2.5	2.4	2.6	2.4	2.5					
Stroke vol (ml)	35.6	20.1	20.1	20.3	19.9	20.9	21.3	18.8	17.9	17.9				
Hepatic A flow (ml/min)	133	109	101	93	109	124	134	143	147	147				
SVR (dyne . sec. cm-5)	2168	3208	3208	3175	3142	2869	2529	2880	3133	2908				

SHAM-NONALCOHOL (Pig 21)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.2	39.4	39.5	39.5	39.5	39.5	39.3	39.4	39.4	39.5	39.5			
Heart rate (beats/min)	171	164	179	176	167	163	205	186	184	174	168			
Mean BP (mmHg)	148	150	150	141	137	136	145	138	134	136	136			
CVP (cm water)	5	4	4	4.5	4.5	4.5	5	5	5	5	5			
PAP (mmHg)	17	23	23	23	21	21	22	21	21	21	20			
PAWP (mmHg)	4	6	5	5	5	5	7	5	5	7	8			
Cardiac output (L/min)	4.71	3.63	4.11	4.3	3.93	4.14	4.71	4.5	4.57	4.57	4.58			
	4.28	3.54	3.91	3.87	3.84	3.86	4.43	4.53	4.57	4.36	4.1			
	4.61	3.77	4.07	3.85	3.87	3.84	4.19	4.32	4.55	4.34	4.12			
Stroke vol (ml)	26.5	22.3	22.5	22.8	23.2	24.2	21.7	23.9	24.8	25.4	25.4			
Hepatic A flow (ml/min)	244	188	202	220	225	245	280	274	265	268	273			
SVR (dyne . sec. cm-5)	2547	3222	2918	2746	2755	2686	2545	2413	2285	2394				

SHAM-NONALCOHOL (Pig 25)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.7	40.3	40.3	40.4	40.5	40.6	40.5	40.3	40.3	40.3	40.2			
Heart rate (beats/min)	176	150	150	147	142	142	135	132	127	127	129			
Mean BP (mmHg)	155	136	136	132	129	115	120	113	113	116	116			
CVP (cm water)	1	4	4	4	5	6	5	6	6	6	6			
PAP (mmHg)	36	34	35	35	39	46	51	52	55	56	55			
PAWP (mmHg)	16	21	20	20	28	36	37	39	40	40	41			
Cardiac output (L/min)	5.5	4.9	5	5.1	4.9	4	4.2	4.6	4	4.3	3.9			
	5.7	4.6	4.9	4.7	4.6	3.8	4.2	4.5	3.7	3.9	3.8			
	5.6	4.6	4.8	4.5	4.5	4	4.2	4.6	3.5	3.7	3.7			
Stroke vol (ml)	31.8	31.3	32.7	32.7	33.1	27.5	31.1	34.8	29.1	31.5	29.5			
Hepatic A flow (ml/min)	285	345	312	302	301	278	297	280	288	284	295			
SVR (dyne . sec. cm-5)	2204	2264	2171	2150	2132	2267	2214	1887	2346	2230				

SHAM-NONALCOHOL (Pig 27)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.6	39.7	39.7	39.6	39.6	39.6	39.6	39.7	39.7	39.7				
Heart rate (beats/min)	179	166	157	143	144	142	140	137	140	141				
Mean BP (mmHg)	110	114	115	118	113	114	113	112	114	114				
CVP (cm water)	6.5	6.5	6.5	6.5	6.5	6.5	6	6.5	6	6				
PAP (mmHg)	19	25	27	28	25	28	27	28	26	26				
PAWP (mmHg)	5	16	17	17	16	17	17	17	17	17				
Cardiac output (L/min)	5.5	4.8	5.2	5.5	4.9	5.3	4.8	5	5	4.6				
	5.6	4.9	5	5	4.9	4.6	4.6	4.6	4.6	4.4				
	5.9	5.1	5.2	4.7	4.8	4.4	5	4.4	4.6	4.6				
Stroke vol (ml)	31.8	29.5	32.5	36.4	34	33.8	34.3	34.3	33.6	31.9				
Hepatic A flow (ml/min)	128	132	131	140	144	157	172	166	182	193				
SVR (dyne . sec. cm-5)	1453	1782	1727	1740	1765	1819	1808	1823	1864	1947				

SHAM-NONALCOHOL (Pig 29)

Pericardial pressure	Baseline	0 cm	5 cm	10 cm	10 cm	10 cm	10 cm	10 cm	12 cm	14 cm	16 cm	18 cm	20 cm	22 cm
Time	0 min	1 hour	1hr10min	1hr20min	1hr35min	1hr50min	1hr65min	1hr80min	1hr90min	1hr100min	1hr110min	1hr120min	1hr130min	1hr140min
Temp (degrees C)	39.9	39.8	39.8	39.7	39.8	39.9	39.9	39.9	39.9	39.6				
Heart rate (beats/min)	149	149	148	137	139	131	142	132	150	142				
Mean BP (mmHg)	152	148	148	147	149	135	138	146	138	130				
CVP (cm water)	5	5	5	5	5	7	7	7	6	6				
PAP (mmHg)	20	15	15	15	15	17	18	18	20	20				
PAWP (mmHg)	7	6	6	6	6	6	6	7	6	7				
Cardiac output (L/min)	3.3	2.7	2.8	2.9	2.8	2.7	3	2.9	3.4	3.1				
	3.2	2.6	2.7	2.7		2.5	2.9	3	3.1	3.2				
	3.3	2.5	2.7	2.8		2.4	2.9	3		3				
Stroke vol (ml)	22.1	17.4	18.2	20.4	20.1	19.1	20.4	22.7	21.7	21.8				
Hepatic A flow (ml/min)	135	147	147	146	146	146	151	145	150	142				
SVR (dyne . sec. cm-5)	3594	4438	4274	4093	4150	4152	3662	3753	3286	3239				