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**Predictors of survival in patients requiring IABP
support following cardiac surgery**

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Dedication

To my wife Shanaz for her continuous support and encouragement throughout the study

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Abbreviations

AD	Adrenaline
ACC time	Aortic Cross Clamp Time
ACT	Activated Clotting Time
AK 200	Renal Dialysis System
AVC	Aortic Valve Closure
AVO	Aortic Valve Opening
AVR	Aortic Valve Replacement
BMI	Body Mass Index
BW	Body Weight
CABG	Coronary Artery Bypass Graft
CAS	Carotid Artery Stenosis
CPB	Cardiopulmonary Bypass
CI	Cardiac Index
CK	Creatine Kinase
CPR	Cardiopulmonary Resuscitation
CVP	Central Venous Pressure
CVVH	Continuous Veno-Venous Hemofiltration
DPTI	Diastolic Pressure Time Index
ECC	Extracorporeal Circulation
ECG	Electrocardiogram
ECMO	Extracorporeal Membrane Oxygenation
EF	Ejection Fraction
Exp (B)	Exponent of the B-coefficient
FiO ₂	Fraction of Inspired Oxygen
HIT	Heparin Induced Thrombocytopenia
HLM	Heart-lung Machine
HOCM	Hypertrophic Obstructive Cardiomyopathy
IAB	Intraaortic Balloon
IABP	Intraoartic Balloon Pump

ICU	Intensive Care Unit
IQR	Interquartile Range
MAP	Mean Arterial Pressure
MARS	Molecular Adsorbent Recirculating System
mPAP	Mean Pulmonary Artery Pressure
MVR	Mitral Valve Replacement
LAP	Left Atrial Pressure
LBBB	Left Bundle Branch Block
LOS	Low Cardiac Output Syndrome
LVAD	Left Ventricular Assist Device
LVEDP	Left Ventricular End Diastolic Pressure
OPCAB	Offpump Coronary Artery Bypass
PAWP	Pulmonary Artery Wedge Pressure
PTCA	Percutaneous Transluminal Angioplasty
PTT	Partial Thromboplastin Time
RVAD	Right Ventricular Assist Device
SD	Standard Deviation
SIRS	Systemic Inflammatory Response Syndrome
SvO ₂	Mixed Venous Oxygen Saturation
SVR	Systemic Vascular Resistance
TAH	Total Artificial Heart
TTI	Tension Time Index
TVR	Tricuspid Valve Replacement
UO	Urine Output
VAR	Ventricular Aneurysm Resection
VF	Ventricular Fibrillation
VSD	Ventricular Septal Defect

1. Introduction

Despite continuous expansion of interventional cardiological procedures, cardiac surgery remains the only life-saving treatment in a significant number of patients with heart disease. Continuous development of surgical and anaesthetic procedures yield positive surgical results, enabling elderly patients to have necessary surgeries (Warner et al., 1997). However low cardiac output and cardiogenic shock are serious and life-threatening complications of this surgery (Baskett et al., 2002).

The intra-aortic balloon pump (IABP) is the most commonly used mechanical assist device in cardiac surgery. The device is used to support patients with low cardiac output. Through an enhancement of stroke volume and favourable diastolic effects, IABP use can increase cardiac output by 20% (Baskett et al., 2002).

The intra-aortic balloon pump has been widely used in the last 40 years to support a number of patients who exhibit any of the following risk factors for heart failure, such as left main stem disease, low ejection fraction, medical refractory unstable angina, and redo surgery (Christenson et al., 1997; Christenson et al., 1999). IABP has been used also to wean patients from the heart lung machine, or to assist postoperative patients after hemodynamic deterioration. According to previous studies, the incidence of IABP use in cardiac surgery ranges between 1.5-17% (Torchiana et al., 1997; Vigneswaran et al., 1985).

However despite the use of IABP, mortality remains high in these patients, either because of multiple risk factors present before the operation or due to the occurrence of either intra- or postoperative complications.

In patients receiving IABP intra- or postoperatively, outcomes tend to be worse than in those receiving IABP preoperatively (Baskett et al., 2002). While preoperative IABP support is usually associated with survival rates of more than 74%, intra- and postcardiotomy IABP support is associated with an overall survival of only 55% (range: 27% to 89%) (Baskett et al., 2002). It has been demonstrated that 40% of the patients receiving an intraoperative IABP ultimately require a ventricular assist device (McGee et al., 1980). Some of these patients are bridged to heart transplantation (Korfer et al., 1996; Loebe et al., 1997), while others receive a ventricular assist device (VAD) as destination therapy, and still a significant number of other patients are successfully weaned from VAD (Hausmann et al., 2002; Loebe et al., 1999).

There are several studies which analyze risk factors of those patients with high mortality after IABP Implantation (Aksnes et al., 1996; Corral et al., 1986; Davies et al., 2001; Hausmann et al., 2001; Naunheim et al., 1992), but these studies lack evaluation of the difference in hemodynamic data and catecholamine doses after IABP implantation with regard to their effect on survival. In one study Ota et al. shows differences in early postoperative cardiac index between CABG and valve operations without measuring other hemodynamic data and catecholamine requirement with regard to their effect on survival (Ota et al., 1992). Moreover, an IABP score which includes adrenaline requirement, left atrial pressure, urine output, and mixed venous saturation, has recently been developed to predict survival early after IABP implantation in cardiac surgery (Hausmann et al., 2002).

Although the IABP score has been validated at the heart centre where it was developed (Hausmann et al., 2002), the usefulness of this score for other heart centres is unclear at present.

It was the aim of this investigation (I) to find predictors of mortality in patients who required IABP intra- or postoperatively, (II) to develop an IABP score in order to predict survival early after IABP implantation, and (III) to assess the early course of hemodynamic parameters and catecholamine requirement in patients who survived the first 30 days after IABP implantation in comparison with non-survivors.

1.1 History of IABP

In 1958, Harken described for the first time a method to treat left ventricular failure by using counterpulsation or diastolic augmentation. He suggested removal of a certain blood volume from the femoral artery during systole and then rapid replacement of this volume during diastole. By increasing coronary perfusion pressure, this concept would augment cardiac output and unload the functioning heart simultaneously (Harken, 1958; Harken, 1976). This method of treatment was limited because of problems with access (need for arteriotomies of both femoral arteries), turbulence and development of massive hemolysis by the pumping apparatus. Even experimental data showed that no augmentation of coronary blood flow was obtained (Dormandy et al., 1969).

Then in the early 1960s Moulopoulos et al. from the Cleveland Clinic developed an experimental prototype of the intra-aortic balloon (IAB) whose inflation and deflation were timed to the cardiac cycle (Moulopoulos et al., 1962; Moulopoulos et al., 1962). In 1968, the initial use in clinical practice of the IABP, and its continued improvement was advanced by Kantrowitz's group (Kahn et al., 1990; Kantrowitz et al., 1968).

In its first years, the IABP required surgical insertion and surgical removal with a balloon size of 15 French. In 1979, after subsequent development in IABP technology, a dramatic headway with the introduction of a percutaneous IAB with a size of 8.5 to 9.5 French was achieved (Bregman, 1980; Hauser et al., 1982). This advance made it possible, even for nonsurgical personnel, to perform an IAB insertion at the patient's bedside. In 1985, the first prefolded IAB was developed.

Today, continued improvements in IABP technology permit safer use, and earlier intervention to provide hemodynamic support. All these progresses have made the IABP a mainstay in the management of ischemic and dysfunctional myocardium.

1.2. Basic Principles of IABP

IABP is instituted by insertion of a distensible polyurethane, nonthrombogenic balloon (usually 40 cc) in the descending thoracic aorta. The balloon is passed retrogradely to a position in situ just below the left subclavian artery, but above the renal arteries. The tip of the catheter is visible radiographically as an opaque rectangle, 3x4 mm, paralleling the walls of the descending aorta. An IABP is correctly positioned with this tip in the proximal descending aorta just below the left subclavian artery (Figure 1).

The balloon is mounted on a vascular catheter, which has multiple pores (Figure 2). Helium gas is shuttled from the balloon pump console into the balloon catheter, before escaping through the pores, and finally inflating the balloon. Helium has a low molecular weight, which minimizes shuttle transfer time, and thus increases system efficiency.

Inflation occurs immediately upon onset of diastole. Deflation occurs during isometric contraction or early systole (Figure 1).

Arterial entry is acquired usually through a femoral artery, but axillary artery or open chest proximal aortic insertions are alternative options. Femoral insertion is most often accomplished percutaneously, but can be achieved also via an arterial cut down.

1.2.1. Impact of Counterpulsation on the Arterial Pressure Waveform

Elevation of intra-aortic pressure during diastole is termed *diastolic augmentation*. This action is reflected by an increase in diastolic arterial pressure, which becomes the highest pressure point of the arterial waveform. Deflation occurs during isometric contraction, since balloon inflation displaces intra-aortic balloon volume, and aortic end-diastolic pressure is lowered during IAB deflation. Console instrumentation allows the operator to adjust points of inflation-deflation manually within defined safety limits in an effort to maximize hemodynamic benefits to the patient. Although the ECG is used in triggering the pump, it is the arterial pressure waveform that must be used to "time" counterpulsation and assess its benefit on the patient's hemodynamics.

1.2.2. Timing of IABP

IABP timing is performed from the ECG or the arterial waveform.

1. *ECG*: Input to the balloon console is provided from skin leads or the bedside monitor. Inflation is set for the peak of the T wave at the end of systole with deflation set just before or on the R wave. The use of bipolar pacing eliminates the interpretation of pacing spikes as QRS complexes by the console.
2. *Arterial waveform*: Inflation should occur at the aortic notch with deflation just before the onset of the aortic upstroke. This method is especially useful in the operating room where electrocautery may interfere with the ECG signal.

1.2.3. Effects of IABP on Myocardial Oxygen Supply and Demand

The primary physiological impact of IABP is on myocardial oxygen supply/demand. Oxygen supply is determined by patency of coronary arteries, autoregulation, diastolic perfusion gradient (Aortic diastolic pressure minus left ventricular end diastolic pressure), and the diastolic pressure time index (DPTI). Balloon counterpulsations effect on improving oxygen supply is best appreciated by examining the diastolic pressure time index (DPTI) and tension time index (TTI) (Moccetti et al., 1982; Philips et al., 1975).

The adequacy of the subendocardial perfusion can be predicted by calculating myocardial supply/demand ratio, defined as the ratio of DPTI divided by the systolic pressure TTI. (Figure 3)

Online monitoring of TTI and DPTI (myocardial oxygen supply/demand) ratios is useful as an indicator of adequate left ventricular subendocardial blood flow as impacted by IABP.

The subendocardial layer receives most or all of its oxygen supply during diastole (Alcan et al., 1984). As a response to myocardial ischemia, coronary vasodilatation occurs, and subendocardial perfusion becomes pressure dependent (Alcan et al., 1984). Myocardial blood flow is regulated by forces affecting aortic diastolic pressure, left ventricular end diastolic pressure, or diastolic duration. DPTI depends upon the pressure-time relationship of these factors and therefore can be used to estimate diastolic and subendocardial blood flow (Alcan et al., 1984).

Intraaortic balloon inflation increases DPTI and myocardial oxygen delivery. Therefore, IABP provides physiologic assistance to the failing heart by decreasing myocardial oxygen demand or unloading the heart by rapid deflation just before ventricular systole and improving coronary perfusion through rapid inflation, just after aortic valve closure (Lazar et al., 1992; Naunheim et al., 1992).

1.2.4. Impact of Balloon Inflation in Diastole on Coronary Artery Perfusion

Coronary perfusion is potentially increased as the balloon inflates in diastole (Figure 3). Effective augmentation of coronary perfusion, however, depends on the degree of vasodilatation within the coronary bed. Myocardial ischemia is a potent stimulus for increasing blood flow and oxygen delivery to the myocardium through vasodilatation. Balloon inflation displaces blood proximally, potentially increasing coronary perfusion. IABP thus can potentially improve coronary perfusion by increasing diastolic pressure and the diastolic perfusion gradient. Coronary artery flow will increase in proportion to pressure rise.

(A) LV Diastole

(B) LV Systole

Figure 1: (A) Balloon inflation during left ventricular diastole increases proximal coronary and cerebral perfusion. (B) Balloon deflation during LV systole decreases LV afterload and myocardial oxygen demand.

Figure 2: The intraaortic balloon is mounted on a vascular catheter, which contains multiple pores.

Figure 3: Schematic representation of coronary blood flow, aortic, and left ventricular pressure wave form with / without IABP. (Effects on DPTI and TTI)

- a) Inflation of the balloon during diastole (augmentation of the aortic diastolic pressure) increases coronary blood flow (DPTI).
- b) Deflation of the balloon occurs just prior to the onset of systole and reduces impedance to left ventricular ejection (TTI).

1.3. Indications

The currently accepted indications for IABP use have expanded to include (Baskett et al., 2002):

1. Ongoing unstable angina refractory to medical therapy
2. Acute myocardial ischemia/infarction associated with percutaneous transluminal angioplasty (PTCA). The criteria for prophylactic IABP implantation before PTCA include (Kahn JK, 1991):
 - a. Left ventricular EF $\leq 30\%$
 - b. Angioplasty of the only functional coronary artery
 - c. Multivessel angioplasty in patients with hypotension
 - d. Left main coronary artery angioplasty, when the left main artery is unprotected by a patent graft
3. Perioperative low cardiac output syndrome
4. Cardiogenic shock after myocardial infarction
5. Congestive heart failure
6. Bridge to heart transplant
7. Ischemic ventricular septal defect
8. Acute mitral valve insufficiency
9. Poorly controlled perioperative ventricular arrhythmias

Although most physicians accept many of these indications, the decision to use an IABP and the timing of its use are not generally agreed.

1.4. Contraindications

The following contraindications of IABP use are well established:

1. Thoracic or abdominal aortic aneurysm
2. Aortic insufficiency
3. Severe pre-existing peripheral vascular disease
4. Lack of definitive therapy for underlying pathology

1.5. Timing of IABP Insertion with Regard to the Operation

The optimal timing of IABP insertion in cardiac surgeries remains controversial and poorly defined (Baskett et al., 2002; Holman et al., 2000). Some of the controversy concerns the definition of a high risk patient. However, much of the benefit derived from preoperative insertion and use of the IABP may be the result of improved myocardial perfusion and stability in the induction of anaesthesia in the early operative period before commencing bypass (Christenson et al., 1997; Gutfinger et al., 1999).

There are some reports which conclude that preoperative IABP insertion in high-risk CABG patients decreased mortality and postoperative length of stay (Christenson et al., 1997; Christenson et al., 1999). High risk was defined as any two of the following: medically refractory unstable angina, ejection fraction $\leq 40\%$, left main stenosis $\geq 70\%$, or redo surgery.

In conclusion, there is class I level "A" evidence that preoperative IABP use in ischemic CABG patients is beneficial. There is class I level "B" evidence for preoperative IABP use in CABG patients with ejection fraction $\leq 25\%$ who are undergoing nonelective operations or reoperation, or who have New York Heart Association class III-IV symptoms (Dietl et al., 1996).

Intraoperative and postoperative IABP insertion is an indication of serious complications, which are often not correctable. Therefore, these patients face a high mortality.

Intraoperative balloon use for weaning from cardiopulmonary bypass is well established, although the specific indications are hard to analyze.

An IABP inserted for low cardiac output rather than ischemia is clearly associated with poorer prognosis (Corral et al., 1986; Torchiana et al., 1997).

In Heart and Diabetes Centre North-Rhine-Westfalia, IABP is used preoperatively in the presence of the aforementioned risk

factors. Meanwhile, it is used intraoperatively to wean patients from the cardiopulmonary machine during medical refractory cardiogenic shock. Postoperatively, the IABP is utilized as the initial mechanical support for patients having low output syndrome (LOS) despite high dosage of inotropics, or after unsuccessful cardiopulmonary resuscitation (>30 minutes), or in patients with recurrent ventricular fibrillation, or prophylactic in patients with postoperative significant ST elevation in ECG. Ultimately, IABP is sometimes used to induce pulsatility in patients with ECMO.

1.6. IABP Complications

The following items are reported as complications related to IABP insertion:

1. Inability to inflate balloon: This could occur due to:

- Unipolar atrial pacing (Interpretation of atrial pacing spikes as QRS complex by the console, resulting in ineffective pumping)
- Rapid cardiac rate
- Arrhythmias
- Volume loss from the balloon detected by the console monitor alarms
- Balloon rupture

2. Vascular complications:

- Aortic dissection or rupture of the iliac artery or aorta
- Embolisation to visceral vessels, especially renal arteries
- Distal ischemia
- Paraplegia

3. Thrombocytopenia

Complications are reported to be primarily associated with the insertion process rather than pumping, removal, or post removal monitoring (Alcan et al., 1983; Kantrowitz et al., 1986). The clinicians technical skills and experience, catheter stiffness, catheter -induced arterial trauma, or combination of thrombotic occlusion and thromboembolism (Alpert et al., 1980) have been implicated as sequelae related to insertion.

The predisposing factors include: gender (more complication in women), age (increased risk with increasing age), pre-existing peripheral vascular disease, duration of IABP therapy, *diabetes mellitus*, method of insertion (percutaneous insertion associated with lower complication rate as open surgical technique), and finally sheathed insertion of the catheter. Other risk factors are also reported, such as hypertension, smoking, obesity, low cardiac index, and elevated systemic vascular resistance (Cohen et al., 2000; Gottlieb et al., 1984; Kantrowitz et al., 1986; Miller et al., 1992; Tatar et al., 1993).

2. Materials and Methods

2.1 Definitions

Abdominal Operations: This refers to laparotomies, performed due to intestinal ischemia.

AF: This acronym is defined as "atrial fibrillation," diagnosed on basis of preoperative ECG.

CVVH (Continuous Veno-Venous Hemofiltration): This technique is performed using an AK 200 machine for patients with oligo-anuria and or patients with high serum creatinine (>8 mg/dl) or blood urea nitrogen (BUN) (>200 mg/dl).

Death after IABP Implantation: This description is used for patients who died in the Heart and Diabetes Centre, North-Rhine-Westfalia and in other hospitals after discharge.

DM: Includes patients with diet, drug controlled, or insulin controlled *diabetes mellitus*.

Emergency Operation: The term "emergency" refers to an operation which occurs directly after diagnosis either due to instable *Angina pectoris* or hemodynamic instability or PTCA induced main stem dissection.

Intraoperative IABP: The IABP device is implanted in the operating room, outside the ICU.

LOS: This acronym refers to "low output syndrome" defined as cardiac index ≤ 2.2 L/min/m².

LBBB: ECG findings of prolonged QRS interval ≥ 120 ms, deep S waves in lead V1, and RsR' waves in lead V6.

MARS (Molecular Adsorbent Recirculating System): This modified dialysis uses an albumin containing dialysate, which is recirculated and perfused online through charcoal and anion exchanger columns. It allows the selective removal of albumin bound substances, and it has been used for patients with high bilirubin values (≥ 10 mg/dl).

Paralytic Ileus: Describes nonmechanical obstruction of the bowel due to paralysis of the bowel wall. It is diagnosed on

the basis of clinical signs with radiological and-or sonographic findings.

Perioperative Myocardial Infarct(PMI): PMI is diagnosed on the basis of perioperative Troponin value of ≥ 15 U/l.

Pneumonia: Pneumonia is diagnosed on the basis of radiological findings of lung infiltrations with clinical signs of infection.

Postoperative Renal Insufficiency: This is defined by either serum creatinine levels ≥ 2 mg/dl and-or CVVH requirement.

Postoperative Liver Insufficiency: This is defined by either bilirubin values of ≥ 2 mg/dl and-or MARS requirement.

Preoperative Myocardial Infarct: This diagnosis pertains to patients with Troponin positive acute coronary syndrome with or without ECG change.

Preoperative Renal Insufficiency: This is defined as patients with preoperative creatinine value of ≥ 2 mg/dl and-or renal dialysis requirement.

Redos: This refers to patients with previous heart operations.

Rethoracotomy: This refers to an additional thoracotomy after the initial cardiac operation due to significant bleeding, pericardial tamponade, or hemodynamic instability with requirement of ECMO or VAD.

Septicemia: This is defined by SIRS in addition to the presence of positive blood culture, urine culture, and-or tracheal secrete culture.

Significant Main Stem Stenosis: Main stem stenosis is characterized by $\geq 70\%$ stenosis, as obtained from coronary angiography.

Significant Carotid Stenosis: This is defined as internal carotid artery stenosis of $\geq 75\%$, as diagnosed using carotid doppler.

Significant Postoperative ECG Change: It is defined as ST elevation in two or more ECG leads or in the presence of a new left bundle branch block.

Significant ST Elevation: This refers to new ST elevation in two or more contiguous leads that is > 0.2 mV.

SIRS: Systemic Inflammatory Response Syndrome is diagnosed by the presence of two or more from the followings:

- Heart rate >90 beats per minute
- Body temperature <36 °C (96.8 °F) or >38 °C (100.4 °F)
- Hyperventilation (high respiratory rate) >20 breaths per minute or, on blood gas, a PaCO₂ <32 mm Hg
- White blood cell count <4000 cells/mm³ or >12000 cells/mm³

2.2. Patients

A retrospective analysis was performed between January 2002 to January 2004 in the department of thoracic and cardiovascular surgery (Heart Centre North Rhine-Westphalia, Ruhr University of Bochum, Germany) to identify patients who received IABP intra and postoperatively, excluding patients who acquired IABP preoperatively or else following heart transplantation.

We identified 140 patients from a total number of 7872 operations (1.77%). In four patients (2.85%), IABP was implanted to generate pulsatility after ECMO implantation, and the hemodynamic data from these patients as well as another 19 patients (13.57%), who required ECMO, were excluded later from the analysis.

Later, prospective evaluation of the newly developed score system was performed for another 145 patients who required IABP either intra or postoperatively between January 2004 and December 2005.

2.3. Methods

A chart review of the patients from local hospitals' archive was performed to discover relevant clinical information.

Data regarding a number of variables were recorded. Preoperative variables were as follows: patients' weight, BMI, age, sex, diagnosis, surgery type, presence of significant main stem disease and percentage of the stenosis, *diabetes mellitus*,

atrial fibrillation, presence of significant carotid stenosis, history of myocardial infarction in the last four weeks, emergency operation, redos, peripheral vascular disease, preoperative renal dialysis requirement, preoperative NYHA class, left ventricular function measured with transthoracic echocardiogram using the planimetric method, and preoperative serum creatinine, measured in mg/dl.

Intra and postoperative variables recorded include: CPB time, ACC time, implantation indication, implantation place (Intraoperatively or in ICU), rethoracotomy, time between admission and IABP implantation, postoperative ECG change, postoperative venous saturation and urine output in the first and at the sixth hour following implantation, postoperative maximum CK, CK-MB, troponin value in U/L, postoperative maximum creatinine in mg/dl, bilirubin in mg/dl, lactate in mmol/L, duration of support, duration of mechanical ventilation, requirement of CVVH or MARS, ECMO (femoro-femoral or transthoracic) and/or VAD (Ventricular assist device) implantation and the type implanted. Postoperative ileus, abdominal operations, septicemia, pneumonia, IABP complication, neurological findings at discharge, and finally duration of ICU stay and total follow-up time were recorded also.

The above mentioned variables were analyzed using Cox regression analysis to identify independent risk factors for mortality.

Afterward, patients who received ECMO after IABP were excluded from the second statistical analysis which included the hemodynamic data and catecholamine requirements. Reasons behind the exclusion stemmed from the performance of most ECMO implantations within one hour after IABP implantation, not to mention the inability to compare hemodynamic data between IABP patients and the ECMO patients. Moreover, it is common practice to reduce the catecholamine doses of patients after ECMO implantation.

The hemodynamic variables, which had been measured from pulmonary artery and systemic arterial catheters, were recorded at 1 hour, 6 hour, 12 hour, and 24 hour intervals, following IABP implantation. The doses of catecholamines required at different times were recorded as well. The variables available within the first 24 hours after IABP implantation were tested using Cox regression analysis in regard to their effect on 30 day mortality. A new score system could be developed from the results of this analysis.

Lastly, after developing the new score system, we prospectively evaluated it for another 145 patients who received IABP either intra or postoperatively between January 2004 and December 2005.

At the Heart and Diabetes Centre, North-Rhine-Westfalia, the pulmonary artery catheter is not used routinely. It is only implanted if there are signs of low output syndrome (LOS) such as oliguria, lactate acidosis, cool periphery, low blood pressure, and $SvO_2 < 60\%$. Ultimately, there was a small group of patients (n=15), who lacked a pulmonary catheter even after IABP implantation.

In July 2005, patients were contacted in order to assess long-term survival. In patients who died during the follow-up period, we requested the medical report from the family physicians or from the emergency hospital to determine the date of death. Causes of death were documented as well.

2.4. Anaesthesia

All patients, except emergency cases, received Lormetazepam (1-3mg dose), Morphine sulphate (7.5-15mg), and Dehydrobenzperidole just one hour before the operation as premedication. Anaesthesia was performed with narcotics, such as Fentanyl (0.1-0.4 mg) and one intravenous anesthetic for example Etomidat or Midazolam, and then the patients were intubated after muscle relaxation. In emergency cases, anaesthesia was carried out with Fentanyl and Midazolam, and only small concentrations of inhalational anaesthetics. After operation, all patients were transferred to the ICU and extubated as soon as possible. Generally, patients that received IABP on basis of resuscitation were extubated relatively late compared with patients who received IABP for other indications. Of course, extubation was performed only in the presence of stable hemodynamics.

2.5. Operation details

All procedures were done under mild hypothermia (Blood temperature 27-34 °C) and hemodilution (Hb 7-10 g/dl) with membrane oxygenation. Anticoagulation performed with heparin (400 I.E./kg), and the effect was controlled by measuring ACT (Activated Clotting Time) every 20 minutes.

The operations were performed with non-pulsatile perfusion, except in patients with significant internal carotid artery stenosis ($\geq 75\%$ stenosis), in which pulsatile perfusion was used.

The extracorporeal circulation (ECC) flow rate ranged between (2.2-2.6 L/min/m²) and the mean perfusion pressure ranged between 40-90 mm Hg. The ECC was performed on pH-stat-basis.

Perioperative antibiotic prophylaxis was performed with Cephazolin (2 gm) prior to skin incision, and it was given for merely one day after CABG operations, for one week following

valve operations, and up to six weeks in patients with endocarditis.

2.6. Anticoagulation

Anticoagulation in patients with IABP was started postoperatively with heparin in absence of significant thoracic bleeding (i.e. when the amount of bleeding ≤ 50 ml/hr). Heparin effect was monitored using PTT with target PTT of 1.5-2 times control. In patients with HIT (Heparin Induced Thrombocytopenia), thrombininhibitors such as, Lepirudin (Refludan) or more recently Argatroban, were used.

2.7. Insertion techniques

A. Percutaneous insertion: Percutaneous insertion is performed by the Seldinger technique, placing the balloon through a sheath and over a guidewire. Generally, the sheath can be left in place or removed from the artery. Only "sheathless" systems were used in the Heart and Diabetes Centre, North-Rhine-Westfalia, to minimize occlusion of the femoral vessels, and the balloon is placed just distal to the left subclavian artery. Use of small (8 French), sheathless catheters, and percutaneous insertion is associated with less complications (Elahi et al., 2005).

B. Surgical insertion: This is accomplished through exposure of the femoral artery and placement of the balloon through a sidearm graft or directly into the vessel, through an arteriotomy or a percutaneous sheath. The transthoracic balloon is inserted via the ascending aorta and the patients are transferred to the ICU with open chest until hemodynamic stabilization (usually after 2-4 days). Then, IABP is removed surgically, and the chest is closed.

In the majority (94.3%) of patients, IABP was inserted via the femoral artery using the Seldinger technique. Transthoracic implantation was performed in four patients (2.85%), and open surgical implantation was performed in only four patients (2.85%) as well.

Two types of commercially available IABP systems were used Datascope (97E, 98XT, and CS100) (Datascope Corporation, Oakland, New Jersey, USA) and Arrow (Auto CAT 2 WAVE and ACAT 1 PLUS) (Arrow Deutschland, Erding, Germany). It is noteworthy that the majority of implanted IABP were from the Datascope company.

2.8. IABP removal

A percutaneous IABP was removed without exposing the femoral puncture site. The balloon catheter was disconnected from the pump and completely deflated using a 50-mL syringe. Using steady pressure over the femoral puncture site, the balloon catheter was withdrawn smoothly, and pressure was maintained over the puncture site for 30 minutes using a special compression device (Pilote). Then, pressure was reduced until reaching a pressure lower than systolic blood pressure. If the balloon was inserted via a cut-down, the balloon was removed in the operating room. The puncture site was closed with sutures. If blood flow to the lower limb was impaired after removal, a local thromboembolectomy using Fogarty catheters and an angioplasty procedure using a vein patch is performed.

3. Statistics

Data was analyzed using SPSS software (SPSS for Windows version 11.0, SPSS Inc.; Chicago, IL). Normal distribution of the data was tested using Kolmogorov-Smirnov test. Normal distribution was considered with p value above 0.05. Cox regression test was applied for univariate analysis of the parameters with regard to their effect on survival. Those parameters demonstrating a marginal significance of $p < 0.1$ were included in multivariate stepwise analysis (Cox regression test) to detect independent predictors of survival. A p value of ≤ 0.05 was considered to be significant. Survival rates were calculated with the Kaplan-Meier product-limit estimator.

In order to assess differences in the hemodynamic data and catecholamine doses between survivors and non survivors, patients who required ECMO after IABP were excluded. The unpaired student t test for normally distributed data and Man Whitney test for not-normally distributed data were used to compare these variables in regard to their effect on 30 day mortality. Time effect within the study groups were evaluated using the Friedman test. For the purpose of finding earlier predictors of survival, the association of statistically significant factors, which were available within the first 24 hours after IABP implantation with 30 day mortality, were tested again in a univariate Cox regression model. Every univariate variable showing marginal significance ($P \leq 0.1$) was then tested in a Cox multivariate model and removed stepwise if no significant influence was discovered. A p -value ≤ 0.05 was considered statistically significant. Based on coefficients of the multivariate analysis, an IABP score formula was determined. All patients were scored using this formula. Data are expressed as mean with standard deviation or median with interquartile range.

4. Results

4.1. Characteristics of the patients:

Between January 2002 to January 2004, 140 patients, from a total of 7872 operations at the Heart Centre, Bad Oeynhausen, received IABP intra or postoperatively (1.77%). Seventy eight patients (55.71%) could be successfully weaned and discharged, while 62 patients (44.28%) died in our ICU. Early mortality (30 days) was 45.7%, median ICU duration was 7 days (IQR: 4-17 days), and mean follow-up time was 337.63 days (± 405.54 SD). One year mortality rate was 55.71% (n=78), while two year mortality rate reached 58.57% (n=82).

Patient age ranged between 37-90 years (mean 69.19 ± 9.4 SD), 75 patients (53.6%) were ≥ 70 years old. There were 72 males (51.42%) and 68 females (48.57%), with body weight ranging from 43-109 kg (mean 74.14 ± 3.36 SD), and BMI ranging between 17.22-39.54 kg/m² (mean 26 ± 3.6 SD). Preoperative measurements recorded EF ranging between 17-87% (mean 53.31 ± 16 SD), 25 patients (17.85%) had EF $\leq 35\%$ before the operation; 50 patients (35.71%) had *diabetes mellitus* preoperative; 31 patients (22.14%) had atrial fibrillation; 25 patients (17.85%) had significant main stem stenosis $\geq 70\%$; 40 patients (28.57%) were redos. In 21 patients (15%), the operations were performed on emergency basis, and 27 patients (19.28%) experienced myocardial infarction in the last 4 weeks before operation.

NYHA preoperative classification was as following: class I, 4 patients (2.85%); class II, 18 patients (12.85%); class III, 89 patients (63.57%); class IV, 29 patients (20.71%). Median preoperative creatinine was 1.1 mg/dl (IQR= 0.9-1.4 mg/dl), while 11 patients (7.85%) had preoperative creatinine value ≥ 2 mg/dl. Five patients (3.57%) were on renal dialysis before the operation. Thirty-five patients (25%) had preoperative peripheral vascular disease. Thirty-one patients (22.14%) had relevant carotid stenosis. One operation was conducted without

cardiopulmonary bypass (OPCAB). The rest of the operations were performed with cardiopulmonary bypass. Cardiopulmonary bypass (CPB) time ranged between 14-357 minutes (mean= 113.46 $\pm$ 55.15 SD). Aortic cross clamp time ranged between 0-145 minutes (mean 44.81 $\pm$ 30.58 SD). The cardiac operations performed are listed in Table 1. Other operations were as follows: one De Vega plastic + subtotal pericardiectomy, one myectomy by HOCM + mitral valve annuloplasty + VSD closure, one ascending aortic replacement, and lastly one patient with ventricle rupture closure following previous CABG operation.

In 47 patients (33.57%), IABP was implanted intraoperatively; in 93 patients (66.42%) IABP implantation was performed in the ICU. Rethoracotomy was performed in 42 patients (30%) due to cardiac tamponade or bleeding.

Implantation indications are shown in Table 2. In 43 patients (30.71%), IABP was implanted during CPR either because of recurrent VF or asystole. Median duration of mechanical ventilation was 4 days (IQR: 1-13 days). Median time between ICU admission and IABP implantation was 4.5 hours (IQR: 1-11 hours). In one patient, IABP was implanted on postoperative day 14 during resuscitation after PTCA trial, IABP median duration of support was 4 days (IQR: 2-6 days). In one patient, it was difficult to wean from IABP, which is why she received an IABP three times. (Her age prevented VAD implantation.) She died due to electromechanical dissociation after 43 days.

In total, 23 (16.42%) patients had the combination of IABP with ECMO, among them 19 patients (13.57%) received ECMO after IABP, while only four patients (2.85%) received IABP after ECMO. VAD implantation was performed in a total of nine patients (6.42%). Four patients (2.85%) received Cardiowest TAH, and another four patients (2.85%) received Thoratec (LVAD or BVAD), while one patient (0.71%) obtained the combination of LVAD (Abiomed)

with RVAD (centrifugal pump). In seven patients (5%), VAD were implanted following previous ECMO support. Whereas in two patients (1.42%), VAD were implanted following IABP implantation without earlier ECMO support, one patient (0.7%) received Cardiowest TAH and the other patient (0.7%) received Thoratec (TAH). Median time between IABP and ECMO or VAD implantation was 1.2 hours (IQR: 1-3 hours).

Early postoperative ECG changes were as follows: 59 patients (42.14%) showed no change, 44 patients (31.42%) had significant ST-elevation, 18 patients (12.85%) had new LBBB, in 19 patients (13.57%) the interpretation was impossible due to AV pacing. Median postoperative maximal CK was 1580 U/L (IQR: 692-3149.5 U/L), median postoperative maximal CK/MB was 77 U/L (IQR: 30.5-227.5 U/L), median postoperative maximal cardiac troponin was 47.8 U/L (IQR: 18.36-103 U/L), and median postoperative maximal lactate was 6.2 mmol/L (IQR: 3.75-10.1 mmol/L). Perioperative myocardial infarction with a troponin value of ≥ 15 U/L was detected in 79.28% of the patients.

Median postoperative maximal creatinine was 2.1 mg/dl (IQR: 1.5-3.2 mg/dl); therefore, 71.42% developed postoperative renal insufficiency and 57.14% required CVVH. Meanwhile, MARS therapy was performed in 10.71% of the patients due to severe liver insufficiency. Exactly 26.42% developed postoperative paralytic ileus, and 12.14% required laparotomy for intestinal ischemia. In one patient (0.71%), laparotomy was performed due to lower gastrointestinal tract bleeding. Septicemia was diagnosed in 42.14% (25% with IABP, 17.14% after IABP explanation). Pneumonia was diagnosed in 15% of the patients, during the follow up in the ICU.

Table 1: Type of Operations Performed

<i>Type of Operation</i>	<i>Total Number Performed</i>	<i>Percentage</i>
CABG*	74	52.85
AVR	15	10.71
MVR	6	4.28
CABG+AVR	20	14.28
CABG+MVR	12	8.57
CABG+AVR+MVR	1	0.71
CABG+VAR	2	1.42
AVR+MVR	3	2.14
TVR	2	1.42
TVR+MVR	1	0.71
Others	4	2.85
Total	140	100

* CABG: Coronary Artery Bypass Graft, AVR: Aortic Valve Replacement, MVR: Mitral Valve Replacement, TVR: Tricuspid Valve Replacement, VAR: Ventricular Aneurysm Resection

Table 2: Implantation Indications

<i>Implantation indication</i>	<i>Total Number</i>	<i>Percentage</i>
LOS*	44	31.42
During CPR	43	30.71
Failure to wean from HLM	39	27.85
Prophylactic due to ST Elevation	7	5.0
Recurrent VF	3	2.14
Pulsatility Induction after ECMO	4	2.85

* LOS: Low Output Syndrome, CPR: Cardiopulmonary Resuscitation, HLM: Heart Lung Machine, VF: Ventricular Fibrillation, ECMO: Extracorporeal Membrane Oxygenation

By the time of discharge, there were 82 patients (58.57%) without neurological abnormality. Twenty one patients (15%) had hemiparesis or were in coma before death or discharge, while 37 patients (26.42%) were on narcotics just before death (Neurological examination could not be performed).

The aforementioned variables were tested in regard to their effect on mortality, and statistically significant prognostic indicators for univariate analysis are shown in Tables 3 and 4. After including variables with p value <0.1 in the multivariate analysis, maximal CK-MB, maximal lactate in the first 24 hours, postoperative ischemia induced paralytic ileus, postoperative renal insufficiency, and implantation after cardiac operations other than CABG and valve operations were the most important predictors of survival. Table 5 shows these variables.

Regarding causes of death, 23 patients (28%) died due to multiple organ failure (MOF); 38 patients (46.4%) died due to cardiogenic shock; 17 patients (20.8%) had septicemia; two patients (2.4%) died due to a central cause (following perioperative cerebral ischemia); and finally two patients (2.4%) died due to other causes.

In this study, 5% IABP related complication rate was recorded, which is comparable to other studies with different IABP related complications rates (2.9 - 47%) (Arafa et al., 1999; Collier et al., 1986; Elahi et al., 2005; Kuki et al., 2001; Scholz et al., 1998). IABP technical failure occurred in three patients (2.14%) and was managed by changing the pump without any negative influence on the outcome; thus, it is not regarded as IABP related complication. One patient died due to IABP related limb ischemia complicated by septicemia.

Table 3: Statistically Significant Prognostic Indicators in Univariate Analysis (Categorical Variables)

Variable	% Survivors (No.=58)	% Non survivors (No.=82)	Exp (B)	95% CI for Exp (B)	P Value*
Female Sex	33.3	59	1.900	1.223-2.952	0.004
Age ≥70 Years	40.4	62.7	1.817	1.164-2.838	0.009
Weight ≤75 Kg	42.1	60.2	1.666	1.072-2.591	0.023
CAS **	15.8	26.6	1.513	0.917-2.496	0.1
Rethoracotomy	15.8	40.7	2.021	1.290-3.166	0.002
Implantation in ICU	57.9	72.3	1.551	0.959-2.511	0.07
Perioperative Infarct	68.4	86.8	2.295	1.178-4.471	0.015
Implantation by Operations other than CABG and Valve	0	4.8	2.786	1.012-7.673	0.047
PO Renal Insufficiency	45.6	90.8	6.235	2.849-13.643	<0.001
PO Liver Insufficiency	42.1	65.8	1.72	1.067-2.773	0.026
MARS Therapy	3.5	15.6	1.869	1.001-3.49	0.05
Paralytic Ileus	8.9	40.3	3.058	1.897-4.93	<0.001
Laparatomy	5.3	16.9	2.154	1.173-3.955	0.013
ECMO Implantation	3.5	25.3	2.491	1.505-4.123	<0.001
Septicemia	22.8	56.6	1.402	1.074-1.831	0.013
Implantation during CPR	19.3	38.6	1.989	1.276-3.102	0.002

* Cox regression analysis, ** Exp (B)= exponent of the B-coefficient, CI = confidence interval, CAS : Internal Carotid Artery Stenosis, ICU : Intensive Care Unit, CABG : Coronary Artery Bypass Graft, PO: Postoperative, MARS : Molecular Adsorbent Recirculating System, ECMO : Extracorporeal Membrane Oxygenation, CPR : Cardiopulmonary Resuscitation

Table 4: Statistically Significant Prognostic Indicators in Univariate Analysis (Continuous Variables)

Variable	Survivors	Non survivors	Exp (B)	95% CI for Exp(B)	P Value*
Height in cm	170.6 (± 8.8 SD)	166.5 (± 9.8 SD)	0.968	0.946- 0.990	0.005
Max. CK-MB level in U/L	47 (IQR:20.5- 90.5)	111.5 (IQR:48- 262.2)	1.001	1.001- 1.002	<0.001
Max. Troponin level in U/L	33.3 (IQR:12.6- 69)	62.5 (IQR:27.8- 36.5)	1.004	1.002- 1.005	<0.001
Max. Lactate in First 24 Hour Postoperative in mmol/L	5.1 (IQR:3.2- 7)	7.7 (IQR:4- 12.5)	1.094	1.060- 1.130	<0.001

*Cox regression analysis

Table 5: Results of Multivariate Analysis

Variable	Exp(B)	95% CI for Exp (B)	P value
Max. CK-MB level	1.001	1.000-1.002	0.004
Max. lactate in First 24 Hour	1.055	1.019-1.092	0.003
Paralytic Ileus	2.389	1.418-4.026	0.001
Postoperative Renal Insufficiency	4.312	1.917-9.699	<0.001
Implantations after Operations other than CABG and Valve	5.967	2.039-17.466	0.001

2.2. Characteristics of the Study Cohort after Excluding ECMO Patients:

As previously mentioned, the hemodynamic data after ECMO implantation could not be assessed. In an effort to obtain earlier predictors of survival depending on available hemodynamic parameters and catecholamine requirements, patients with ECMO were excluded from the second statistical analysis. The characteristics of the remaining 117 patients are shown in Table 6.

In the univariate analysis, various parameters were predictors of 30-day mortality (Table 7). While in the multivariate analysis, four parameters remained statistically significant. These parameters were MAP at 6 hours, adrenaline dose at 6 hours, CVP at 6 hours, and blood lactate concentration at 6 hours of IABP use (Table 8). From these variables, a new IABP score was calculated, designated Bad Oeynhausen IABP score, to predict death or survival in our cohort of patients.

The new IAPB score was calculated as follows: $I(AD > 0.04 \mu\text{g/kg body weight/min}) + I(\text{MAP} < 60 \text{ mm Hg}) + I(\text{CVP} > 14 \text{ mm Hg}) + I(\text{Lactate} > 6 \text{ mmol/l})$, whereas $I(X)$ denotes the indicator function, being equal to one, only if X holds true, and otherwise substitute zero.

Figure 4 demonstrates the accuracy of the newly developed score system to discriminate between survivors and non survivors. Patients who scored 3 or 4 points had no probability of surviving 30 days, whereas patients with a score of zero had a survival probability of 84.4%. The area under the ROC curve was 0.81 (0.72 - 0.90).

After developing the score system, another 145 patients, who received IABP intra-or postoperatively from January 2004 through December 2005, were evaluated prospectively. The types

of operations performed in this control group are shown in Table 10. The probability of survival according to the score is shown in Figure 5. According this data, the investigation confirmed the validity of the score. Notably, the control group of patients included only one patient who survived the first 30 days with a score of 3. However, this patient needed long term nursing care, which is why we consider our new score to be highly accurate and predictable.

In Table 9 and Figure 6 A-D, differences amongst hemodynamic parameters are shown for patients who survived 30 days after operation and non survivors. Only the survivors showed a significant increase in MAP and CI values. The other parameters remained unchanged. However, CVP was significantly higher in the non survivors, compared to survivors before IABP implantation ($p= 0.05$). With the exception of the mPAP values, all other parameters differed significantly at the 24 hour interval between survivors and non-survivors.

Regarding catecholamine and their relation to 30 day mortality, dopamine and epinephrine dosage were the most important predictors, with significant difference in dopamine requirement starting early before IABP implantation. Patients who required dopamine doses ≥ 7 $\mu\text{g/kg/min}$ before IABP implantation had 52% thirty day mortality versus 30.6% in patients with preimplantation dopamine of < 7 $\mu\text{g/kg/min}$ ($p= 0.02$), yet epinephrine requirement before implantation was not statistically significant ($p= 0.17$). Patients with dopamine requirement of ≥ 8.5 $\mu\text{g/kg/min}$ one hour following implantation had 60.5% thirty day mortality versus 28.9% in the other group of patients with dopamine < 8.5 $\mu\text{g/kg/min}$ ($p= 0.002$). Moreover, 30 day mortality in patients with epinephrine doses of ≥ 0.05 $\mu\text{g/kg/min}$ 1 hour after implantation was 65.2% versus 33% in patients with epinephrine doses < 0.05 $\mu\text{g/kg/min}$ ($p= 0.008$).

Meanwhile, statistically significant differences in dobutamine and norepinephrine requirements between survivors and non survivors could be detected only 24 hours following implantation.

Table 6: Characteristics of the study cohort after excluding ECMO patients

<i>Parameter</i>	<i>Total Number</i>	<i>Percentage</i>
Sex		
Male	60	51.28
Female	57	48.71
Age ≥ 70 years	65	55.55
Type of Operation		
Coronary Artery Bypass Grafting	62	52.99
Valve	23	19.65
Combined coronary artery bypass grafting and valve	29	24.78
Others	3	2.56
Concomitant Diagnosis		
<i>Diabetes mellitus</i>	40	34.18
Atrial Fibrillation	26	22.22
Left Main Stem Stenosis $\geq 70\%$	22	18.80
Myocardial Infarction within 4 Weeks Before Surgery	25	21.36
Emergency Operation	19	16.23
Redos	30	25.64
Preoperative Renal Insufficiency	11	9.40
Preoperative Dialysis	5	4.27
Peripheral Vascular Disease	27	23.07
Indication for IABP use		
Low Cardiac Output Syndrome	40	34.18
During Cardiopulmonary Resuscitation	33	28.20
Failure to Wean from Cardiopulmonary Bypass	34	29.05
Others	10	8.54
Preoperative NYHA functional class	4	3.41
I	17	14.52
II	70	59.82
III	26	22.22
IV		
Left ventricular ejection fraction	20	17.09
$\leq 35\%$		

Table 7: Results of Univariate Analysis after Excluding ECMO Patients and Including Hemodynamic Data and Catecholamine Requirements

Parameter	Exp (B)	95% CI for Exp (B)*	P-value
Female sex	1.786	1.001-3.189	0.05
Age ≥ 70 years	2.092	1.136-3.854	0.018
Body Mass Index (BMI) ≤ 28 kg/m ²	2.305	1.033-5.139	0.041
CABG Operation	0.523	0.293-0.933	0.028
Valve Operation	1.73	0.899-3.33	0.1
Implantation in the Intensive Care Unit	2.043	1.042-4.006	0.038
Implantation During Resuscitation	2.352	1.317-4.201	0.004
Dopamine Dose Immediately Before IABP Use ≥ 7 μ g/kg BW/min.	1.956	1.092-3.505	0.024
MAP at 1 h ≤ 65 mm Hg	2.89	1.43-5.841	0.003
CVP at 1 h ≥ 12 mm Hg	2.858	1.276-6.404	0.011
mPAP at 1 h ≥ 30 mm Hg	2.35	1.18-4.68	0.015
Dopamine Dose at 1 h ≥ 8.5 μ g/kg BW/min.	2.744	1.527-4.93	0.001
Adrenaline dose at 1 h ≥ 0.05 μ g/kg BW/min.	2.841	1.526-5.288	0.001
Urine Volume at 1 h ≤ 100 ml/h	1.694	0.931-3.083	0.085
MAP at 6 h ≤ 60 mm Hg	3.855	2.095-7.093	<0.001
CVP at 6 h ≥ 14 mm Hg	3.8	1.941-7.441	<0.001
PAWP at 6 h ≥ 23 mm Hg	3.65	1.60-8.29	0.002
mPAP at 6 h ≥ 32 mm Hg	2.12	1.11-4.07	0.023
Dopamine Dose at 6 h ≥ 7.5 μ g/kg BW/min.	2.008	1.095-3.682	0.024
Adrenaline Dose at 6 h ≥ 0.04 μ g/kg BW/min.	3.817	2.064-7.061	<0.001
Urine Volume at 6 h ≤ 50 ml/h	3.204	1.774-5.787	<0.001
Blood Lactate at 6 h ≥ 6 mmol/l	2.364	1.286-4.347	0.006
MAP at 12 h ≤ 65 mm Hg	3.122	1.669-5.843	<0.001
CVP at 12 h ≥ 12 mm Hg	3.21	1.418-7.268	0.005
mPAP at 12 h ≥ 28 mm Hg	1.995	1.04-3.825	0.038
PAWP at 12 h ≥ 18 mm Hg	2.846	1.5-5.402	0.001
Dopamine Dose at 12 h ≥ 7 μ g/kg BW/min.	2.114	1.136-3.937	0.018
Epinephrine need at 12 h	3.155	1.684-5.913	<0.001
MAP at 24 h ≤ 65 mm Hg	2.971	1.568-5.63	0.001
CVP at 24 h ≥ 12 mm Hg	2.959	1.301-6.728	0.01
PAWP at 24 h ≥ 18 mm Hg	2.646	1.37-5.111	0.004
CI at 24 h ≤ 2.4 L/min/m ²	3.247	1.671-6.31	0.001
Dopamine Dose at 24 h ≥ 7 μ g/kg BW/min.	2.917	1.531-5.557	0.001
Epinephrine need at 24 h	3.924	2.07-7.434	<0.001

* Exp (B)= exponent of the B-coefficient; CABG= Coronary Artery Bypass Graft;

MAP= Mean Arterial Pressure; BW= Body Weight; CI= Cardiac Index; CVP= Central Venous Pressure;

PAWP = Pulmonary Artery Wedge Pressure; mPAP = mean Pulmonary Artery Pressure

Table 8: Results of Multivariate Analysis after Excluding ECMO Patients

<i>Parameter</i>	<i>Exp (B)</i>	<i>95% CI of Exp (B)*</i>	<i>P-value</i>
CVP at 6 h ≥ 14 mm Hg	3.946	1.917 – 8.125	<0.001
MAP at 6 h ≤ 60 mm Hg	2.655	1.365 – 5.162	0.004
Adrenaline at 6 h ≥ 0.04 $\mu\text{g/kg BW/min}$	2.591	1.333 – 5.036	0.005
Lactate at 6 h ≥ 6 mmol/l	2.096	1.072 – 4.096	0.030

*CI = confidence interval; Exp (B) = exponent of the B-coefficient; MAP= Mean Arterial Pressure; BW= Body Weight; CVP= Central Venous Pressure

Table 9: Hemodynamic Differences Between 30 Day Survivors and Non-survivors

<i>Hemodynamic</i>	<i>Mean ($\pm$ SD)</i> <i>Non-survivors</i>	<i>Mean ($\pm$ SD)</i> <i>Survivors</i>	<i>P Value*</i>
MAP (Pre)	55 (11.7)	55 (11)	0.9
CVP (Pre)	15 (5)	13.1 (4.3)	0.05
mPAP (Pre)	31 (8)	28.1 (5.5)	0.5
PAWP (Pre)	19.6 (6)	18.4 (2.5)	0.8
CI (Pre)	1.93 (0.3)	2 (0.4)	0.3
MAP (1)	57.62 (12.8)	66.86 (11.7)	<0.001
CVP (1)	14.62 (3.5)	12.6 (3.6)	0.004
mPAP (1)	29.14 (7.12)	25.9 (4.1)	0.02
PAWP (1)	17.52 (5)	15.56 (3.94)	0.06
CI (1)	2.32 (0.77)	2.42 (0.57)	0.5
MAP (6)	62.21 (10.73)	70 (8.8)	<0.001
CVP (6)	15.26 (3.76)	12 (3)	<0.001
mPAP (6)	29.67 (7.81)	26.66 (4.75)	0.03
PAWP (6)	17.37 (4.98)	14.63 (4)	0.005
CI (6)	2.38 (0.78)	2.63 (0.6)	0.09
MAP (12)	65 (14.4)	73.7 (10.94)	0.002
CVP (12)	14.57 (3)	11.97 (3.5)	<0.001
mPAP (12)	29.78 (7.57)	25.9 (6.56)	0.01
PAWP (12)	17.68 (5.85)	14.53 (4.42)	0.006
CI (12)	2.6 (0.66)	2.76 (0.5)	0.18
MAP (24)	66.26 (11.75)	74 (9.52)	<0.001
CVP (24)	14.55 (3.47)	11.66 (3.38)	<0.001
mPAP (24)	28.61 (6.96)	26.67 (6.58)	0.18
PAWP (24)	17.86 (5)	15.2 (4.33)	0.01
CI (24)	2.74 (0.66)	3.16 (0.6)	0.002

* Unpaired student t-test; (Pre)= Preimplantation; (1)= 1 hour after IABP implantation; (6)= 6 hours after implantation; (12)= 12 hours after implantation; (24)= 24 hours after implantation; MAP= Mean Arterial Pressure; CI= Cardiac Index; CVP= Central Venous Pressure; PAWP = Pulmonary Artery Wedge Pressure; mPAP = mean Pulmonary Artery Pressure

Table 10: Type of Operation Performed in the Control Group of Patients (2004 and 2005)

<i>Operation</i>	<i>Total Number Performed</i>	<i>Percentage</i>
CABG*	106	73.10
Valve Operation	21	14.48
CABG + Valve Operation	16	11.03
VSD closure	2	1.42
Total	145	100.00

*CABG= Coronary Artery Bypass Graft; VSD= Ventricular Septal Defect

n = 117

Figure 4: Probability of 30 Days Survival According to the New Scoring System

n = 145

Figure 5: Probability of Survival after Prospective Score Evaluation (2004-2005)

Figure 6-A

Figure 6-B

Figure 6-C

Figure 6-D

Figure 6-E

Figure 6 A-E: Mean arterial pressure (A) and hemodynamics (B-E) of survivors and non survivors during the first 24 hours after IABP implantation; Data are given as mean +/- standard deviation. (■) survivors; (●) non-survivors. * $P < 0.05$, ** $P < 0.01$ *** $P < 0.001$ vs. survivors at the same time point (Unpaired student t- test).

5. Comment

Despite continuous improvement in surgical and anaesthetic techniques, including myocardial protection, the morbidity and mortality of this group of patients who require intra and /or postoperative IABP remains high.

In this study, 62 patients (44.28%) died in the ICU. The 30 day mortality rate was 45.7%, a value which is comparable to the mortality rates of 21-73% in other reported studies (Baskett et al., 2002; Creswell et al., 1995; Ghali et al., 1999). Overall, only 1.77% from the entire patient group received IABP either intra or perioperatively, and 30.7% of implantations were done on emergency basis in the ICU during CPR either due to VF or asystole.

Nearly all published studies have demonstrated that patients receiving preoperative IABPs have better outcomes than those receiving IABPs intraoperatively or postoperatively (Ali et al., 2005; Creswell et al., 1995; Gutfinger et al., 1999; Holman et al., 2000; Pfeiffer et al., 2005; Ramnarine et al., 2005). Yet, this study includes patients who have received IABPs both intraoperatively and postoperatively, which also contributes to the relative high mortality rate after long term follow up.

After 1 year follow up, the mortality rate was 55.71% (n=78), while the 2 year mortality rate was 58.57% (n= 82). Considering these high mortality rates, it is enormously important to identify any factor which predicts mortality in these patients.

There are several factors, reported in other studies, that predict survival such as higher age, female gender, preoperative renal insufficiency, myocardial infarction in the last 4 weeks, preoperative nitro-glycerine use, preoperative reduced left ventricular ejection fraction, LVEDP, NYHA class, combined CABG and valve operations, prolonged CPB and ACC time, small balloon size, transthoracic insertion, prolonged duration

of support, postoperative use of isoproterenol or digoxin, perioperative myocardial infarction, the need for dialysis, postoperative high lactate level in first 8 hours of implantation (Baldwin et al., 1993; Corral et al., 1986; Davies et al., 2001; Hedenmark et al., 1989; Naunheim et al., 1992; Pi et al., 1995; Scanlon et al., 1976; Sturm et al., 1980). Moreover, Norman et al. and Hausmann et al. developed scoring systems to predict mortality in these patients (Hausmann et al., 2001; Norman et al., 1977).

Regarding the predictors of survival in this study, maximal level of CK-MB could be recognized as an important factor ($p=0.004$, $RR=1.001$). Ultimately, this reflects the degree of cardiac damage in these patients, especially a maximal CK-MB level of 520 U/L which predicted 100% mortality regardless of the preoperative left ventricular ejection fraction. In addition, the postoperative maximal troponin level was significant in univariate analysis, but it was not predictive in multivariate analysis.

The type of operation performed was another important factor which predicted survival in these patients requiring IABP. This can be observed from the differences in the mortality rates. The 30 day mortality rate was 35.5%, 55.6%, 54.5% and 100% for CABG, valve, CABG + valve, and other operations, respectively. The worst outcome seen in patients receiving IABP after operations other than CABG and valve operation was one of the important factors contributing to mortality in this cohort ($p=0.001$, $RR=5.967$). Moreover, the outcome was better in patients who received IABP after CABG than after valve operation. This result is also reported in other studies (Baskett et al., 2002; Ota et al., 1992).

Among other important factors, postoperative renal insufficiency is considered to be highly predictive ($p = <0.001$, $RR = 4.312$). The important reported causes of postoperative renal insufficiency are low output state and hypotension or potent vasopressor use. The previously described risk factors for development of postoperative renal insufficiency include: pre-existing renal dysfunction, older age, left ventricular dysfunction, emergency operation, as well as any combination of the following: hypertension, diabetes and peripheral vascular disease, concomitant CABG-valve operations, mitral valve operations, use of deep hypothermic circulatory arrest, and longer duration of bypass and total cross clamp time (Andersson et al., 1993; Corwin et al., 1989; Gaudino et al., 2005; Khilji et al., 2004; Zanardo et al., 1994). Significant risk factors for development of postoperative renal insufficiency in this study includes: age ($p = 0.009$, $RR = 1.035$), ECMO implantation ($p = <0.001$, $RR = 2.910$), paralytic ileus ($p = <0.001$, $RR = 2.618$), maximum lactate in first 24 hours ($p = 0.001$, $RR = 1.061$), and postoperative liver insufficiency ($p = 0.03$, $RR = 1.665$).

Another important predictor was the occurrence of postoperative paralytic ileus due to non occlusive mesenteric ischemia ($p = 0.001$, $RR = 2.389$). This constitutes the most catastrophic gastrointestinal complication, following cardiac surgery with a high mortality rate (Mangi et al., 2005). In this study, 26.42% developed paralytic ileus, 41.7% of them required laparotomy, and mortality in these patients with ileus was very high (86.1%). This mesenteric ischemia results from splanchnic hypoperfusion due to a low cardiac output state or a long pump run, atherosclerotic embolism, or mesenteric thrombosis less commonly. The known risk factors for the development of mesenteric ischemia include: peripheral vascular disease, triple vessel disease, operation type, history of smoking, IABP use, renal insufficiency, use of inotropics, and prolonged

cardiopulmonary and-or aortic cross clamp time (Ghosh et al., 2002; Venkateswaran et al., 2002). In this cohort of patients, age ($p = <0.001$, RR= 1.095), BMI ($p = 0.005$, RR= 0.872), NYHA class ($p = 0.017$, RR= 2.614), maximal lactate level in the first 24 hours ($p = 0.001$, RR= 1.1), and postoperative septicemia ($p = <0.001$, RR= 2.48) were important predictors of this lethal complication. The early diagnosis of this lethal complication is still difficult and can be made merely by mesenteric arteriography which can identify or exclude thromboembolic causes and allow for the infusion of mesenteric vasodilators (Papaverine)(Kaleya et al., 1992; Klotz et al., 2001). Furthermore, Straub et al. described CW-Doppler sonography to be helpful in the diagnosis of this complication (Straub et al., 2004).

Postoperative lactate levels in the first 24 hours, with metabolic acidosis, reflects the degree of tissue damage due to low cardiac output with peripheral vasoconstriction, poor peripheral perfusion, or intra-abdominal catastrophes, such as mesenteric ischemia secondary to low-flow state or renal causes. It is well known that the normal myocardium utilizes glucose and degrades lactate produced by glycolysis to pyruvate so that in normal heart at rest, no lactate is formed in the coronary sinus blood. Once myocardial hypoxia occurs, there is a decrease in aerobic glycolysis. As a result, anaerobic metabolism will ensue causing production of lactate. In this cohort of patients, serum lactate levels were identified to be highly predictive of mortality. Lactate levels after six hours of IABP implantation are an important parameter, which are also included in the newly developed Bad Oeynhausen scoring system. Davies et al. reported in a small group of patients with maximal level of lactate in the first 8 hours after IABP implantation of 10 mmol/L to be a 100% predictor of mortality (Davies et al., 2001). Moreover, MAP less than 60 mm Hg just

eight hours after IABP implantation was approximately 90% predictive of in-hospital mortality. Compared to this study, MAP values less than 60 mm Hg after 6 hours of IABP showed only 69% predictive values for mortality. Regarding lactate levels, 100% mortality was achieved only if the concentrations were higher than 16 mmol/L. Data support the medical progress in the treatment of patients with severe cardiac complications as well as different treatment strategies at different heart centres.

The above mentioned factors are essential to consider, but the fact that they occur relatively late in follow up instigated a search for other predictive variables, which are available early after IABP implantation, and can be included in a score system. This might help the anesthesiologist/surgeon to find an optimal patient-specific treatment. Information could be achieved in this study through inclusion of hemodynamic parameters and catecholamine requirements early after IABP implantation. Yet for this purpose, patients with ECMO had to be excluded from the second statistical analysis.

A newly developed Bad Oeynhausen IABP score demonstrated reliability in prediction of the 30-day survival in this cohort of patients. It is noteworthy that all parameters of the Bad Oeynhausen IABP score can be assessed easily and do not need the use of a Swan-Ganz catheter.

All four parameters of the Bad Oeynhausen IABP score may indicate cardiac dysfunction. The need for high adrenaline doses as well as low MAP values are indicators of low cardiac output, whereas high CVP values reflect right ventricular dysfunction either primarily or secondarily due to left ventricular dysfunction. Moreover, high lactic acid concentrations can result from low cardiac output.

The higher incidence of several complications such as paralytic ileus, laparotomy, septicemia, and postoperative renal insufficiency in the non-survivors compared to the patients who survived the first 30 days may also have been influenced by the more pronounced cardiac dysfunction of the non-survivors.

Hausmann and associates demonstrated the results of a clinical study aimed to discover predictors of survival in patients after IABP implantation (Hausmann et al., 2002; Hausmann et al., 2001). A scoring system was developed that includes the adrenaline requirement, left atrial pressure, urine output, and mixed venous saturation (SvO_2), beginning just one hour after IABP implantation. However, this scoring system was not able to predict the mortality in Heart centre Bad Oeynhausen, simply because no patients had more than 3 points from a total of 5 points (which then predicts 100% mortality). Maximum adrenaline dose in Heart Centre Bad Oeynhausen was $<0.3 \mu\text{g/kg/min}$, whereas the Hausmann score system which depicts that two points can be obtained from an adrenaline dose of $\geq 0.5 \mu\text{g/kg/min}$. These results explain the differences in therapy strategies between the Heart Centres. However, apart from SvO_2 , the other parameters of the Hausmann IABP score were also predictors in this study for the univariate analysis, at least 6 hours after IABP implantation. SvO_2 can be used to assess the adequacy of tissue perfusion and oxygenation, and to serve as an indirect predictor of low cardiac output. It has been reported that SvO_2 measurement is unreliable and insensitive method of predicting cardiac output (Sommers et al., 1993). This stems from consistent fluctuation amongst factors that affect oxygen supply and demand, such as shivering, low temperature, anaemia, alteration in FiO_2 and the efficiency of alveolar gas exchange.

A rise in filling pressure (PAWP) or left atrial pressure to about 18-20 mm Hg will optimize the preload required to achieve a satisfactory cardiac output, but on the other hand, it reflects low ventricular performance. Left atrial pressure in the low 20s is recommended usually for patients with poor left ventricular function, a stiff hypertrophied ventricle with diastolic dysfunction, a small left ventricular chamber, or pre-existing pulmonary hypertension from mitral valve disease. A high LAP is one of the important parameters in the Hausmann scoring system, with LAP ≥ 15 mm Hg being highly predictive. In our study, PAWP recorded one hour after implantation was not a significant parameter. Elevation in PAWP after the sixth hour from implantation was significant in univariate analysis.

Regarding changes in cardiac index (CI) following IABP implantation, a significant difference between survivors and non survivors starts relatively late in follow up (after 24 hours). This fact is also mentioned in some other studies (Ida et al., 1984; Nasu et al., 1991). However, CI ≤ 2.4 L/min./m² about 24 hours after implantation was significant only in univariate analysis with no effect in multivariate analysis. Therefore it is not possible to rely on cardiac index alone as a predictive mortality parameter early in the follow up.

Mean arterial pressure (MAP) is an extremely sensitive factor predicting survival in this study. There is a continuous significant difference in mean arterial pressure throughout the course of follow up between survivors and non survivors. This can be explained by the indirect relation of the arterial pressure to the cardiac output and systemic vascular resistance (Blood Pressure = Cardiac Output x Systemic Vascular Resistance). However in the early postoperative period, myocardial function may be marginal despite normal or elevated blood pressure due to an elevated SVR resulting from augmented

sympathetic tone and peripheral vasoconstriction. Ultimately, a deterioration in blood pressure indirectly reflects marginal cardiac output. It has been recognized that the myocardial function generally declines for about 6-8 hours following cardiac surgery, presumably from ischemic/ reperfusion injury before returning to baseline after 24 hours (Breisblatt et al., 1990), and it is obvious in this study that deterioration might be worse in patients who require IABP after cardiac surgery. Moreover, low blood pressure will cause systemic hypoperfusion leading to end organ dysfunction. Among the most important organ systems affected which influences survival are myocardial, cerebral, renal, and mesenteric blood supply, resulting in ischemia and organ dysfunction. It is noteworthy that MAP and CI increased significantly during the first 24 hours only in the survivors of this study cohort.

The severe damage of the heart in these patients also becomes obvious by the observation that the hemodynamic parameters showed significant differences between survivors and non-survivors already within the first 24 hours of IABP use. Data further suggests that patients with profound hemodynamic compromise persisting after IABP implantation will likely survive only with a VAD system (Baldwin et al., 1993; Torchiana et al., 1997). In this study cohort, only a few patients with intra or postoperative IABP ultimately received a VAD system. Furthermore, it is difficult to rule out that 30-day survival would have been enhanced if more patients had received a VAD system. At present, VAD implantation in Heart Centre Bad Oeynhausen is performed in patients who fail to recover after ECMO implantation, in patients with end-stage heart failure, or in patients with fulminant myocarditis.

It is also important to consider the catecholamine requirements in the early hours after IABP implantation, because they

reflect a pertinent dichotomy. On one hand, it suggests the degree of hemodynamic deterioration, while on the other hand higher doses lead to more drug related complications. The higher mortality in patients with greater catecholamine requirement is documented in some other studies (Hausmann et al., 2002; Nasu et al., 1991). Among the most important catecholamines in this study are dopamine and epinephrine, which were significant throughout the follow up time. Epinephrine requirement from ≥ 0.04 $\mu\text{g/Kg BW/min}$ six hours following implantation is one of the most important predictive factors of mortality in these patients.

However, differences in kind and severity of complications in the patients of this study and the patients of earlier studies, as well as different treatment strategies may have influenced multivariate analysis differences. Both the differences in baseline characteristics between patient groups as well as the differences in treatment strategies may make it difficult to develop a generally applicable IABP score. At present, it seems that each Heart Centre has to develop its own IABP score.

IABP related complications were recorded in 5%. This low complication rate stems from the fact that 94.3% of the implantations were percutaneous, using Seldinger technique. Open surgical implantation was used only in four patients (2.85%), while four implantations (2.85%) were transthoracic. Another important contributing factor is the use of smaller catheters in this series (8 French). Elahi et al. demonstrated significant decrease in IABP related complication rate in the last years due to the increasing number of IABP used, evolving technology in IABP design, less invasive insertion techniques, and appropriate anticoagulation therapy (Elahi et al., 2005). Previously described risk factors for IABP related complications include female sex, peripheral vascular disease,

diabetes mellitus, duration of IABP support, smoking, and hypertension (Gottlieb et al., 1984; Cohen et al., 2000; Miller et al., 1992). None of the aforementioned risk factors were significant in this series of patients, but lactate level ≥ 6 mmol/L in the first 6 hours of IABP implantation was an independent risk factor of IABP related complications ($p=0.013$).

In summary, our data demonstrate that a score can be helpful to predict 30 day lethality of patients with intra or postoperative IABP implantation. In order to develop a generally applicable IABP score, it is necessary that there is easy access to essential parameters. However, before such a generally applicable score can be developed, uniform recommendations for preoperative, intraoperative, and postoperative IABP use and treatment strategies must exist. The fact that myocardial function declines for about 6-8 hours following cardiac surgery (presumably from ischemic/reperfusion injury) (Breisblatt et al., 1990) might further confirm the applicability of the new score system, since the risk factors presented several hours after IABP implantation were more reliable to predict the mortality as factors available immediately after implantation.

This study represents four years of experience in a quaternary level Heart Centre. Moreover, data are in general agreement with the results of recently published studies (Davies et al., 2001; Hausmann et al., 2002). Although satisfactory results could be demonstrated in these patients, they continue to have high mortality, especially patients receiving IABP postoperatively. This may encourage insertion of IABP early before the operation in patients with multiple risk factors (Baskett et al., 2002; Christenson et al., 1997; Christenson et al., 1997; Holman et al., 2000). The trends should favour

prophylactic use to avoid rather than to treat ischemia, or else to think about other alternatives, for example, implementation of various VAD systems in the early postoperative period.

6. Summary

This study deals with patients receiving IABP intra and/ or postoperatively following cardiac operations. Generally, these patients have a high mortality rate even after implantation of this device. This study contains both retrospective and prospective elements, aimed to identify predictors of survival after IABP implantation, which may be helpful to adjust the future management strategy.

Significant risk factors in this study were as follows: implantation after operations other than CABG and valve operations, postoperative high levels of lactate and/ or CK/MB levels, postoperative complications such as renal insufficiency and ischemic paralytic ileus.

After excluding patients who received ECMO, the parameters available within the first twenty-four hours after IABP implantation were tested by Cox regressions analysis to pinpoint independent risk factors which could be included in a new score system. Mean arterial pressure (MAP), central venous pressure (CVP), lactate levels and epinephrine requirement six hour after IABP implantation were the most significant factors in the multivariate analysis to predict the 30 day mortality. Based on this finding, a new Bad Oeynhausen scoring system could be developed which is able to predict a 100% 30 day mortality by maximal score of 3 or 4. The new IABP score was calculated as follows: $I(AD \geq 0.04 \text{ } \mu\text{g/kg/min}) + I(MAP \leq 60 \text{ mm Hg}) + I(CVP \geq 14 \text{ mm Hg}) + I(\text{Lactate} \geq 6 \text{ mmol/l})$, whereas $I(X)$ denotes the indicator function, being equal to 1 if X holds and zero otherwise.

After development of the aforementioned score system, the sensitivity and predictability were evaluated prospectively in another control group. The acquired results of this investigation confirmed the applicability of the score.

Lack of a previously developed score system, able to predict patient survival in Bad Oeynhausen Heart Centre, might be due to different treatment strategies in different Heart Centres. However it is advantageous to develop a generally applicable IABP score. Moreover, it is desirable that the parameters, which are needed to calculate such a score, can be assessed easily. Yet, before such a generally applicable score can be developed, uniform recommendations for preoperative, intra-operative, and postoperative IABP use and treatment strategies must exist.

The data in this study demonstrate that the Bad Oeynhausen score system predicts 30 day fatality in patients with IABP implantation. Such a score can be useful to find an optimal patient-specific treatment. Therefore, this new risk score will be used in the future to select patients, who probably will benefit from an early VAD implantation.

7. References

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