Use of Impedance Cardiography in Anaesthesia and Intensive Care in Children

Ph.D. thesis

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List of abbreviations

ASA	**-**	**American Society of Anesthesiologists**
CI	**-**	**cardiac index**
CO	**-**	**cardiac output**
CVP	**-**	**central venous pressure**
E	**-**	**voltage difference**
ECG	**-**	**electrocardiography**
$ETCO_2$	**-**	**end tidal carbon dioxide pressure**
HI	**-**	**Heather Index**
HR	**-**	**heart rate**
I	**-**	**electrical current**
IAP	**-**	**intra-abdominal pressure**
ICG	**-**	**impedance cardiography**
l	**-**	**inner distance between the voltage detecting electrodes**
LVET	**-**	**left ventricular ejection time**
MABP	**-**	**mean arterial blood pressure**
NIBP	**-**	**non invasive blood pressure**
PEEP	**-**	**positive end expiratory pressure**
P_{aw}	**-**	**airway pressure**
PIP	**-**	**peak inspiratory airway pressure**
PP	**-**	**pneumoperitoneum**
PPV	**-**	**positive pressure ventilation**
SV	**-**	**stroke volume**
SVI	**-**	**stroke volume index**
S_vO_2	**-**	**mixed venous oxygen saturation**
$S_{cv}O_2$	**-**	**central venous oxygen saturation**
SVR	**-**	**systemic vascular resistance**
SVRI	**-**	**systemic vascular resistance index**
TEB	**-**	**thoracic electrical bioimpedance**
Z	**-**	**impedance/resistance**
Z_0	**-**	**baseline thoracic impedance**
ρ	**-**	**resistivity the conducting material**
dZ/dT_{max}	**-**	**maximum rate of change of impedance during systole**

I. Introduction

I.1. Background

The evaluation of the haemodynamic state of the patient during anaesthesia and intensive care is essential. The primary goal of haemodynamic monitoring is to determine the adequacy of oxygen delivery, as the most important function of the circulation is to provide transport of oxygen and substrates to and from the tissues (1). Since oxygen transport is determined by the arterial perfusion pressure, arterial oxygen content and cardiac output, these parameters are called “vital signs”. While determination of blood pressure, heart rate, respiratory rate and oxygen saturation is readily available in most clinical settings, assessment of the true haemodynamic state from an analysis of these measurements alone is difficult (1). Cardiac output (CO) is considered the most important factor in oxygen delivery. The use of thermodilution (right heart catheterisation, pulse contour cardiac output) to measure cardiac output is the ‘gold standard‘ technique but it is invasive. The convergence of escalating concerns over the safety of invasive haemodynamic monitoring and the developments in microprocessors and signal analysis technology has culminated in a renewed interest in some of the noninvasive monitoring methods (2). One of them is impedance cardiography (ICG) has been used to measure CO for decades, and holds the promise of rapid and continuous measurement of cardiac output (3,4).

I.2. Electrophysiologic principles of impedance cardiography

Ohm’s Law states that the flow of an electrical current (I) is equal to a voltage drop (E) between the two ends of a circuit divided by the resistance or impedance (Z) to current flow (5) .

$$I=E/Z \quad \text{or} \quad Z=E/I$$

If the current remains constant, then changes in voltage across the circuit are equal to changes in the impedance to current flow. Furthermore, if the impedance (Z) is dependent upon the

cross sectional area (A), the length (L), and resistivity (ρ) of the conducting material, then changes in Z can be related to changes in volume (V) of the conductor by the expression:

$$Z=\rho(L/A) \text{ or } Z=\rho(L^2/V)$$

In this equation, V= A· L and resistivity (where ρ is a constant specific to the composition of the material) is measured in Ω cm. This supposition is the fundamental principle behind the concept of ICG (5).

Kubicek and others investigated the possibility of measuring total blood flow within the aorta (representing cardiac output) by examining impedance changes across the thoracic cavity under the influence of a constant magnitude , high frequency measurement current and used the term “thoracic electrical bioimpedance” (TEB). In his original model, Kubicek used the simple assumption of the thorax as a cylinder of cross-sectional area (A) and length (L) that would serve as an electrically nonhomogeneous bulk conductor of some constant injected current circuit (3). The human thorax is composed of mostly muscle, lung, fat, skin, bone and air; all of which have very high resistivity (R=200-5000 Ωcm). By contrast, blood, with its electrolyte-rich fluid base, has a very low resistivity (plasma: R=65 Ωcm; whole blood: R=130 Ωcm), though it composes a much smaller portion of the total volume of the thorax (~ 15%). However, since electrical currents tend to take the path of least resistance, it can be postulated that the majority of the current flowing through the thorax would travel up the blood-filled aorta and vena cava, since they would serve as natural conduits. Kubicek then considered that the changes in impedance observed to occur within this thorax conductor would also reflect changes in the volume within the great vessels.

Using information derived from the changing impedance during the cardiac cycle (time dependent waveform), Kubicek estimated the stroke volume in a method similar to the pulse contour method. Since the area under the arterial pressure waveform accurately reflects stroke volume, this area can be estimated if the peak pressure change dP/dt_{max} is multiplied by the

total ejection time. The equation for peak flow can then be transformed into the Kubicek expression:

$$SV=\rho \cdot (l^2 \cdot Z_0{}^{-2}) \cdot dZ \cdot dt_{max}{}^{-2} \cdot LVET$$

where SV=stroke volume (ml), ρ=resistivity of blood (Ωcm), l=inner distance between the voltage detecting electrodes (cm), Z_0= baseline thoracic impedance (Ω), $dZ \cdot dt_{max}{}^{-2}$ = maximum rate of change of impedance during systole (Ω/s) and LVET= left ventricular ejection time (ms) (3).

Although considerable efforts has been made to eliminate some of the assumptions of the Kubicek model (i.e. the thorax is truncated) mainly by Bernstein (4), most commercially available devices use a modified Kubicek equation. Regardless of which equation or model used, a reasonable estimation of the stroke volume can be ascertained if we are able to determine the two important variables of $dZ \cdot dt_{max}{}^{-2}$ and LVET.

I.3. ICG setup, origins of the impedance signal and waveform

Most modern ICG devices use a tetrapolar lead system of electrodes, separating the current pathway from the sensing pathway by at least 4 centimetres. One set of the external surface electrodes placed on the upper abdomen and the upper neck is the source of constant high-frequency (50-100 kHz) low magnitude (0.2-0.5 mA) current that provides coverage of the thorax with a homogeneous electrical field. The voltage is sensed by two pairs of electrodes placed at the beginning of the thorax (the line of the root of the neck) and the end of the thorax (the xyphoid process level) (Figure 1.). As blood is pumped out of the heart and into the aorta during the cardiac cycle, the volume of this fluid in the thoracic conduit and therefore the impedance to flow of the current change dramatically with time. ICG technology converts the

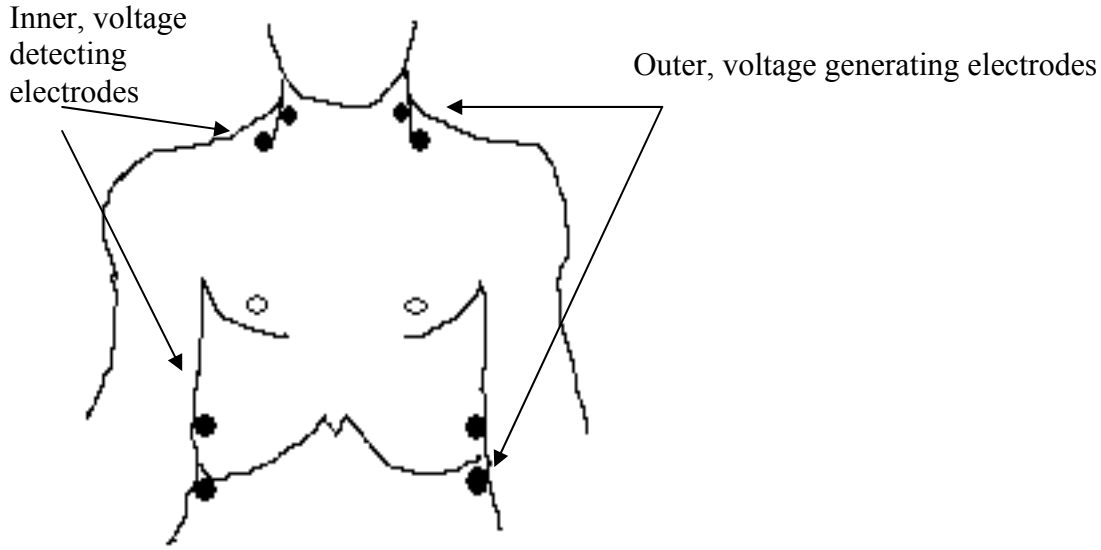

Figure 1. Tetrapolar electrode configuration used during impedance cardiography.

time-varying measurements of Z electrical resistance of the thorax into waveform from which a variety of parameters derived. The important parameters required to compute stroke volume and cardiac output are dZ/dt and LVET. While the ECG shows the electrical events of the heart, the ICG waveform is a fingerprint of the mechanical events of cardiac contraction (Figure 2.). The standard points of impedance waveform are: "A," beginning of electromechanical systole; "B," opening of aortic valve; "C," maximal mechanical contraction (dZ/dt_{max}); "X," closing of aortic valve; "Y," closing of the pulmonary valve; and "O," mitral valve opening (6).

Z_0 is the baseline impedance of the thoracic tissues, fluid and air, with an average normal value in man of around 25 Ω. As Z_0 does not change acutely with time, $Z_R(t)$ (respiration) and $Z_H(t)$ (haemodynamic) determine the impedance waveform changes. The respiratory component $Z_R(t)$ typically induces a change about 1 Ω. The haemodynamic component is in the range of 0.1 to 0.2 Ω, which is only 0.3-0.5% of the total thoracic impedance. dZ/dt_{max} was initially measured directly from the slope of the simple impedance waveform, but this

method proved to be too variable for routine clinical use. The first derivative of these impedance changes with respect to time ($\delta Z/\delta t$) were found to eliminate much of the variations in the baseline due to respirations and largely reflects $Z_H(t)$ only. This is explained by the fact that $Z_H(t)$ has a much higher frequency than $Z_R(t)$ (average heart rate of 70 beats · min^{-1}, compared with a normal respiratory rate of 14 breaths · min^{-1}). Using this derivative methodology, it has been determined that almost all of the impedance changes were derived from changes in the systemic thoracic aorta alone. Therefore, the rate of cardiovascular TEB changes (dZ/dt) (i.e. the first derivative of impedance) is an image of the aortic blood flow and its maximum value dZ/dt_{max} is proportional to the aortic blood peak flow (6).

The impedance cardiograph ICG-M401 used in our studies is a unique device concerning its special software using electromechanical components (phono-head), beat to beat analysis when it is compared with an invasive technique that uses intermittent data collection with statistical correction (7, 8). Using ICG to measure stroke volume non-invasively on a beat to beat basis showing trends helps in clinical decision making (9, 10). The instrument (ICG-M401) used in our study was tested by Pianosi who compared impedance measurements of CO with carbon dioxide rebreathing measurement of CO in healthy children and children with cystic fibrosis during exercise. He found that ICG provided reliable estimation of CO with good correlation of indirect Fick (CO_2) method (11, 12). There is strong correlation between the results of ICG and of invasive methods (dye dilution, thermodilution), in adults (13) and paediatric patients under mechanical ventilation, in various clinical settings (14-16).

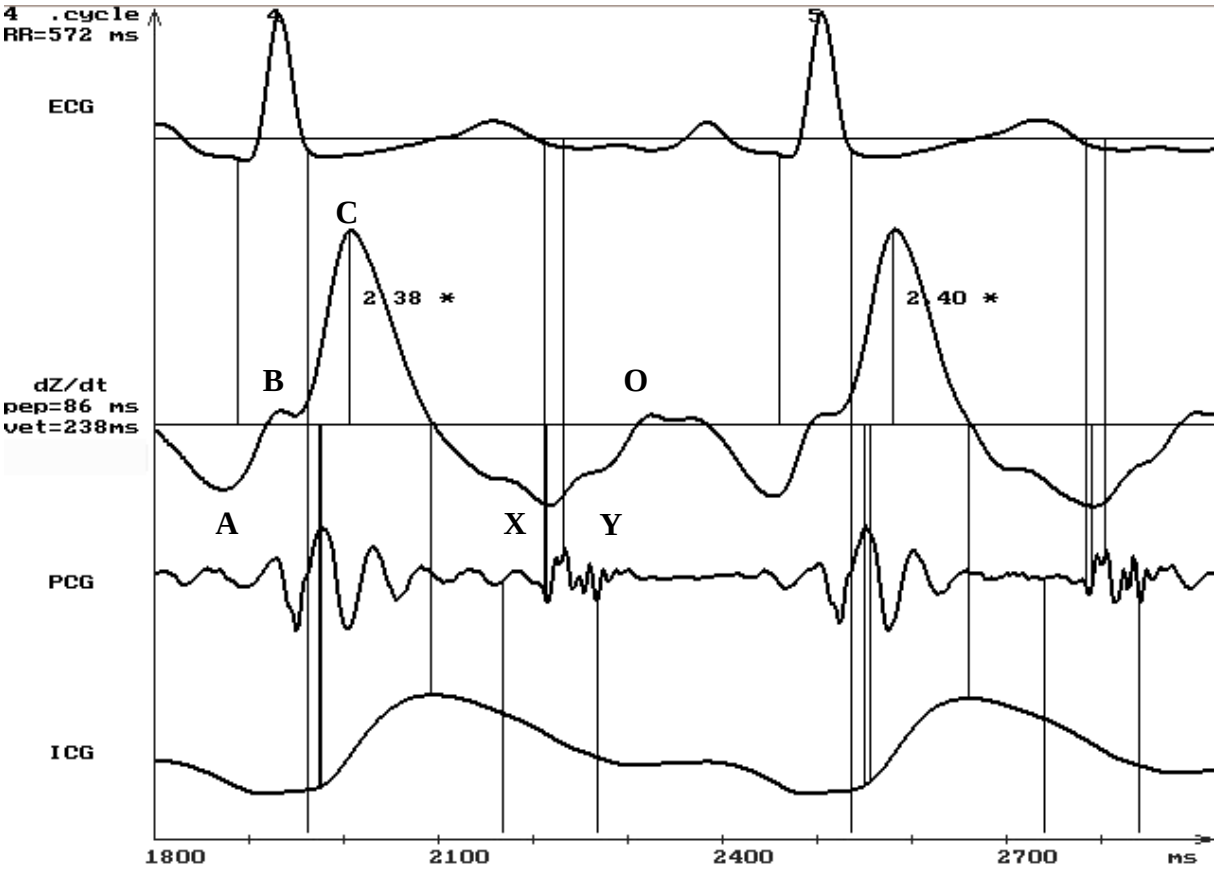

Figure 2. Graphic waveforms of two cardiac cycle processed by the ICG M-401. Upper trace is ECG, second is dZ/dt, third is phonocardiogram (PCG) and lower trace is thoracic electric bioimpedance (ICG). The calculated numeric value of dZ/dt (2.38 and 2.40) is shown for two individual heartbeats. The vertical lines are used to compute the preejection period (pep) and ventricular ejection time (vet). The standard points of impedance waveform: A: beginning of electromechanical systole; B: opening of aortic valve; C: maximal mechanical contraction (dZ/dt_{max}); X: closing of aortic valve; Y: closing of the pulmonic valve; and O: mitral valve opening.

II. Aims

II.1. Haemodynamic changes related to pneumoperitoneum (PP) in children.

Laparoscopy is widely used in paediatric surgery for the diagnosis and treatment of many surgical conditions such as varicocele, gastro-oesophageal reflux, testicular retention (17). However, proper haemodynamic monitoring during these operations is not easy. Data are limited of the intraoperative and postoperative changes related to pneumoperitoneum (PP) in children. Pulmonary artery catheter to measure cardiac output during laparoscopy is techniqually difficult and rarely used in this age of group. Transthoracic electric bioimpedance has been used to measure cardiac output for decades. The aim of the present study was to evaluate whether ICG is an applicable method to track the trends in cardiovascular parameters during laparoscopy in children.

II.2. Trendelenburg positioning and anaesthesia induction with propofol in children.

The induction of general anaesthesia with propofol and fentanyl is safe and widely used in paediatric practice, however is often associated with a decrease in blood pressure and cardiac output (18, 19). While this decrease in cardiac performance is rarely clinically important in healthy individuals, this may not be the case in patients in whom hypotension may critically reduce tissue perfusion (hypovolaemia, shock states). Trendelenburg positioning is often the first clinical step to treat heamodynamically unstable patients when hypovolaemia is suspected. The aim of this manoeuvre is to increase central blood volume, and thereby cardiac preload, by autotransfusion. However, the effects of the Trendelenburg position on cardiac performance have been studied with controversial results (20-22), data are limited with respect to the cardiovascular effects related to head-down tilt in children (23). The use of thermodilution (right heart catheterisation, pulse contour cardiac output) to measure cardiac output in these patients is too invasive. The objective of our study was to determine with the

use of impedance cardiography whether Trendelenburg positioning would prevent or attenuate the decrease in blood pressure and cardiac output caused by intravenous induction of anaesthesia with propofol and fentanyl in children.

II.3. Haemodynamic effects of positive pressure ventilation in children.

Continuous mechanical ventilation with positive end expiratory pressure (PEEP) is part of the routine management of gas exchange disturbances in intensive care. The haemodynamic effects of positive pressure ventilation (PPV) have been studied in animal models and in several clinical settings. It has been widely accepted that increases in airway pressure (P_{aw}) induced by PPV can decrease cardiac output (24-26). The primary mechanism responsible for this effect is presumed to be a decrease in right ventricular filling due to a decrease in pressure gradient for the systemic venous return. Data are limited with respect to the haemodynamic changes related to PEEP in children (27, 28), especially with normal, or improving lung function. Cardiac output strongly determines oxygen supply to the tissues. Monitoring mixed venous oxygen saturation (S_vO_2) via right heart catheterisation is widely used to monitor the balance between oxygen supply and demand in adult patients. Central venous catheters are more routinely used in paediatric intensive care, with a lower less risk of complications. Central venous oxygen saturation ($S_{cv}O_2$) correlates well with S_vO_2 and is easily monitored (29).

The objective of our study was to evaluate the relationship between a) CO and P_{aw} with the use of impedance cardiography, and b) CO and $S_{cv}O_2$ in ventilated paediatric patients without pulmonary disease.

III. Materials and methods

Impedance cardiography was performed in all of the studies (with 12 electrodes and a phono head) using ICG-M401 impedance cardiograph (Askit Ltd, Budapest, Hungary). The ICG-M401 uses a tertrapolar lead system with paired inner -voltage detecting- electrodes placed on either side in the supraclavicular fossa just above the level of the suprasternal notch, and along the midaxillary line at the level of the xyphoid. The outer -voltage generating-electrodes are placed 4 cm cephalad and caudad, respectively (Figure 1). Leads for the electrocardiogram were placed on the right and left pectoral areas and on the right and left lower quadrants of the abdomen. Finally a microphone was attached at a site above the heart where the second heart sound was loudest in order to record phonocardiogram. Stroke volume was calculated as follows, using ICG:

$$SV=\rho \cdot (l^2 \cdot Z_0{}^{-2}) \cdot dZ \cdot dt_{max}{}^{-2} \cdot LVET$$

where SV=stroke volume (ml), ρ=resistivity of blood (Ωcm), l=inner distance between the voltage detecting electrodes (cm), Z_0= baseline thoracic impedance (Ω), dZ/dT_{max}= maximum rate of change of impedance during systole (Ω/s) and LVET= left ventricular ejection time (ms). Stroke volume index (SVI) and cardiac index (CI) were calculated using the built-in software of the ICG-M401. Three 8-second impedance measurements were made during the last minute of each period, and averaged to provide a single value for SV.

III.1. Study design of haemodynamic changes related to PP in children.

After approval of the Hospital Ethics Committee and obtaining parental consent, 30 ASA I boys scheduled for elective laparoscopic varicocelectomy were enrolled in the study; patients' characteristics were (mean±SD):age 13±2.3 years, weight 46.6±14.8 kg. Children had been fasting for 6 hours before surgery and a premedication of 0.3-0.5 $mg \cdot kg^{-1}$ oral midazolam 60

minutes prior to induction of anaesthesia was given. In the operating theatre following the standard monitoring devices (ECG, Pulse oxymetry, NIBP), the 12 electrodes and the phono head of the impedance cardiograph were attached. The ICG was then used in continuous monitoring mode. Anaesthesia was induced with midazolam (0.1 $mg \cdot kg^{-1}$): propofol (2 $mg \cdot kg^{-1}$): fentanyl (2 $\mu g \cdot kg^{-1}$) and vecuronium (0.1 $mg \cdot kg^{-1}$) was used to facilitate intubation. Anaesthesia was maintained by continuous propofol infusion. Mechanical ventilation was started using volume controlled mode with expired tidal volume of 8-10 $mg \cdot kg^{-1}$ to achieve end tidal CO_2 pressure ($ETCO_2$) of 4-5.2 kPa (30 to 40 mmHg). PEEP was not administered. The ratio of inspiratory time to expiratory time was 1:2. During pneumoperitoneum $ETCO_2$ higher than 5.8 kPa (45 mmHg) was considered as hypercapnia and minute ventilation was then increased to achieve the desired range of $ETCO_2$. Pneumoperitoneum was created as follows: after a small incision below the umbilicus the Veress' needle was inserted into the peritoneal cavity, and the abdomen was insufflated with CO_2 to the desired intra-abdominal pressure (IAP) of 12-13 mmHg and this was maintained automatically. Two other trocars were inserted under laparoscopic guidance to locate and clip the dilated testicular vein(s). During surgery, patients were laying in a 15˚ head-down position. No further opioids after the initial dose of 2$\mu g \cdot kg^{-1}$ fentanyl were required. The values of heart rate (HR), mean arterial blood pressure (MABP), $ETCO_2$, peak inspiratory airway pressure (PIP), stroke volume (SV), stroke volume index (SVI), CO, cardiac index (CI), systemic vascular resistance (SVR) and systemic vascular resistance index (SVRI) were recorded every minute. The course of anaesthesia was divided into 4 periods (T1-4):T1, before induction; T2, between induction and incision; T3, during insufflation; T4, after desufflation of PP until awake. The mean values of PIP, CI, SVI, MABP, HR and SVRI of the four periods were compared using paired T-test.

III.2. Study design of Trendelenburg positioning and anaesthesia induction with propofol in children.

After approval of the Hospital Ethics Committee and obtaining informed parental consent thirty ASA I children of both sexes scheduled for elective minor orthopaedic surgery were enrolled in the study. Patients were fasted for 6 hours before surgery and premedication of 0.3-0.5 $mg \cdot kg^{-1}$ oral midazolam about 1 hour prior to induction of anaesthesia was given. In the operating room standard monitoring devices and the electrodes and phono head of the impedance cardiograph were attached. A 20 or 22-gauge cannula was inserted into a vein. Anaesthesia was induced with fentanyl (1.5 $\mu g \cdot kg^{-1}$) and propofol (3 $mg \cdot kg^{-1}$) and the appropriate size laryngeal mask airway (LMA) was inserted. Mechanical ventilation was started using the pressure control mode with 70% nitrous oxide in oxygen to achieve $ETCO_2$ of 4.3-5.2 kPa (35-40 Hgmm). Peak airway pressure ranged from 12-to 14 cmH_2O. During the study period, ventilatory settings were kept constant in each group and anaesthesia was maintained with continuous propofol infusion (8 $mg \cdot kg^{-1} \cdot h^{-1}$). Impedance cardiography was performed as mentioned above (III). Beside the haemodynamic variables of SVI and CI the Heather Index (HI) was measured, which represents a direct reflection of acceleration expressed as $\Omega \cdot s^{-2}$ for aortic ejection and thus contractility (30). Heather Index ($\Omega \cdot s^{-2}$) as the ratio of dZ/dT_{max} to RZ, where RZ(ms) is the interval between the peak of ECG R wave and the peak of dZ/dT wave, stroke volume index (SVI) and cardiac index (CI) were calculated using the built-in software of the ICG-M401. Three 8-second impedance measurements based on all cardiac cycles were made and averaged to provide a single value for SV and HI.

The study protocol was as follows: After baseline measurements in awake patients anaesthesia was induced. Patients were allocated to one of two positions using computer generated numbers: 20° head-down tilt (head-down group, HDG, n=15) or supine (supine group, SG, n=15). Patients' characteristics were [median (range)]: HDG; age 12 (7-16) years,

weight 42 (32-70) kg; SG; age 12 (7-16) years, weight 39 (26-76) kg. HDG patients were tilted into Trendelenburg position for 5 min, 30 s after LMA insertion. The SG remained in the supine position. During the study period no intravenous fluids or muscle relaxants were given and no movement or surgical stimulations was permitted. During the course of anaesthesia in each group, the values of HR, MABP, $ETCO_2$, SVI, CI, SVRI and HI were recorded before induction (B) and three (A_3) five (A_5) and eight (A_8) minutes after LMA insertion. Surgery was started after the last recording (A_8).

Statistical analysis: The first period (B) was used as the baseline. Analysis of variance (ANOVA) for repeated measures was used to compare time effects. Posthoc paired samples t-tests with Bonferroni correction were performed for the haemodynamic variables (HR, MABP, CI, SVI, SVRI, HI) to determine if variables obtained at A_3, A_5, and A_8 were significantly different from those obtained at B and from each other. Independent samples t-test was used to evaluate differences between groups at each levels. A p-level<0.05 was regarded as statistically significant.

III.3. Study design of haemodynamic effects of positive pressure ventilation in children.

After approval of the Hospital Ethics Committee and obtaining informed parental consent twelve children requiring mechanical ventilation in the Paediatric Intensive Care Unit were enrolled in the study. The median weight of the patients was 13 kg (range 9-16 kg), the median age was 41 months (range 7-65 months). None of the patients had pulmonary diseases. Four of them underwent head-neck surgery, three laparotomy, one surgery for tracheal stenosis, and four children were treated with complicated febrile convulsion. Haemoglobin and hematocrit values were normal in all patients. The ventilator used was a Siemens-Servo 300A (Siemens-Elema, Sweden) working in pressure-control (PCV) mode with the tidal volume (TV) of 6-8 $ml \cdot kg^{-1}$ to achieve an end-tidal CO_2 pressure of 4.3-5.2 kPa

(35-40 mmHg). Baseline PEEP was set to 5 cmH_2O. All patients were sedated intravenously with i.v. midazolam (0.1-0.2 $mg \cdot kg^{-1} \cdot h^{-1}$) and fentanyl (1-2 $\mu g \cdot kg^{-1} \cdot h^{-1}$). ECG, periferial oxygen saturation, MABP, $ETCO_2$ and central venous pressure (CVP) were monitored using a Datex-Ohmeda patient monitor (model S/5 Helsinki, Finland). All patients had a central venous catheter via the subclavian approach as a routine part of their management. The locations of cathetertips were in the lower part of the superior vena cava as confirmed by chest X-ray. Impedance cardiography was performed using ICG-M401 impedance cardiograph.

The study protocol was as follows: neuromuscular blockade was achieved by vecuronium 0.1 $mg \cdot kg^{-1}$ i.v. in the anaesthetized children. After a 5 min resting period with PEEP 5 cmH_2O (P_{b5}) with stable ventilatory and circulatory condition the following end-expiratory pressures were applied for 5 mins consecutively: PEEP 10 cmH_2O (P_{i10}); PEEP 15 cmH_2O (P_{i15}); PEEP10 cmH_2O (P_{d10}) and PEEP 5 cmH_2O (P_{d5}). The respiratory rate was adjusted [18 (2.5) at P_{b5}, 19 (2.7) at P_{i10}, 21 (3.0) at P_{i15}, 18 (2.7) at P_{d10} and 17 (1.9) at P_{d5} $breaths \cdot min^{-1}$, respectively] to obtain an $ETCO_2$ between 35 and 40 mmHg. Thus, the minute ventilation was maintained constant for each patient. Levels of PEEP and P_{aw} were registered from the ventilator. The values of HR, MABP, $ETCO_2$, CVP, P_{aw}, CI and SVI were recorded at the end of each time period. Central venous oxygen saturations were measured from venous sample with a blood-gas analyser (Stat Profile-pHOx-Plus, Nova Biomedical Co, Waltham, USA) at the end of each time period. All data are presented as mean (SD).

Statistical analysis: The first period (P_{b5}) was used as the baseline. Analysis of variance (ANOVA) for repeated measures was used to compare time effects. Posthoc paired samples t-tests with Bonferroni correction were performed for the haemodynamic variables (HR, MABP, CI, SVI), P_{aw} and $S_{cv}O_2$ to determine if variables obtained at P_{i10}, P_{i15}, P_{d10} and P_{d5} were significantly different from those obtained at P_{b5} and from each other. A p-level< 0.05

was regarded as statistically significant. The SPSS software, (version 12 for Windows, SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

IV. Results

IV.1. Results of haemodynamic changes related to PP in children.

Results are reported as mean ± standard deviation (SD). The average IAP was 12.4±2.1 mmHg. The average insufflation time was 16±4.5 min. After the induction of anaesthesia HR, MABP and CI decreased, the SVI remained unaffected. The decrease in CI was 11%, caused mainly by the decrease in HR. The insufflation resulted in a significant decrease in stroke volume and a further reduction in CI. Total reduction in CI was 25%. Following PP HR did not change. The MABP and the SVR increased significantly (Table 1). After desufflation the CI, SVI increased and the SVRI decreased significantly, but only the SVI returned to the baseline values. As a result of decreased thoracic compliance PIP elevated significantly during PP. No significant changes of $ETCO_2$ were noted during surgery (Table 2).

Heamodynamic changes	T1 Before induction	T2 Induct.-incision	T3 Insufflation	T4 After desufflation
HR, beat min^{-1}	97.7±16.6	82.4±15.5*	80.6±13.3	80.2±13.7
MABP, mmHg	79.5±10.6	64.3±5.7*	79.0±9.4**	78.6±9.4
CI, l min^{-1} m^{-2}	3.0±0.5	2.7±0.5*	2.2±0.5**	2.7±0.8***
SVI, ml m^{-2}	33.6±7.6	32.8±5.2	27.4±4.8**	33.3±8.1***
SVRI, dyns $sec^{-1}cm^{-5}m^{-2}$	2194±505	2100±486	2970±783**	2512±821***

*p<0.001 as compared with T1 **p<0.001 as compared with T2 ***p<0.001 as compared with T3

Table 1. The average results (mean±SD) of the measured (HR, MABP) and calculated (CI, SVI, SVRI) values of the four periods.

	T1	T2	T3	T4
PIP (cmH_2O)		19,8±2.6	23.1±3.0*	
$ETCO_2$ (mmHg)		33.3±3.7	35.5±7.6	

*p<0.01 as compared with T2

Table 2. Respiratory changes during anaesthesia

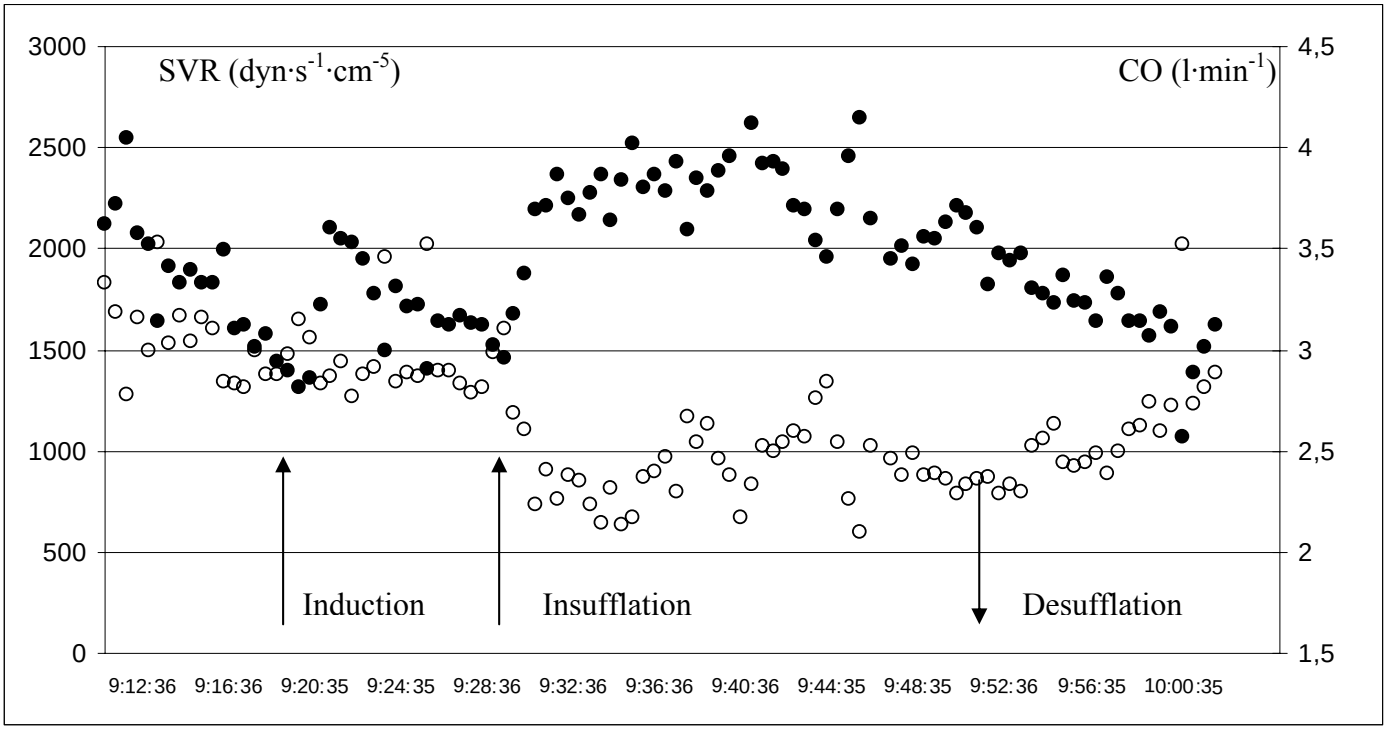

Figure 3. The values of CO (○) and SVR (●) in a patient during laparoscopy.

IV.2. Results of Trendelenburg positioning and anaesthesia induction with propofol in children

The changes in haemodynamic parameters are shown in Figs 4 and 5, and Table 3. Baseline haemodynamic variables were not significantly different between the groups.

After induction of anaesthesia, a significant ($p<0.05$) decrease in HR (32% in HDG and 16% in SG at A_3), MABP (25% HDG and 23% SG at A_3) and CI (24% HDG and 16% SG at A_3) were recorded in each group compared with baseline (B). The reduction in HR was more pronounced in the HDG at A_3 [66(13) vs. 78(17) beat $\cdot$ min^{-1} respectively, $p=0.039$]. The differences in CI and MABP between the groups were not significant. SVI did not change in the supine group while statistically but not clinically significant SVI elevation was observed in the HDG at A_3 as compared to the baseline [38.8(5.4) at B vs 42.9(6.4) ml $\cdot$ m^{-2} at A_3 $p=0.021$]. No significant differences in SVRI were found between and within the groups, while induction resulted in a significant decrease in HI in each group (Table 3, Figs 4 and 5). After induction, the end-tidal CO_2 concentrations in the HDG were higher than those is SG, and the differences were significant at A_3 and A_5 but not at A_8 (Table 3).

	Before Induction B		3 min after LMA A_3		5 min after LMA A_5		8 min after LMA A_8	
	HDG	SG	HDG	SG	HDG	SG	HDG	SG
HR(beat min^{-1})	97(11)	93(15)	66(13)*,†	78(17)*	67(13)*	75(16)*	68(13)*	75(17)*
MABP (mmHg)	82(7.5)	87.6(7.6)	63.1(7)*	65.3(8.3)*	62.6(5.9)*	64.3(7.9)*	63 (6.6)*	64.3(7.9)*
CI(l min^{-1} m^{-2})	3.7(0.5)	3.6(0.7)	2.8(0.4)*	3.0(0.5)*	2.9(0.5)*	3.0(0.5)*	2.7(0.5)*	3.0(0.5)*
SVI (ml m^{-2})	38.8(5.4)	38.5(5.4)	42.9(6.4)*	40.6(5.3)	42.4(5.3)	41.2(6.9)	40(6.2)	41.1(5.3)
SVRI(dyn s^{-1} cm^{-5} m^{-2})	1769(275)	2002(303)	1836(298)	1785(340)	1826(309)	1750(310)	1887(282)	1773(326)
HI (Ω s^{-2})	25(6)	23(7)	18(5)*	19(5)*	18(4)*	19(5)*	16(5)*	18(6)*
$ETCO_2$ (kPa)			5.6(0.5)†	4.8(0.5)	5.8(0.4)†	4.7(0.4)	5.4(0.4)	4.7(0.5)

*p<0.05 vs BI (baseline); †p<0.05 vs SG

Table 3.
Measured (HR, MABP) and calculated (SVI, CI, SVRI, HI) values of haemodynamic changes, and $ETCO_2$ of the four periods [mean(SD)].

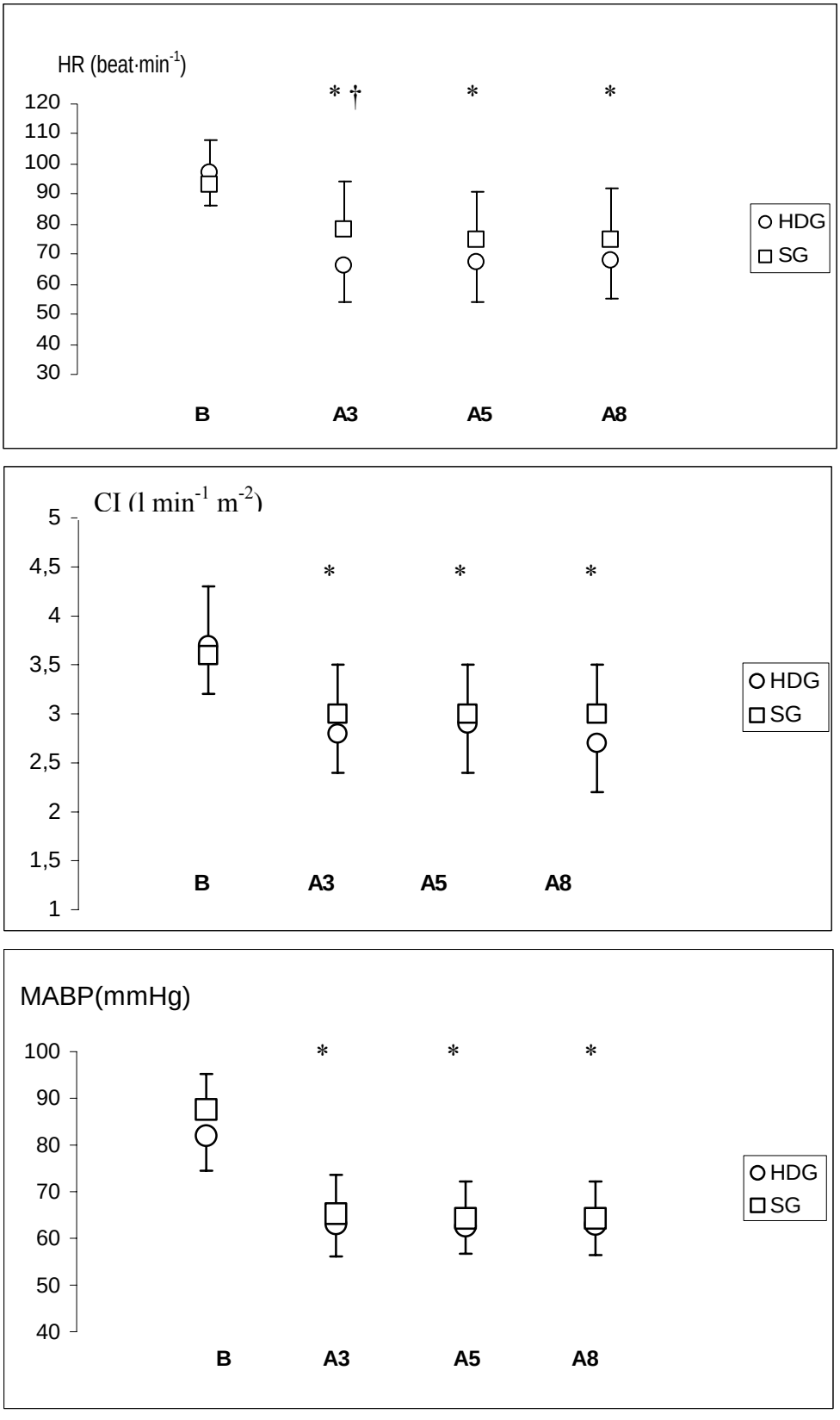

Figure 4.Changes in HR, CI and MABP after induction of anaesthesia in the two groups. Data are mean (SD).All values are significantly decreased at A_3, A_5 and A_8 as compared to baseline (B) (*$p<0.05$ vs B). In the HDG at A_3 HR is significantly lower compared to the SG (†$p<0.05$).

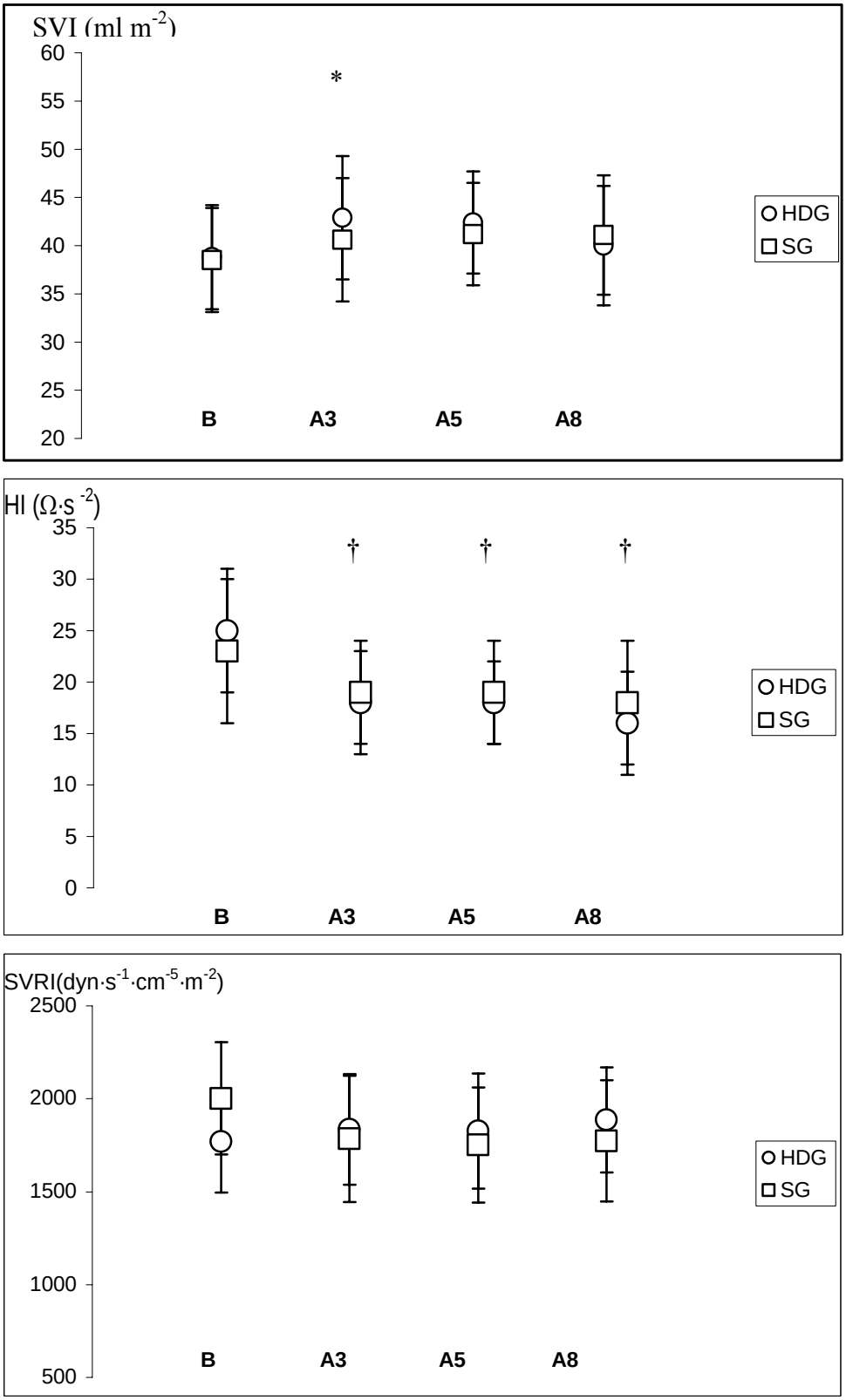

Figure 5. Values of SVI , HI and SVRI of the four time periods. Data are mean (SD). In HDG SVI statistically significantly increased at A_3 as compared to B (*$p<0.05$ vs B). The values of HI significantly decreased after propofol administration in each group (†$p<0.01$ vs B). SVRI values remained unchanged.

IV.3. Results of haemodynamic effects of positive pressure ventilation in children.

Increasing the P_{aw} did not result in significant changes in SVI and CI at P_{i10} and P_{i15} compared to P_{b5} as a baseline. PEEP reduction (P_{d5}) resulted in a statistically significant increase in SVI as compared to P_{i15} [26(5.1) at P_{i15} vs 30.3(4.2) ml · m^{-2} at P_{d5}]. The increase in CI was significant at P_{d5} [2.8(0.6) at P_{i15} vs 3.2(0.5) l · min · m^{-2} at P_{d5}]. CVP increased significantly after PEEP elevation [7.6(1.6) at P_{b5} vs 8.8(1.5) at P_{i10} than 11(1.7) mmHg at P_{i15}] and returned to the baseline when PEEP decreased. CI, HR, MAP and $ETCO_2$ did not change significantly. CO, HR, MAP and $ETCO_2$ did not change significantly. The values of $S_{cv}O_2$ decreased non-significantly after PEEP elevation (Table 4.).

Haemodynamic changes and $S_{cv}O_2$	P_{b5} PEEP:5	P_{i10} PEEP:10	P_{i15} PEEP:15	P_{d10} PEEP:10	P_{d5} PEEP:5
HR(beat·min^{-1})	106±14	105±14	107±14	104±12	105±11
CI(l·min·m^{-2})	2.8±0.6	2.8±0.5	2.8±0.6	3.0±0.4	3.2±0.5*
SVI (ml·min·m^{-2})	26.5±5.3	26.4±4.2	26.0±5.1	28.9±4.2	30.3±4.2*
CVP (mmHg)	7.6±1.6	8.8±1.5	11.0±1.7**	9.6±1.7	8.4±1.3
MABP (mmHg)	61±4.6	59.5±3.6	62.3±4.5	63.3±3.4	60.1±3.3
P_{aw}(cmH_2O)	8.8±1.6	14.3±1.0	19.4±1.4**	14.1±1.2	9.5±1.3
$ETCO_2$ (mmHg)	36.8±2.6	35.7±3.3	36.9±4.1	35.7±4.4	37.0±3.2
S_{cv}O2 (%)	76.5±3.6	74.6±4.7	73.5±5.1	74.5±5.5	74.9±5.0

*$p<0.05$ compared to T_{i15}; **$p<0.01$ compared to T_{b5},T_{i10},T_{d10} and T_{d5}

Table 4.
The measured (HR, CVP, MABP) and calculated (SVI, CI) values of haemodynamic changes, respiratory changes (P_{aw} and $ETCO_2$) and values of $S_{cv}O_2$ of the five periods.

V. Discussion

V.1 Discussion on haemodynamic changes related to PP in children.

This study demonstrates that the cardiovascular effects of carbon dioxide peritoneal insufflation can be measured using ICG in children during laparoscopic varicocelectomy. We found significant decrease in CI after induction of anaesthesia, partly the result of the decrease in heart rate as SVI did not greatly change (Table 1.). However during PP a significant reduction in SVI and CI and increase in SVRI and MABP was observed. Our results are similar to those reported using different techniques in adults. Using thermodilution method, claimed to be the gold standard in estimating CO, authors observed a significant reduction in CO, and SV during peritoneal insufflation (22, 31, 32). Another popular technique is oesophagus Doppler monitor (ODM), which is a semi-invasive method using an orally introduced Doppler head to measure aortic blood flow. Using ODM the results are similar to those measured by thermodilution (33, 34, 35). The results using transoesophageal echocardiography is controversial. De Agustin found minimal increase in CI in children (36), while Portera (32) and Cunningham (37) demonstrated no significant changes in left ventricular ejection fraction and left ventricular function throughout laparoscopy in adults. Studies in adults using impedance cardiography (38, 39) to monitor CI in patients undergoing laparoscopic surgery found significant decrease in stroke volume and cardiac output, similar to those measured by invasive techniques. On the other hand little data can be found on haemodynamic measurements in children. Using standard monitoring devices Tobias found minimal disturbance in cardiorespiratory function while examining fifty-five paediatric patients undergoing elective laparoscopy (40). Sfez examined 25 children scheduled for elective laparoscopic fundoplication. He reports no major cardiovascular or respiratory

changes intraoperatively (41). In our study the procedure was tolerated well by all the patients. No significant episodes of hyper-, or hypotension was observed. There were minimal changes in respiratory function, manifested by an increase in PIP required to achieve the desired $ETCO_2$ level. Despite the fact that laparoscopy seems to be a safe and well tolerated technique in children, an accurate method is required to monitor haemodynamic changes during PP even in healthy patients (prolonged insufflation, etc.). Impedance cardiography, measuring the pulsatile change in resistance to microcurrents to calculate stroke volume, especially useful in children. Being non-invasive it can be widely used under various circumstances (in the OR, ICU, ambulance service). The use of dermal electrodes does not cause discomfort to the patient, and has the potential for prolonged use in the same patient, but it can not be used during open chest procedures and chest wall surgery. It is a truly beat to beat measurement, giving continuous information about cardiac performance. Although ICG has been compared with several other techniques, where correlation was good (11, 12, 14) or relatively poor, especially in critically ill (42, 43), ICG-M401 is a unique device concerning its special software using electromechanical components (phono-head), beat to beat analysis when it is compared with an invasive technique that uses intermittent data collection with statistical correction. Using ICG to measure stroke volume non-invasively on a beat to beat basis showing trends helps in clinical decision making (44) (Figure 3). The instrument (ICG-M401) used in our study was tested by Pianosi who compared impedance measurements of CO with carbon dioxide rebreathig measurement of CO in healthy children and children with cystic fibrosis during exercise. He found that ICG provided reliable estimation of CO with good correlation of indirect Fick (CO_2) method (11, 12).

Pneumoperitoneum has multiple effects: it mechanically compresses the abdominal caval vein resulting in preload reduction (45) and on the other hand several studies suggest the release of humoral factors such as catecholamines and vasopressin behind the SVR elevation, partly

caused by intraoperative hypercapnia (46, 47). During laparoscopy the position of the diaphragm is influenced by both the head-down position and PP. We suspect that the increased minute ventilation necessary for CO_2 elimination counteracts the former effects, thus estimation of SV using unchanged electrode position during PP is reliable. We found decreased SVRI after desufflation of PP (Table 1), but remained elevated as compared with the values of T1. We suspect that moderately elevated SVRI after desufflation is partly the result of humoral factor release caused by insufflation. The increase in minute ventilation to avoid hypercapnia associated with a decrease in thoracic compliance resulted in significant PIP elevation. Some reports suggest that during mechanical ventilation in patients with PP the transmural right atrial pressure (TRAP, i.e., the pressure within the right atria minus the extracardiac pressure) should be used rather than directly measured central venous pressure (CVP) as an indicator of venous return to the heart. These studies found that TRAP does not change significantly as compared to that measured before insufflation (31, 48). The observation of a significant decrease of SV, despite the unchanged TRAP can be the result of elevated SVRI. We found remarkable increase in SVRI, but only a clinically insignificant change in PIP. Thus, we think that the reduction in CI in our study was minimally influenced by the unavoidable elevation of PIP to maintain normocapnia during PP. The usual cardiovascular monitoring techniques during anaesthesia (blood pressure, heart rate, pulse oximetry, capnography) give no accurate information on the changes in SVR and CO. We found similar MABP values before induction of anaesthesia and during insufflation while cardiac index decreased by 25% at the same time.

V.2. Discussion on Trendelenburg positioning and induction of anaesthesia with propofol in children.

After intravenous induction of anaesthesia using propofol and fentanyl, a 20° Trendelenburg positioning compared with supine did not clinically attenuate haemodynamic changes.

This study used non-invasive impedance cardiography to determine stroke volume, cardiac output and myocardial contractility. We could not find any reports describing the use of ICG to monitor on the effects of Trendelenburg positioning on SVI and CI in children. In paediatric intensive care patients good correlation was found between ICG and dye dilution (14), thermodilution (15) and the direct Fick method (16) in the measurement of cardiac output. The ICG-M401 has been validated for comparing impedance measurements of cardiac output (CO) with carbon dioxide rebreathing measurement of CO in healthy children (11) and children with cystic fibrosis during exercise in the supine position (12). ICG provided reliable estimation of CO and a good correlation with the indirect Fick (CO_2) method.

A decrease in arterial pressure after induction of anaesthesia with propofol is well recognized, and is one of its most frequently criticized characteristics in both children and adults (18, 19). We found significant decrease in CI in both groups (24% in HDG and 16% in SG) after induction of anaesthesia, probably as a result of the decrease in heart rates as SVI did not greatly change (Table 3, Figures 4, 5). Our results are similar to those reported by Aun et al, they found a significant (15%) reduction in cardiac index using two-dimensional echocardiography and pulse Doppler after propofol induction in children (19). However the mechanism of propofol induced hypotension has yet to be elucidated. Many studies have demonstrated substantially reduced systemic vascular resistance, reduced sympathetic nervous system activity resulting in venodilatation and thus decreasing venous return (19, 49). Some studies found that propofol causes a significant reduction in myocardial contractility (50). In our study no clinically important changes in SVRI were observed after induction while the

significant decrease in HI suggests direct myocardial depression. This reduced myocardial contractility may have contributed to CI decrease in our patients rather than the decreased systemic vascular resistance.

Fentanyl was used to supplement induction of anaesthesia with propofol. In combination with propofol there is some evidence that the addition of low-dose fentanyl may cause a slower heart rate when compared with those patients who have received propofol only for induction (51). Similarly to nitrous oxide the haemodynamic effects of fentanyl would also apply to both groups equally in our study.

The Trendelenburg position has been used for decades as a first-step manoeuvre to treat haemodynamic instability as a consequence of reduced preload. The extent of the resulting preload increase, the autotransfusion effect and the desired cardiac output increase has been investigated using several different techniques. However the results have been conflicting. Terai et al. examined healthy volunteers using two-dimensional echocardiograms. They found a 16% increase in CO followed by the increase in left ventricular end-diastolic volume (LEDV) at 1 minute after head-down tilting, although these changes disappeared after 10 minutes of tilting (52). Reuter et al. used transpulmonary thermodilution technique to measure SVI, CI and volumetric preload parameters (intrathoracic blood volume index) during Trendelenburg position in postoperative cardiac patients. They found only slight increase of preload volume without improving cardiac function (21). Data are limited with respect to the haemodynamic effect of head-down tilt in children and adolescents. Our results are in line with those reported using different techniques mainly in adults (21, 22). We found statistically significant elevation in SVI in the head-down group at A_3 as compared with B. The only clinically significant difference between the two groups was found in HR which decreased more in the HDG than in the SG at A_3. The possible explanation is that carotid and aortic baroreceptors respond to an increase in hydrostatic pressure with systemic vasodilation and

bradycardia (53). In our study the slight increase in preload volume did not result in CI elevation because of the marked decrease in HR during head-down tilt.

As a consequence of pressure-controlled ventilation, a significant increase in $ETCO_2$ was observed in the HDG after induction of anaesthesia at A_3 and A_5. We used pressure-controlled ventilation to keep P_{aw} constant after a change in body position to avoid the possible negative haemodynamic effects of volume controlled ventilation when lung compliance decreased. As a consequence, CO_2 elimination was diminished in the HDG, but the moderate hypercarbia probably did not affect the haemodynamic response to head-down tilt.

One important limitation of this study is that the ICG-M401 instrument has not been validated in head-down tilt. Although body posture may alter the volume of electrically participating thoracic tissue, agreement was found between the results of ICG measured SV by other instruments and of standard techniques in tilted positions (54).

V.3. Discussion on the haemodynamic effects of positive pressure ventilation in children.

High PEEP levels in ventilated children without pulmonary pathology did not result in significant haemodynamic changes. Mechanical ventilation strategies using PEEP for optimal alveolar recruitment remain the mainstay for managing respiratory failure in children. Although the haemodynamic effects of mechanical ventilation and ventilatory manoeuvres like PEEP have been studied extensively, we could not find any reports describing the use of ICG to monitor the effects of IPPV and PEEP on SVI and CI in children. The accuracy and reliability of ICG in adults with no primary pulmonary pathology under mechanical intermittent positive-pressure ventilation with PEEP are reported to be good (13), and in paediatric intensive care patients good correlation was found between ICG and dye dilution,

thermodilution and the direct Fick method (14, 15, 16). Impedance cardiography, measuring the pulsatile change in resistance to microcurrents to calculate stroke volume is especially useful in children. Being non-invasive it can be widely used under various circumstances (in the OR, ICU, ambulance service).

We found no significant decrease in SVI, CI and $S_{cv}O_2$ after PEEP elevation. Our results are not in line with those reported using different techniques in children and infants. Gullberg et al. used Doppler technique to measure blood flow velocity in the ascending aorta and thus SVI (55). They found a significant (12.6%) decrease in CI in otherwise healthy infants when P_{aw} was increased by increasing PEEP to the maximum of 6 cmH_2O. Shekerdemian et al. used the direct Fick method to calculate CI during intermittent positive pressure ventilation followed by negative pressure ventilation postoperatively in infants and children requiring open heart surgery (56). They found that negative pressure ventilation has heamodynamic advantages over conventional IPPV. Our findings suggest that normovolaemic children with normal lung compliance can compensate the negative effects of elevated PEEP on venous return. The PEEP-induced increase in intrathoracic pressure might have been blunted by the high lung elastance, resulting in relatively low pericardial pressures. Oesophageal pressure changes as an indicator of transmission of intrapulmonary pressures to the mediastinal area were found to be minimal in an animal model (57). We did not measure the intra-abdominal pressure, but the unchanged SVI and CI after P_{aw} elevation can be the result of an in-phase-associated pressurisation of the abdominal compartment with compression of the liver and squeezing of the lungs as reported in adults (58). The circulation is a closed-loop, autoregulated circuit, which attempts to maintain the perfusion pressure of the organs and blood flow by altering the autonomic tone. Several studies have suggested that humoral factors such as cathecolamines and vasopressin are released during IPPV with PEEP (59, 60). We measured SVI 5 minutes after P_{aw} was altered. It is difficult to differentiate between

primary and secondary effects of increased PEEP leading to a new haemodynamic steady-state. The altered autonomic tone probably contributed to the fact, that CI remained stable at P_{i15} and that SVI and CI increased significantly at T_{d5} when airway pressure returned to normal.

We measured $S_{cv}O_2$ to determine the changes in the balance of O_2 supply/demand. Although mixed venous oxygen saturation (S_vO_2) as a gold standard indicates the accuracy of the tissue oxygenation, several reports have shown that S_vO_2 and $S_{cv}O_2$ are closely related and interchangeable in various clinical settings (61, 62, 63). Oxygen demand remained unchanged during the study. The constant values of ScvO2 are in line with the lack of significant changes in CO as measured by ICG.

VI. Conclusions

VI.1. Conclusions of haemodynamic changes related to PP in children.

Our findings suggest, that significant haemodynamic changes occurring in healthy children caused by peritoneal insufflation can be monitored by impedance cardiography. Our patients tolerated the cardiovascular effects of these short peritoneal insufflations well. Further investigations are needed to examine the circulatory effect of PP in younger children and the effect of prolonged insufflation on haemodynamic changes. Proper monitoring is essential for children with impaired cardiac function undergoing laparoscopy. In these cases impedance cardiography can be a useful method to monitor trends in cardiac function. Comparison of ICG monitoring to thermodilutions techniques is warranted in the future.

VI.2. Conclusions of Trendelenburg positioning and anaesthesia induction with propofol in children.

Using ICG to determinate cardiac output, we found that (a) reduced myocardial contractility is responsible for the decrease in cardiac output following propofol-fentanyl induction of anaesthesia, and (b) a 20° head-down tilt does not prevent a decrease in cardiac output after induction of anaeshesia using a combination of propofol and fentanyl in healthy children.

VI.3. Conclusions of haemodynamic changes of positive pressure ventilation in children.

Using ICG to determine cardiac output, we found that short-term PEEP elevation from 5 up to 15 cmH_2O does not cause a significant decrease in CI in ventilated normovolaemic children without lung injury. The unchanged values of $S_{cv}O_2$ indicate that changes in P_{aw} did not influence the balance of oxygen supply and demand.

VII. References

1. Wo CCJ, Shoemaker WC, Appel PL, Bishop MH, Kram HB, Hardin E. Unreliability of blood pressure and heart rate to evaluate cardiac output in emergency resuscitation and critical illness. *Crit Care Med* 1993;**21**:218-223.
2. Dalen JE, Bone RC. Is it time to pull the pulmonary artery catheter? *JAMA* 1996; **18**:916-918.
3. Kubicek WG, Patterson RP, Witsoe DA: Impedance cardiography as a non invasive method of monitoring cardiac function and other parameters of the cardiovascular system. *Ann NY Acad Sci* 1970;**170**:724-729.
4. Bernstein DP : Continuous non invasive real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. *Crit Care Med* 1986;**14**:898-900.
5. Winter UJ, Klocke RK, Kubicek WG, Niederlag W (eds).Thoracic Impedance measurements in Clinical Cardiology. New York: Thieme Medical Publishers, 1994.
6. Summers RL, Shoemaker WC, Peacock WF, Ander DS, Coleman TG. Bench to bedside: Electrophysiologic and clinical principles of noninvasive hemodynamic monitoring using impedance cardiography. *Acad Emerg Med* 2003;**10**:669-680.
7. Naszlady A. Impedancia kardiográfia alkalmazási lehetőségei *Aneszteziológia és Intenzív Terápia Supplementum* 1995. **25**. 1. sz.: 4-8
8. Gömöry A., Horváth S., Thöring J., Fésüs L, Asbóth R., Naszlady A.: Non-invasive determination and follow up of circulatory parameters by means of impedance cardiography. *Orv Hetil* 1988; 129;2083-2089

9. Kerekes L, Nagy I, Varga V. The analysis of haemodynamic changes measured by the method of impedance cardiography during spinal anaesthesia. *Cardiol Hung* 1993. **22**. suppl.p. 8-11.

10. Melczer L., Brolly M., Farkasfalvi K, Komócsi A. Frekvencia-válaszos (rate responsive) pacemakerek programozása impedancia kardiográfiával. *Aneszteziológia és Intenzív Terápia. Supplementum* 1995; **25**: 33-39.

11. Pianosi P, Garros D. Comparison of impedance cardiography with indirect Fick (CO_2) method of measuring cardiac output in healthy children during exercise. *Am J Cardiol* 1996;**77**:745-749.

12. Pianosi P. Impedance cardiography accurately measures cardiac output during exercise in children with cystic fibrosis. *Chest* 1997;**111**:333-337.

13. Castor G, Molter G, Helms J, Niedemark I, Altmayer P. Determination of cardiac output during positive end-expiratory pressure-Noninvasive electrical bioimpedance compared with standard thermodilution. *Crit Care Med* 1990;**18**:544-546.

14. O'Connel AJ, Tibbals J, Coulthard M. Improving agreement between thoracic bioimpedance and dye dilution cardiac output estimation is children. *Anaesth Intensive Care* 1991;**19**:434-440.

15. Introna RP, Pruett JK, Crumrine RC, Cuadrado AR. Use of transthoracic bioimpedance to determine cardiac output in pediatric patients.*Crit Care Med* 1998;**16**:1101-1105.

16. Braden DS, Leatherbury L, Treiber FA, Strong WB. Noninvasive assessment of cardiac output in children using impedance cardiography. *Am Heart J* 1990;**120**:1166-1172.

17. Georgeson KE, Owings E. Advances in minimally invasive surgery in children. Am J Surg. 2000;**180**:362-364.

18. Assuncao Braga AF, Braga FSS, Poterio GMB, Filier PR, Cremonesi E. The effect of different doses of propofol on tracheal intubating conditions without muscle relaxant in children. *Eur J Anaesth* 2001;**18**:384-388.
19. Aun CST, Sung RYT, O'Meara ME, Short TG, Oh TE. Cardiovascular effects of intravenous induction in children: comparison between propofol and thipentone. *Br J Anaesth* 1993;**70**:482-485.
20. Wilcox S, Vandam LD. Alas, poor Trendelenburg and his position! A critique of its uses and effectiveness. *Anesth Analg* 1998;**67**:574-578.
21. Reuter DA, Felbinger TW, Schmidt C et al. Trendelenburg positioning after cardiac surgery: effects on intrathoracic blood volume index and cardiac performance. *Eur J Anaesthesiol* 2003;**20**:17-20 .
22. Hirvonen EA, Nuutinen LS, Kauko M. Haemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laparoscopic hysterectomy. *Acta Anaesthesiol Scand* 1995;**39**:949-955.
23. Manner T, Aantaa R, Alanen M. Lung compliance during laparoscopic surgery in paediatric patients. *Paediatr Anaesth* 1998;**8**:25-29.
24. Cournand A, Motley H, Werko L, Richards D. Physiologic studies of the effects of intermittent positive pressure breathing on cardiac output in man. *Am J Physiol* 1948;**125**:261-273.
25. Diebel LN, Myers T, Dulchavsky S. Effect of increasing airway pressure and PEEP on he assessment of cardiac preload. *J Trauma* 1997;**42**:585-590.
26. Jellinek H, Krafft P, Fitzgerald RD, Schwarz S, Pinsky MR. Right atrial pressure predicts hemodynamic response to apneic airway pressure. *Crit Care Med* 2000;**28**:672-678.

27. Gullberg N, Winberg P, Selldén H. Changes in stroke volume cause change in cardiac output in neonates and infants when mean airway pressure is altered. *Acta Anaethesiol Scand* 1999;**43**:999-1004.

28. Shekerdemian LS, Bush A, Lincoln C, Shore DF, Petros AJ, Redington AN. Cardiopulmonary interactions in healthy children after simple cardiac surgery: the effects of positive and negative pressure ventilation. *Heart* 1997;**78**:587-593.

29. Rivers EP, Ander DS, Powell D. Central venous oxygen saturation monitoring in the critically ill patient. *Curr Op Crit Care* 2001;**7**:204-211.

30. Mezzacappa ES, Kelsey RM, Katkin ES. The effects of epinephrin administration on impedance cardiographic measures of cardiovascular function. *J Appl Physiol* 1999; **31**:189-196.

31. Joris JL, Noirot DP, Legrand MJ, et al : Haemodynamic changes during laparoscopic cholecystectomy. *Anesth Analg* 1993;**76**:1067-1071.

32. Portera CA, Compton RP, Walters DN *et al*. Benefits of pulmonary artery catheter and transesophageal echocardiographic monitoring in laparoscopic cholecystectomy patients with cardiac disease. *Am J Surg* 1995; **169**:202-206.

33. Dexter SP, Vucevic M, Gibson J *et al*. Haemodynamic consequences of high- and low-pressure capnoperitoneum during laparoscopic cholecystectomy. *Surg Endosc* 1999; **13**:376-381.

34. Elliot S, Savill P, Eckersall S. Cardiovascular changes during laparoscopic cholecytectomy: a study using transoesophageal Doppler monitoring. *Eur J Anaethesiol* 1998;**15**:50-55.

35. Haxby EJ, Gray MR, Rodriguez C *et al.* Assessment of cardiovascular changes during laparoscopy hernia repair using oesophageal Doppler. *Br J Anaesth* 1997;**78**:515-519.

36. De AgustinJC, Zabala JI, Zunzunegui JL *et al.* Alteraciones hemodinamicas durante la cirugia laparoscopica. Estudio preliminar. *Cir Pediatr* 1999;**12**:30-32.

37. Cunningham A, Turner J, Rosenbaum S. Transoesophageal echocardiographic assessment of haemodynamic function during laparoscopic cholecystectomy. *Br J Anaesth* 1993;**70**:621-625.

38. Westerband A, Van De Water J, Amzallag M *et al.* Cardiovascular changes during laparoscopic cholecystectomy. *Surg Gynecol Obstet* 1992;**175**:535-538.

39. Critchley LA, Critchley JA, Gin T. Haemodynamic changes in patients undergoing laparoscopic cholecystectomy: measurment by transthoracic electrical bioimpedance. *Br J Anaesth* 1993;**70**:681-683.

40. Tobias JD, Holcomb GW, Brock JW et al: Cardiorespiratory changes in children during laparoscopy. *J Pediatr Surg* 1995;**30**:33-36.

41. Sfez M, Guérard A, Desruelle P,: Cardiprespiratory changes during laparoscopic fundoplication in children. *Ped Anest* 1995;**5**:89-95.

42. Young J, McQuillan P. Comparison of thoracic electrical bioimpedance and thermodilution for the measurement of cardiac index in patients with severe sepsis. *Br J Anaesth* 1993;**70**:58-62.

43. Genoni M, Pelosi P, Romand J. et al. Determination of cardiac output during mechanical ventilation by electrical bioimpedance or thermodilution in patients with acute lung injury: Effect of positive end-expiratory pressure. *Crit Care Med* 1998;**26**:1441-1445.

44. Vereczkey G. Assessment of Tissue Oxygenation in a Cardiovascular ICU with Radiometer's ABL-625, Siggaard Andersen's OSA and ASK*IT*'s NHMS. In: Eke A, Deply DT, eds. *Oxygen Transport to Tissue XXI* .Kluwer Academic/Plenum Press, 1999;453-468.

45. Ortega AE, Richman MF, Hernandez M, Peters JH, Anthone GJ, Azen S, Beart RW Jr. Inferior vena caval blood flow and cardiac haemodynamics during carbon dioxide pneumoperitoneum. *Surg Endosc* 1996;**10**:920-924.

46. Punnonen R, Viinamaki O,: Vasopressin release during laparoscopy: role of increased intraabdominal pressure. *Lancet* 1982;**1**:175-176.

47. Rasmussen JP, Dauchot PJ, De Palma RG, Sorensen B, Regula G, Anton AH, Gravenstein JS. Cardiac function and hypercarbia. *Arch Surg* 1978;**113**:1196-1200.

48. Diamant M, Benumof JL, Saidman LJ. Haemodynamics of increased intra-abdominal pressure. *Anaesthesiology* 1978;**48**:23-27.

49. Ebert TJ. Sympathetic and haemodynamic effects of moderate and deep sedation with propofol in humans. *Anesthesiology* 2005;**103**: 20-24.

50. Mulier JP, Wouters PF, Van Aken H, Vermaut G, Vandermersch E. Cardiodynamic effects of propofol in comparison with thiopental assessment with a transesophageal electrocardiographic approach. *Anesth Analg* 1991;**72**:28-35.

51. Van Aken H, Meinhausen E, Prien T, Beussel T, Heinecke A, Lawin P. The influence of fentanyl and tracheal intubation on the heamodynamic effect of anaesthesia induction with propofol/N_2O in humans. *Anesthesiology* 1988;**68**:157-166.

52. Terai C, Anada H, Matsushima S, Shimiziu S, Okada Y. Effects of mild Trendelenburg on central hemodynamics and internal jugular vein velocity, cross sectional area, and flow. *Am J Emerg Med* 1995;**13**:255-258.

53. Sibbald WJ, Paterson NA, Holliday RL, Baskerville J. The Trendelnburg position: hemodynamic effects in hypotensive and normotensive patients.*Crit Care Med* 1985; **7**:218-224.

54. Cybulski G, Michalak E, Kozluk E, Piatkowska A, Niewiadomski W. Stroke volume and systolic time intervals: beat-to-beat comparison between echocardiography and

ambulatory impedance cardiography in supine and tilted positions. *Med Biol Eng Comput* 2004;**42**:707-711.

55. Gullberg N,Winberg P, Selldén H. Changes in stroke volume cause change in cardiac output in neonates and infants when mean airway pressure is altered. *Acta Anaethesiol Scand* 1999;**43**:999-1004.
56. Shekerdemian LS, Bush A, Lincoln C, Shore DF, Petros AJ, Redington AN. Cardiopulmonary interactions in healthy children after simple cardiac surgery: the effects of positive and negative pressure ventilation. *Heart* 1997;**78**:587-593.
57. Luecke T, Roth H, Herrmann P, Joachim A, Weisser G, Pelosi P, Quintel M. Assessment of cardiac preload and left ventricular function under increasing levels of positive end-expiratory pressure. *Intensive Care Med* 2004; **30**:119-126.
58. Van den Berg, Paul C.M., Jos R.C. Jansen, Michael R. Pinsky. Effect of positive pressure on venous return in volume-loaded cardiac surgical patients. *J Appl Physiol* 2002;**92**:1223-1231.
59. Kaczmarczyk G, Vogel S, Krebs M, Bunger H, Scholz A. Vasopressin and renin-angiotensin maintain arterial pressure during PEEP in nonexpanded, conscious dogs. *Am J Physiol* 1996;**271**:1396-1402.
60. Payen DM, Brun-Buisson CJ, Carli PA, HuetY, Leviel F, Cinotti L, Chiron B. Hemodynamic, gas exchange, and hormonal consequences of LBPP during PEEP ventilation. *Am J Physiol* 1987;**62**:61-70.
61. Reinhart K, Rudolph T, Bredle DL, Hannemann L, Cain SM. Comparison of central-venous to mixed-venous oxygen saturation during changes in oxygen supply/demand. *Chest* 1989;**95**:1216-1221.

62. Schou H, Perez de Sá V, Larsson A. Central and mixed venous blood oxygen correlate well during acute normovolaemic hemodilution in anaesthetized pigs. *Acta Anaesthesiol Scand* 1998;**42**:172-177.
63. Ladakis C, Myrianthefs P, Karabinis A, Karatzas G, Dosios T, Fildissis G, Goga J, Baltopoulos G. Central venous and mixed venous oxygen saturation in crtically ill patients. *Respiration* 2001;**68**:279-285.

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IX. Publications of the author

IX.1. The thesis is based on the following papers

1. **Kardos A,** Vereczkey G, Pirot L, Nyiradi P, Melker R. Use of impedance cardiography to monitor haemodynamic changes during laparoscopy in children. *Paed Anaesth* 2001; **11**:175-179. **IP**: **0.88**

2. **Kardos A,** Vereczkey G, Szentirmai C. Haemodynamic changes during positive pressure ventilation in children. *Acta Anaesthesiol Scand* 2005; **49**:649-653. **IP: 1.837**

3. **Kardos A,** Foldesi C, Nagy A, Saringer A, Kiss A, Kiss G, Marschalko P, Szabo M. Trendelenburg positioning does not prevent a decrease in cardiac output after induction of anaesthesia with propofol in children *Acta Anaesthesiol Scand* 2006; **50**:869-874. **IP**: **1.863**

IX.2. Other papers

1. Kardos A , Kiss A, Mekler R. Harmadfokú AV blokkal, miokardiális és hepatocelluláris érintettséggel járó infectio öt hónapos csecsemőnél. *Pediáter* 1999; **8**: 159-162.

2. Szentirmai Cs, **Kardos A.** Súlyos koponyasérültek kezelése. *Gyermekaneszteziológia és Intenzív Terápia,* 2003 ;**3**:13-23

3. Máté M, **Kardos A**. A parapneumoniás folyadékgyülem kezelése fibrinolysissel. *Gyermekaneszteziológia és Intenzív Terápia,* 2003;**3**:24-30

4. Vatasescu R, Shalganov T, **Kardos A**, Jalabadze K, Paprika D, Gyorgy M, Szili-Torok T. Right Diaphragmatic Paralysis Following Endocardial Cryothermal Ablation of Inappropriate Sinus Tachycardia. *Europace* 2006 ;**8**:904-6.

5. Shalganov TN, Paprika D, Vatasescu R, **Kardos A**, Mihalcz A, Kornyei L, Szatmari A, Szili-Torok T. Mid-term echocardiographic follow up of left ventricular function with permanent right ventricular pacing in pediatric patients with and without structural heart disease. *Cardiovasc Ultrasound*. 2007 **12**;5:13.

6. Kiss A, Polovitzer M, Merksz M, **Kardos A**, Schaffer P, Apor A, Huttl K. Treatment of posttraumatic high-flow priapism in 8-year-old boy with percutaneous ultrasound-guided thrombin injection. *Urology*. 2007;**69**:779.e7-9.

7. **Kardos A**, Foldesi C, Ladunga K, Toth A, Szili-Torok T. Pulmonary vein isolation without left atrial mapping.*Indian Pacing Electrophysiol J*. 2007 1;**7**:142-7.

8. Bauernfeind T, **Kardos A**, Foldesi C, Mihalcz A, Abraham P, Szili-Torok T. Assessment of the maximum voltage-guided technique for cavotricuspid isthmus ablation during ongoing flutter. *J Interv Card Electrophysiol*. 2007 ; **19**:195-199.

IX.3. Abstracts

1. Kardos A, Stegeman B, Foldesi C, Mihalcz A, Csakany L, Szili-Torok T. Comparison of coupled and paired pacing for rapid rate control during atrial fibrillation. *JAAC* 2007; 49 (Supplement A); 13A:903-241.

2. Kardos A, Kornyei L, Foldesi C, Szili-Torok T. Cryomapping offers advanteges for ablation near to the atrioventricular junction in paediatric patients. *Europace* 2007; 9 (Supplement 3) 39.

3. Foldesi C**, Kardos A**, Mihalcz A, Szili-Torok T. Electrophysiology study before cardiac resynchronisation device implantation: pre-implant coronary sinus canulation offers advantages for cardiac resynchronization procedural outcome. *Europace* 2007; 9 (Supplement 3) 338.

4. Bauernfeind T, **Kardos A**, Foldesi C, Mihalcz A, Szili-Torok T. Assessment of the maximum voltage-guided technique for cavotricuspid isthmus ablation during ongoing atrial flutter. *Europace* 2007; 9 (Supplement 3) 754.