Cardiovascular effects of thoracic epidural anaesthesia

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Chapter 6

Effect of increasing age on the hemodynamic response to Thoracic Epidural Anaesthesia

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Introduction

Thoracic epidural anaesthesia (TEA) combined with general anaesthesia is considered to be the gold standard anaesthetic approach in lung surgery. The cardiac sympathetic outflow emerges from C5 to T5 levels, with the main supply to the ventricles from T1 to T4[1]. TEA results in blockade of these nerves and changes in heart rate, left and right ventricular function and myocardial oxygen demand may occur. TEA might provide cardiac protection[2], has been successfully used in humans to treat refractory angina[3] and may increase the diameter of stenotic epicardial coronary arteries in patients with coronary artery disease[4]. However, TEA decreases arterial and venous vessel tone influencing pre-and afterload of the heart and may directly affect myocardial performance[5]. Ageing is accompanied with a greater sensitivity to volume status of the cardiovascular system[6] due to impaired autonomic nervous system control and impaired diastolic function[7]. These factors suggest that elderly patients may be particularly vulnerable to the hemodynamic side effects of TEA, however, remarkably few data exist on the relationship between age and the hemodynamic response to TEA. In a previous study we did not find that age effected the total amount of spinal segments blocked after TEA with a fixed dose of ropivacaine at the T3-T4 interspace[8].

In the present study we tested the hypothesis that TEA results in more profound cardiovascular effects in the elderly as compared to younger patients. Using contemporary echocardiographic techniques to assess diastolic and systolic function we quantified the effects of TEA on biventricular function in a wide age-spectrum of patients presenting for lung surgery.

Methods

Patients

The protocol of this study was reviewed and approved by the Committee on Medical Ethics of the Leiden University Medical Centre (reg. no: P09060), Leiden, the Netherlands (Chairperson Prof. Dr. A.J. Rabelink) on 6 July 2009 and approved by the Centrale Commissie Mensgebonden Onderzoek (CCMO), as Competent Authority for the review of clinical trials in the Netherlands, NL27041.058.09. The subjects reported in this study have been previously reported in an article presenting data on the effects of age on the segmental spread of local anesthetics[8].

Patients scheduled for pulmonary surgery (full lateral thoracotomies and in case of pleural rubbing video assisted thoracoscopic surgery procedures) under thoracic epidural anaesthesia and general anaesthesia were included in this open, observational, single-center study. All study measurements were done in awake patients. After written informed consent, patients were stratified in one of three age groups (Group 1: 18-45 years; Group 2: 46-65; Group 3: 66 years and older) to ensure an even age distribution across the age spectrum. Patients with a contraindication for epidural anaesthesia and pregnant women were excluded from the study. The groups were not matched with regard to antihypertensive or anti-arrhythmic medication in order to have a population sample that resembles clinical reality, which implies “natural

confounding" of age and use of medication. For the same reason, we did not exclude patients with hypertension, diabetes or patients using anti-arrhythmic drugs. None of the patients included in this study had a history or signs of coronary artery disease.

Procedures

Patients were fasting from midnight before surgery. Antihypertensive medication was continued on the day of surgery. Patients were premedicated with midazolam 7.5 mg (if < 65 yr) or 5 mg (if > 65 yr) orally, 45 min before induction of epidural anaesthesia. A 14-gauge intravenous (IV) catheter was placed in the arm for administration of fluids and medication. A colloid infusion (Voluven®, Hydroxyethyl starch 130/0.4, Fresenius Kabi, Bad Homburg, Germany) was administered at a rate of 10 ml.kg^{-1} over a 40-min period beginning 10 min before the epidural injection of ropivacaine to maintain preload[9]. Epidural puncture was performed with the patient in the sitting position at the T3-T4 interspace, using a paramedian approach. A 20-gauge lateral eye catheter was introduced5 cm into the epidural space in the cephalad direction. In case of signs of intravascular puncture during epidural needle or catheter placement or signs of dural puncture from the epidural needle or catheter, patients were excluded from the study. After catheter insertion patients received 8 ml ropivacaine 0.75% through the catheter. During the echocardiographic examination before and after TEA patients were placed in the left lateral decubitus position.

Measurements

Analgesia was assessed bilaterally by temperature discrimination using ice-cubes. An arterial line 20 G was inserted after local infiltration with lidocaine 1% in the radial artery to monitor arterial blood pressure (Edward Lifesciences LLC, Irvine, Ca, USA). Mean arterial pressure (MAP), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured immediately before (baseline) and 30 minutes after epidural injection of ropivacaine. Heart rate (HR) was monitored continuously from the electrocardiogram. If the systolic blood pressure decreased more than 30% below baseline value or to less than 90 mm Hg, ephedrine 5 mg was given IV. Bradycardia (HR< 55 beats per minute (bpm)) was treated with atropine sulphate, 0.25-0.5 mg IV.

Echocardiography

Standard transthoracic two-dimensional, pulsed, color-flow and M-mode Doppler echocardiographic examination was performed with a Vivid 7 ultrasound machine (GE Medical Systems) equipped with a multifrequency phased array transducer. Recordings were made immediately before placement of an epidural catheter and 45 minutes after thoracic epidural injection of ropivacaine. All measurements were acquired from parasternal long axis (PLAX), apical 4 (A4C) – and 2-chamber (A2C) views and apical long- axis view with the patients in lateral decubitus positioning. For Doppler variables, we aimed for correct alignment (< 20°) of the beam of interrogation with the motion of blood and tissue under investigation. All measurements

were carried out unblinded by one examiner certified in TTE by the European Association of Echocardiography (EAE). Echocardiographic images were stored digitally for subsequent off-line analysis with EchoPac software (EchoPAC Dimension version 7.0.0, GE Vingmed Ultrasound AS, Horten, Norway).

Left Ventricular (LV) function:
Interventricular septum thickness at diastole (IVSd) and left ventricle posterior wall thickness at diastole (LVPWd) were measured from M-mode echocardiographic recordings at the mid-ventricular level in the parasternal long-axis view. A minimum of three beats were measured and averaged for all Doppler variables. In the A4C view using pulsed wave Doppler at the tips of the mitral leaflets the following parameters were obtained: peak velocity during early filling phase (MV E), peak velocity during atrial contraction phase (MV A), the ratio of E to A (MV E/A ratio) and the time interval required for the E velocity to decline from its peak to the baseline (MV E deceleration time or MV DT). Left ventricle end- diastolic volume (LVEDV) and left ventricle end-systolic volume (LVESV) were obtained by tracing the end-diastolic and end-systolic endocardial borders in the A2C and A4C views calculating ejection fraction (EF) with biplanar Simpson's rule. Stroke volume (SV) and Cardiac output (CO) were calculated using the LV outflow velocity time integral, heart rate and LV outflow tract diameter. Cardiac index (CI) was calculated by dividing the CO with the body surface area (BSA).

Long-axis function of the heart was evaluated by measuring the longitudinal velocity of the mitral annulus at the medial and lateral site using 2D-colour coded tissue Doppler imaging (TDI). Off line reconstruction of a myocardial velocity-time curve provided the following parameters: systolic velocity of the lateral (MV S' lateral) and medial (MV S' medial) mitral annulus, early and late diastolic velocity of the mitral annulus at the lateral (resp. MV E' lateral and MV A' lateral) and medial site (resp. MV E' medial and MV A' medial), isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT) and ejection time (ET) (**Figure 1**). LV myocardial performance index or Tei index (MPI-LV)is considered a global index for systolic and diastolic ventricular performance, and calculated using the formula: MPI = ([ICT + IRT] / ET)10 (**Figure 1**). E/E' ratio served as a surrogate for left ventricle end-diastolic pressure (LVEDP)[11-13].

Right ventricular (RV) function:
Tricuspid inflow velocities were obtained by placing the sample volume of the pulsed-waved Doppler at the tips of the tricuspid leaflets in the A4C view. Parameters recorded were peak velocity during early filling phase (TV E), peak velocity during atrial contraction phase (TV A) and the ratio of E to A (TV E/A ratio). Continuous wave Doppler was used to calculate the maximal systolic pressure gradient from the tricuspid regurgitation (TR max PG) using the modified Bernouilli equation[14]. RV systolic function was assessed by measuring the Tricuspid Annular Plane Systolic Excursion of the lateral tricuspid annulus (TAPSE) towards the apex in the A4C view. Color-coded TDI of the tricuspid valve annular velocity was recorded in the A4C view for

offline measurement of systolic (TV S'), early diastolic (TV E') and late diastolic (TV A') tricuspid lateral annular velocities, myocardial acceleration during isovolumic contraction (IVA) and myocardial performance index of the RV (MPI-RV)[10, 15, 16].

Statistics

This study was an explorative study with unknown prior effects of age on TEA induced changes in echocardiographic parameters, making sample size calculations unfeasible. Regarding baseline characteristics frequencies or group percentages were compared using the overall χ^2-test when data were categorical and one way ANOVA when data were continuous. The paired student's t-test was used to compare the means of continuous variables before and after TEA. Data are presented as mean (SD) or mean (range). We used the Kolmogorov-Smirnov test for normality. To investigate the relationship between age and echocardiographic variables we used linear regression analysis. Data from linear regression are presented as corresponding regression coefficients for age with 95%- confidence interval and a Pearson's correlation coefficient. P-values less than 0.05 were considered significant. All statistics were calculated using the software package SPSS Statistics 17.0 (SPSS Inc, Chicago, IL). Graphs were made using SigmaPlot 11.0 (Systat Software Inc, San Jose, CA).

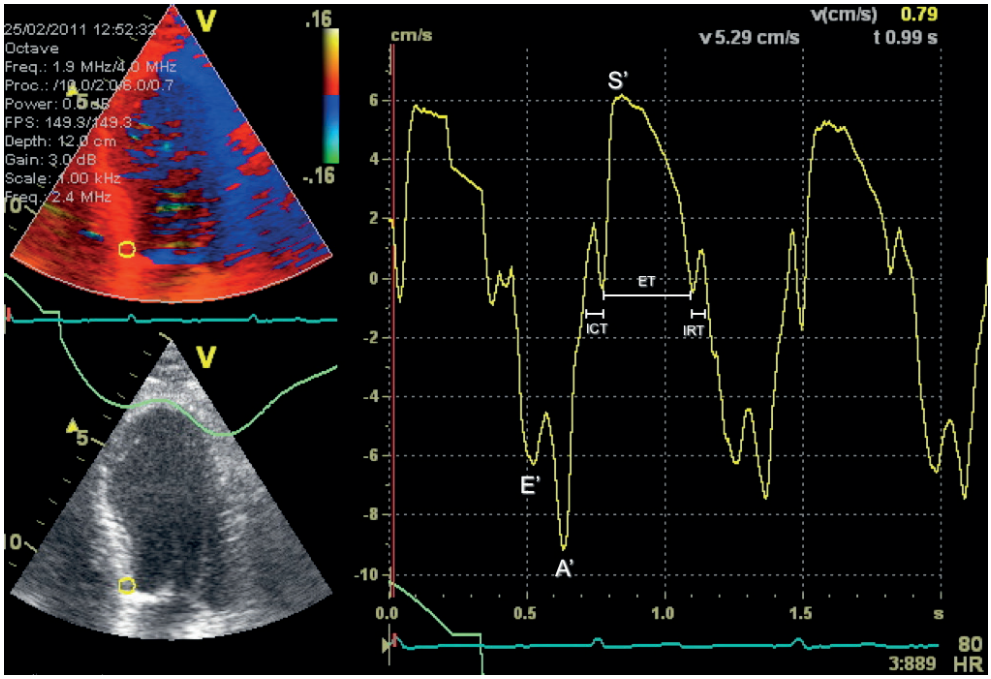

Figure 1. Myocardial velocity-time curve from tissue Doppler recording (TDI) of the medial mitral annulus. MPI is calculated from the time intervals as: MPI = ([ICT + IRT] / ET).

Results

Forty-two patients were asked to participate, of which thirty-five patients gave their written informed consent and were included in this study. Five patients were excluded because either the placement of the epidural catheter technically failed (4 patients) or the rostral border of analgesia only included two (T4-T5) of the thoracic segments innervating the heart (1 patient). All data were normally distributed. Demographic data and characteristics of the groups are presented in **Table 1**. The three groups were comparable according to their height, weight, gender, ASA classification, prevalence of diabetes mellitus (DM), use of antihypertensives and LVPWd. The groups were different with regard to prevalence of hypertension (P=0.02) and use of anti-arrhythmics (P=0.02). Anti-arrhythmics used by patients in this study solely consisted of β-blockers. The group of antihypertensives being used by patients in this study was composed of β-blockers, ACE inhibitors, calcium channel blockers and thiazides.

Table 1. Demographic data and characteristics of patients.

	Group 1 (18-45 years) (*n* = 10)	Group 2 (46-65 years) (*n* = 10)	Group 3 ((≥ 66 years) (*n* = 11)	Total (*n* = 30)
Age (years)	33 (21-43)	57 (47-65)	73 (67-79)	54 (21-79)
Gender (M/F) 6/4 6/4 5/5 17/13	6/4	6/4	5/5	17/13
ASA (I/II/III)	7/3/0	2/7/1	2/6/2	11/16/3
Height (cm)	177 (7)	176(12)	174 (8)	176 (9)
Weight (kg)	71 (13)	85 (17)	74 (11)	77 (15)
Diabetes 0/10 2/8 0/10 2/28	0/10	2/8	0/10	2/28
Hypertension (y/n)*	0/10	2/8	7/3	9/21
Antihypertensives (y/n)	0/10	2/8	4/6	6/24
Anti-arrhythmic (y/n)**	0/10	0/10	5/5	5/25
IVSd (mm)	7.7 (1.9)	9.6 (2.4)	10.6 (2.9)	9.1 (2.6)
LVPWd (mm)	7.9 (2.0)	7.5 (1.6)	8.6 (1.6)	7.9 (1.7)

Data are presented as mean (range), mean (SD) or n. * Overall comparisons,= 12.4; P = 0.002. ** Overall comparisons $\chi 2$ = 12.0; P = 0.002. ASA, American Society of Anesthesiologists' physical status; IVSd, interventricular septum thickness at diastole; LVPWd, left ventricle posterior wall thickness at diastole.

All catheters were placed in the T3-T4 interspace. The mean number of dermatomal segments blocked 30 minutes after epidural injection of 8 ml of ropivacaine 0.75 % was 19.6 (3.5) with a mean cephalad spread to C4 (C2-T1) dermatomal level and a mean caudal spread to L2 (T10-S1) dermatomal level. Thirty minutes after induction of TEA systolic, diastolic and mean arterial blood pressure after 30 minutes decreased in all patients ($P<0.001$) (table 2) and the magnitude of change was similar in all groups. HR only decreased between 0 and 30 minutes and was unchanged 30 minutes after induction of TEA. Bradycardia and/or hypotension occurred in six patients for whom atropine 0.5 mg and ephedrine 5 mg (n=2), 5 mg ephedrine (n=2) and 10 mg ephedrine (n=2) was needed shortly after the injection of ropivacaine. HR and MAP were minimally affected with exclusion of these patients from post-treatment analysis, and therefore these patients were included for analysis. There was a time window of at least 15 minutes between the last administration of vasoactive medication and start of the echocardiographic exam.

Table 2. Haemodynamic and echocardiographic parameters before and 45 min after induction of thoracic epidural anaesthesia

	Group 1 (18-45 years) n=10		Group 2 (46-65 years) n=10		Group3 (≥66 years) n=10		Total n=30	
	Baseline	TEA	Baseline	TEA	Baseline	TEA	Baseline	TEA
Variables of analgesia								
Cephalad border (derma-tome)		C4 (C2-C7)		C4 (C2-T1)		C4 (C2-C8)		C4 (C2-T1)
Caudal border (derma-tome)		L1 (T10-L5)		L4 (T11-S1)		L3 (T12-S1)		L2 (T10-S1)
Maximum number of dermatomes blocked		18.1 (3.3)		20.4 (3.6)		20.3 (3.5)		19.6 (3.5)
Hemodynamic variables								
HR (bpm)	72.7 (9.3)	68.8 (11.7)	73.8 (19.2)	73.6 (14.2)	69.8 (9.4)	68.4 (9.7)	72.1 (13.1)	70.3 (11.8)
SBP (mmHg)	128.9 (14.0)	113.7 (18.4)†	135.3 (21.2)	114.6 (22.8)#	147.8 (24.7)	117.5 (24.6)†	137.3 (21.3)	115.3 (21.4)‡
DBP (mmHg)	66.6 (11.0)	59.2 (8.6)†	66.9 (11.8)	60.2 (9.7)	70.5 (12.1)	57.3 (11.7)#	68.0 (11.4)	58.9 (9.8)‡
MAP (mmHg)	84.4 (15.8)	77.7 (10.6)	91.1 (14.3)	80.5 (14.6)	98.0 (16.3)	79.5 (15.2)†	91.2 (16.0)	79.2 (13.2)‡
LV systolic function								
Ejection Fraction (%)	62.2 (8.8)	62.4 (10.3)	64.0 (6.3)	70.2 (5.5) †	59.9 (7.3)	64.3 (8.2)	62.1 (7.5)	65.6 (8.7) †
MV S' medial (cm sec-1)	6.8 (1.0)	6.9 (1.1)	6.0 (1.1)	6.4 (1.0) †	5.6 (0.8)	6.0 (0.9)	6.1 (1.1)	6.4 (1.0)
MV S' lateral (cm sec-1)	8.9 (1.4)	8.3 (1.4)	6.8 (1.9)	7.0 (2.2)	6.3 (1.7)	6.4 (1.4)	7.3 (2.0)	7.2 (1.8)
Stroke Volume (ml)	79.9 (10.9)	86.0 (19.2)	73.6 (14.6)	84.0 (18.6)#	65.8 (13.5)	77.7 (17.5)#	73.1 (13.9)	82.6 (18.2) †
Cardiac Index (l min-1 m-2)	3.0 (0.6)	3.1 (1.0)	2.6 (0.5)	2.9 (0.6)#	2.4 (0.4)	3.0 (0.7)#	2.7 (0.5)	3.0 (0.8) †
MPI-LV	0.35 (0.07)	0.38 (0.11)	0.42 (0.13)	0.36 (0.08)	0.37 (0.15)	0.37 (0.07)	0.38 (0.12)	0.37 (0.08)
LV diastolic function								
MV E (cm sec-1)	67.5 (16.1)	90.0 (19.8) ‡	58.2 (9.7)	76.8 (14.4) †	54.0 (14.8)	81.3 (13.6) ‡	60.0 (14.7)	82.9 (16.6) ‡
MV DT (ms)	176.9 (40.3)	169.9 (27.1)	200.0 (24.7)	172.9 (22.8)	224.2 (51.4)	199.7 (47.9)	201.2 (44.0)	181.5 (36.5)
MV A (cm sec-1)	53.0 (11.8)	59.4 (8.8)	72.7 (13.2)	75.1 (14.0)	74.0 (17.0)	83.3 (15.0)#	66.3 (16.9)	72.5 (16.1)†
MV E/A ratio	1.4 (0.5)	1.6 (0.5)	0.8 (0.09)	1.0 (0.16) †	0.8 (0.4)	1.0 (0.3)#	1.0 (0.5)	1.2 (0.4) †
MV E' medial (cm sec-1)	9.0 (2.2)	9.6 (1.3)	5.4 (1.0)	6.7 (1.1)#	4.7 (0.8)	5.8 (0.8) ‡	6.4 (2.4)	7.4 (2.0) ‡
MV E' lateral (cm sec-1)	10.5 (2.7)	11.2 (2.4)	6.5 (1.9)	7.8 (1.5)#	5.3 (1.3)	6.5 (1.1) †	7.5 (3.0)	8.5 (2.6) ‡
MV A' medial (cm sec-1)	7.2 (2.0)	6.8 (1.5)	8.7 (2.2)	8.1 (1.9)#	7.6 (1.6)	7.7 (2.0)	7.8 (2.0)	7.5 (1.8)
MV A' lateral (cm sec-1)	6.6 (2.0)	5.7 (1.4)#	8.1 (1.8)	8.6 (2.2)	8.4 (2.3)	8.2 (2.4)	7.7 (2.1)	7.4 (2.4)
MV E/E' medial	7.6 (1.5)	9.7 (1.9)#	11.2 (3.7)	11.9 (4.0)	11.9 (4.3)	13.3 (3.5)	10.2 (3.8)	11.6 (3.5) †
MV E/E' lateral	6.5 (1.1)	8.3 (1.5) †	10.2 (5.5)	10.3 (3.3)	11.7 (4.0)	12.9 (3.6)	9.4 (4.4)	10.5 (3.4)#
LVEDV (ml)	102.8 (17.1)	108.5 (26.7)	103.0 (19.6)	100.0 (17.5)	81.0 (11.0)	93.9 (13.6)	96.4 (18.9)	101.3 (20.7)
RV systolic function								
TAPSE (mm)	21.4 (4.2)	22.2 (3.9)	20.1 (4.5)	22.9 (4.3)#	21.0 (4.8)	25.1 (3.8) ‡	20.7 (4.4)	23.2 (4.1) ‡
TV S' (cm sec-1)	8.8 (1.5)	10.7 (1.2) #	9.5 (2.3)	10.8 (2.1)	9.7 (1.8)	10.7 (1.5)#	9.3 (1.9)	10.7 (1.6) ‡
MPI-RV	0.46 (0.11)	0.37 (0.06) †	0.49 (0.14)	0.43 (0.09)	0.44 (0.12)	0.45 (0.09)	0.46 (0.12)	0.41 (0.08)
IVA (m s-2)	1.7 (0.5)	1.5 (0.7)	2.4 (0.8)	1.9 (0.7)	2.0 (0.27)	1.6 (0.32)#	2.0 (0.6)	1.7 (0.6) †
TR max PG (mmHg)	15.6 (4.3)	19.0 (3.5)	15.6 (5.1)	18.8 (2.8)	23.1 (3.6)	23.1 (6.3)	18.1 (5.4)	20.3 (4.5)#
RV diastolic function								
TV E (cm s-1)	51.2 (8.6)	58.1 (10.7)#	47.8 (4.1)	59.0 (11.2)#	43.2 (16.0)	57.4 (13.3)#	47.2 (11.1)	58.1 (11.4) ‡
TV A (cm s-1)	36.6 (8.4)	41.1 (6.3)	47.9 (17.6)	52.9 (22.3)	40.0 (11.0)	47.4 (13.9)	41.4 (13.3)	47.1 (15.7)#
TV E/A ratio	1.5 (0.5)	1.5 (0.4)	1.1 (0.3)	1.3 (0.5)	1.1 (0.3)	1.2 (0.2)	1.2 (0.4)	1.3 (0.4)
TV E' (cm s-1)	8.9 (1.2)	11.4 (1.4)†	6.9 (1.1)	8.8 (1.1) ‡	6.0 (1.5)	8.4 (2.0) ‡	7.0 (2.1)	9.3 (2.5) ‡
TV A' (cm s-1)	7.9 (2.9)	9.2 (2.1)	11.5 (2.0)	11.2 (3.6)	11.3 (1.9)	12.8 (1.9) ‡	10.2 (2.8)	11.1 (3.0)
TV E/E'	5.9 (1.5)	5.2 (0.8)	7.1 (1.1)	6.9 (1.9)	7.4 (2.3)	7.0 (1.8)	6.8 (1.8)	6.4 (1.8)

Data presented as mean (SD) or mean (range). Difference between baseline values and values 45 min after induction of TEA. HR, heart rate; IVA, isovolumic acceleration; LV, left ventricle; MAP, mean arterial pressure; RV, right ventricle; TAPSE, Tricuspid Annular Plane Systolic Excursion. # P <0.05, † P <0.01, ‡ P <0.001.

Systolic LV function

TEA increased LV EF (P=0.008), SV (P=0.001) and CI (P=0.005). TDI measurements showed no change in MV S' or MPI 45 minutes after induction of TEA (**Table 2**).

Diastolic LV function

MV E (P<0.001), MV A (P=0.005) and E/A ratio (P=0.001) increased significantly 45 minutes after induction of TEA (Table 2). TDI parameters MV E' medial (P<0.001) and MV E' lateral (P<0.001) increased whereas MV A' medial and MV A' lateral (P=0.287) did not change. E/E' RATIO increased. LVEDV remained the same.

RV systolic function

Right ventricular systolic performance measured by TAPSE (P<0.001) and TV S' (P<0.001) showed improvement 45 minutes after induction of TEA while IVA decreased (P=0.002)(**Table 2**). Tricuspid regurgitation pressure gradient (TR max PG), was measurable in only 12 patients and increased from 18.1 ± 5.4 to 20.3 ±4.5 (P=0.042).

RV diastolic function

TEA significantly increased TV E (P<0.001) and TV A (P=0.018), while TV E/A ratio was preserved. Tissue Doppler data showed increases in TV E' (P<0.001) but no changes in TV A' (P=0.094) or TV E/E' (**Table 2**).

Influence of age

There was no effect of age on baseline LV systolic function except for minor decreases in MV S', SV and CI (**Table 3 and 4**). All baseline parameters of LV diastolic function showed a decline with increasing age: MV DT and MV A increased, while MV E decreased. MV E' decreased (0.104 $cm.s^{-1}year^{-1}$; P<0.001; r=-0.79 and 0.13 $cm.s^{-1}year^{-1}$; P<0.001; r=-0.75 for medial and lateral respectively). Finally, MV E/E' increased for the medial (P=0.009) and lateral (P=0.002) wall. LVEDV was not affected by age.

Right ventricular parameters showed an increase in TAPSE with 0.088 mm $year^{-1}$ (P=0.003, R=0.53) but no other changes regarding systolic variables. Diastolic function decreased with advancing age as reflected by a decline in TV E/A ratio (0.1 per 10 years; P=0.021, r=-0.43) and TV E' (0.07 $cm.s^{-1}year^{-1}$, p<0.001) and an increase in TV A' (0.1 $cm.s^{-1}year^{-1}$; P<0.001, r=0.13). There was effect of age on TV E, TV A and TV E/E'.

Except for TAPSE, age did not influence effects of TEA on any echocardiographic parameter (**Table 4**). Linear regression showed that for each additional year, the absolute increase in TAPSE after TEA was 0.09 mm (P=0.003, R=0.53) (**Figure 2**).

Table 3. Correlation between age and baseline echo parameters

	Age coefficient	95%-Confidence Interval	R	P-value
Systolic LV				
Ejection Fraction (%)	0.028	(-0.140 0.196)	0.07	0.736
MV S' medial (cm s^{-1})	-0.022	(-0.044 0.000)	0.37	0.047
MV S' lateral (cm s^{-1})	-0.058	(-0.094 - 0.021)	0.52	0.003
Stroke Volume (ml)	-0.297	(-0.575 - 0.019)	0.38	0.037
Cardiac Index (l $min^{-1}m^{-2}$)	-0.013	(-0.024 - 0.002)	0.44	0.018
MPI-LV	0.000	(-0.003 0.003)	0.04	0.847
Diastolic LV				
IVSd (mm)	0.08	(0.03 0.13)	0.53	0.004
LVPWd (mm)	0.02	(-0.02 0.06)	0.18	0.383
MV E (cm s^{-1})	-0.353	(-0.639 -0.068)	0.44	0.017
MV DT (ms)	1.236	(0.391 2.081)	0.51	0.006
MV A (cm s^{-1})	0.501	(0.194 0.809)	0.54	0.002
MV E/A	-0.014	(-0.022 -0.005)	0.55	0.002
MV E' medial (cm s^{-1})	-0.104	(-0.137 -0.072)	0.79	<0.001
MV E' lateral (cm s^{-1})	-0.13	(-0.17 -0.082)	0.75	<0.001
MV A' medial (cm s^{-1})	0.023	(-0.019 0.066)	0.21	0.271
MV A' lateral (cm s^{-1})	0.054	(0.012 0.095)	0.46	0.013
MV E/E' medial	0.099	(0.027 0.171)	0.48	0.009
MV E/E' lateral	0.116	(0.032 0.200)	0.54	0.009
LVEDV (ml)	-0.345	(-0.746 0.056)	0.33	0.089
Systolic RV				
TAPSE (mm)	0.000	(-0.010 0.090)	0.00	0.98
TV S' (cm/s)	0.021	(-0.021 0.060)	0.20	0.296
IVA (ms-2)	0.007	(-0.008 0.022)	0.21	0.348
MPI-RV	-0.001	(-0.003 0.002)	0.02	0.644
Diastolic RV				
TV E (cm s^{-1})	-0.195	(-0.425 0.034)	0.32	0.092
TV A (cm s^{-1})	0.093	(-0.195 0.381)	0.13	0.513
TV E/A	-0.010	(-0.018 0.002)	0.43	0.021
TV E' (cm s^{-1})	-0.070	(-0.097 0.043)	0.71	<0.001
TV A' (cm s^{-1})	0.098	(0.050 0.146)	0.62	<0.001
TV E/E'	0.000	(0.000 0.001)	0.35	0.070

Data are presented as regression coefficient for age, 95% CI and Pearson's correlation. CI, confidence interval; IVA, isovolumic acceleration; RV, right ventricle; TAPSE, Tricuspid Annular Plane Systolic Excursion.

Discussion

Our data show that TEA increases global hemodynamic performance but has limited effect on Doppler- derived indices of biventricular systolic function. Indicators of diastolic performance showed a modest improvement for both the left and right ventricle after TEA although these changes could have been affected by the mildly elevated preload. Indeed, we used preventive volume loading during TEA, to account for expected reductions in preload, as this is usual clinical practice in order to avoid severe hypotension.

The increase in E/E' ratio, which has been shown in cardiology patients to correspond to increased LV filling pressures[11-13], and the tendency for LVEDV to increase as well, suggest that the amount of colloids administered before TEA was large enough to produce a mild rise in preload. This condition, combined with the documented systemic vasodilatory effects of TEA may largely explain the observed increase in cardiac output present in all age groups studied. Previous reports have shown a decrease in cardiac output with TEA when mild volume loading had no effect on preload[17]. Differences in study design, loading conditions, echo parameters used and patient population all may contribute to these discrepancies.

Tissue Doppler measurements of mitral annular peak velocity are generally considered to be load independent parameters of diastolic function in patients with reduced LV function but are load dependent in hearts with normal function[18]. It therefore appears that the observed increase in mitral and tricuspid annular velocity after TEA combined with volume loading in our study does not necessarily indicate an improvement in diastolic performance but may at least partially be explained by the mild concomitant increase in preload. In any case, these changes are not consistent with, and even directionally opposite to those expected to occur with a deterioration of diastolic function after TEA.

Table 4. Correlation between age and change of echo values 45 minutes after induction of TEA

	Age coefficient	95 % Confidence Interval	R	P-value
Diastolic LV				
MV E (cm s-1)	0.071	(-0.184 0.326)	0.11	0.573
MV DT (ms)	-0.534	(-1.662 0.593)	0.19	0.339
MV A (cm s-1)	0.084	(-0.150 0.318)	0.14	0.467
MV E/A	-0.001	(-0.008 0.005)	0.07	0.733
MV E' medial (cm s-1)	0.014	(-0.0130.041)	0.20	0.289
MV E' lateral (cm s-1)	0.010	(-0.0150.036)	0.16	0.398
MV A' medial (cm s-1)	0.006	(-0.0150.026)	0.11	0.581
MV A' lateral (cm s-1)	0.014	(-0.014 0.041)	0.19	0.324
MV E/E' medial	-0.015	(-0.071 0.042)	0.10	0.600
MV E/E' lateral	-0.014	(-0.073 0.044)	0.10	0.616
LVEDV (ml)	0.182	(-0.217 0.581)	0.19	0.356
Systolic LV				
Ejection Fraction (%)	0.074	(-0.063 0.210)	0.22	0.277
MV S' medial (cm s-1)	0.005	(-0.014 0.025)	0.11	0.566
MV S' lateral (cm s-1)	0.012	(-0.014 0.038)	0.172	0.363
Stroke Volume (ml)	0.088	(-0.2060.382)	0.12	0.544
Cardiac Index (l min -1 m2 -1)	0.006	(-0.0080.020)	0.17	0.388
MPI-LV	-0.001	(-0.004 0.002)	0.15	0.478
Diastolic RV				
TV E (cm s-1)	0.106	(-0.185 0.396)	0.15	0.461
TV A (cm s-1)	0.032	(-0.231 0.295)	0.05	0.802
TV E/A	0.004	(-0.004 0.012)	0.21	0.275
TV E' (cm s-1)	0.001	(-0.030 0.031)	0.01	0.963
TV A' (cm s-1)	-0.013	(-0.071 0.044)	0.09	0.640
TV E/E'	0.004	(-0.036 0.044)	0.04	0.850
Systolic RV				
TAPSE (mm)	0.088	(0.033 0.142)	0.53	0.003
TV S' (cm s-1)	-0.017	(-0.056 0.023)	0.16	0.401
IVA (m/s2)	-0.003	(-0.013 0.008)	0.11	0.610
MPI-RV	0.002	(-0.001 0.005)	0.30	0.159

Data are presented as regression coefficient for age, 95% CI and Pearson's correlation. CI, confidence interval; IVA, isovolumic acceleration; RV, right ventricle; TAPSE, Tricuspid Annular Plane Systolic Excursion.

The effect of age, however, on baseline diastolic performance was unambiguous and consistent with previous publications in cardiology, showing significant decreases in biventricular E', increases in LV E/E' and typical changes in transmitral and transtricuspid flow patterns[19-24]. Most importantly, regardless of baseline function and age, the effects of TEA were similar in all ages. Consequently these data allow us to reject the primary hypothesis and major concern, i.e. that TEA has unfavorable effects in the elderly population because of the age-associated impairment in baseline diastolic performance. In fact we found no influence of age on TEA effects for any of the variables studied with one possible exception for TAPSE. TAPSE is a standard performance indicator for RV ejection and has been widely used to assess RV function in a wide range of pathophysiological conditions. TEA caused increases in TAPSE in all patients but regression analysis showed that the magnitude of change was larger in elderly then in younger patients.

To our knowledge, this is the first study in humans to assess the effects of TEA on RV systolic and diastolic function. Animal studies using invasive measurement techniques to measure contractile performance have found no significant effects of TEA on baseline RV inotropic state[25]. Since TAPSE is a load-dependent ejection index of RV function, the observed increase could be due to either an increase in contractile performance, and/or an increase in RV preload as well as a reduction in RV afterload. Estimated RV systolic pressures, a surrogate for RV afterload slightly increased after TEA in our study while Doppler indices of systolic function were inconclusive. Whereas tricuspid S' increased, IVA which has been proposed as a load-independent index of contractility decreased. Hence, the only possible explanation for the observed increase in TAPSE is the slight increase in preload, induced by the concomitant volume load, and the increased cardiac output secondary to the reduction in LV afterload. It is important to note that some authors have shown IVA to decrease with increased preload[26], a finding that would further support our explanation. However, we have no explanation for the age-related improvement of TAPSE after TEA. Perhaps discrete differences in the effects of volume loading on preload in the elderly could be invoked but further studies are required to address this.

There was a decrease in MAP but not in HR in all patients 30 minutes after induction of TEA. The average decrease in MAP was less than 20% in all age groups. Although the prevalence of pre-existing hypertension was higher and the use of β-blockers was more frequent in the older age group, the decreases in MAP and HR 30 minutes after induction of TEA were not different between the age groups.

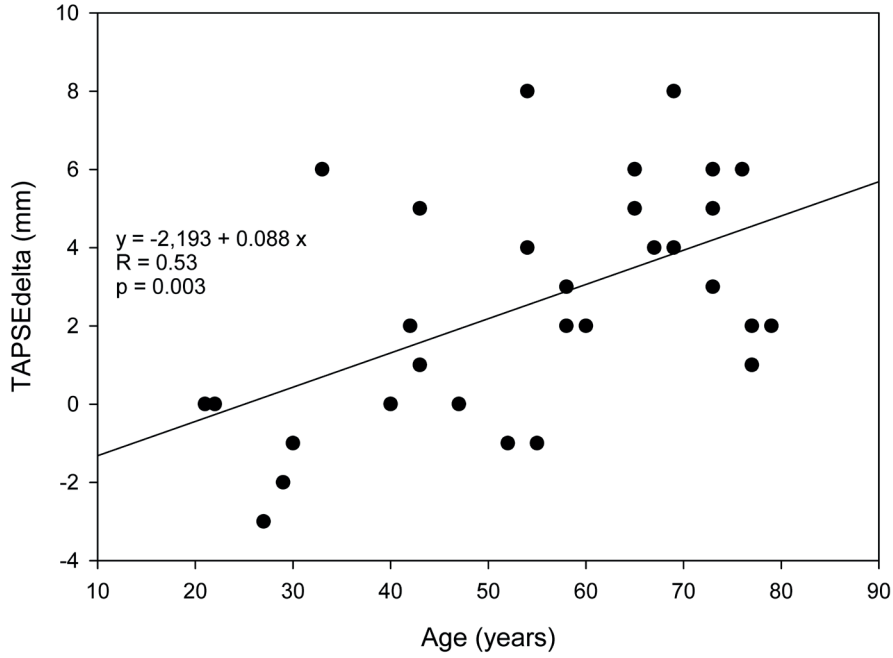

Figure 2. Correlation between delta TAPSE 45 minutes after induction of TEA and age TAPSE, tricuspid annular plane systolic excursion.

Increasing age had no effect on the total amount of spinal segments blocked after TEA with a fixed dose of ropivacaine at the T3-T4 interspace[8].

Discrepancies exist between our study and epidural studies that have evaluated the decrease in MAP and HR in patients following epidural administration of local anesthetic agents. Both with TEA[27] and lumbar epidural anesthesia (LEA)[28] the decrease in MAP and HR was more pronounced in the elderly patients.
Greater extension of the block in the elderly, the type and dose of local anesthetics, preloading, intensity of neural blockade and study design may all have contributed to these age related hemodynamic changes.

Limitations of the study:

Firstly, the analgesic spread after TEA was extensive and certainly not confined to selective blockade of the cardiac sympathetic fibers. To our knowledge there are no data on the spread of analgesic blockade after an epidural loading dose at the T3-T4 level. We aimed for analgesic blockade adequate for lung surgery using a bolus of ropivacaine according to clinical routine. This resulted in an unexpected high amount of blocked spinal segments. Consequently changes in echocardiographic variables might not solely be attributed to sympathicolysis of the cardiac sympathetic fibers, but also to changes in pre- and afterload because of vascular sympathicolysis.

In order to maintain preload and to prevent severe hypotension after TEA we used a high volume load with hydroxyethyl starch (HES) as part of clinical routine and clinical experience[9]. This volume load, despite extensive analgesic blockade, resulted in mildly elevated preload, though LVEDV was not changed.

Six patients needed atropine and/or ephedrine for treatment of hypotension, possibly influencing measurements. In our study population HR before TEA and 30 minutes after TEA was similar. With a time window of at least 15 minutes between the last administration of vasoactive drugs and start of the echocardiographic exam, a substantial influence of this medication on echocardiographic measurements seems unlikely.

Five patients were using anti-arrhythmic drugs (all B-blockers) and six patients were using antihypertensives, possibly influencing hemodynamic parameters. Besides having more difficulties in the inclusion of older patients, excluding older patients using anti-arrhythmic drugs or antihypertensives might introduce selection bias, as stated in the methods section. Moreover, excluding these patients from analysis did not result in significant changes in TEA effects on MAP, HR and echocardiographic indices.

The time point of dermatomal testing (30 min) and that of the echo examination (45 min) varied. The time period of 30 minutes for measurement of neural blockade was based on TEA [27] and LEA[28] studies showing maximal dermatomal spread to occur within 20-30 minutes. According to fig. 2 in our previous article[8], the spread of neural blockade had not yet stopped at 30 min. Consequently the extension of neural blockade might have been larger at the start of the echocardiographic exam at 45 minutes. However we think the progression of neural blockade after 30 minutes most likely was minimal, making the 30 minute values in this study acceptable.

Finally, the echocardiographic variables used in this study all are sensitive to changes in preload and afterload. However, TDI is a sensitive and relatively load-independent[29, 30] method in assessing systolic function and diastolic relaxation[31]. Furthermore, it is non-invasive and equivalent for invasive diastology in cardiology[12, 13] which renders it the current gold standard method for clinical studies.

In conclusion, our data show that TEA is associated with beneficial circulatory effects which are not modified by ageing. Biventricular systolic and diastolic function remain intact and overall cardiovascular performance improves after TEA when volume substitution is used to stabilize preload. The age-related deterioration of diastolic function has not detrimental effects on the hemodynamic response to TEA in elderly patients.

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Chapter
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