Effect of thoracic epidural anesthesia (TEA) on right ventricular function and ventricular-pulmonary coupling

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Right ventricular function will be assessed by invasive pressure-volume loop analysis using combined pressure-conductance catheters [27,28]. The response of right ventricular function to increased afterload, induced by brief, partial clamping of the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON34048

Source
ToetsingOnline

Brief title
Effect TEA on ventricular-pulmonary coupling

Condition

- Other condition

Synonym
lungcancer, lungresection

Health condition

fysiologisch: invloed van sympathisch ZS op ventriculo-pulmonale koppeling

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: RV function, thoracic epidural anesthesia, Ventricular-pulmonary coupling

Outcome measures

Primary outcome

General hemodynamics and right ventricular function are determined from RV pressure-loops. Pressure*volume signals acquired during steady state yield end-diastolic and end-systolic volume (EDV, ESV), ejection fraction (EF), end-diastolic and end-systolic pressure (EDP, ESP), stroke work (SW), dP/dtMAX and dP/dtMIN, and isovolumic relaxation time constant Tau. Load-independent indices of systolic and diastolic RV function are determined from pressure* volume relations obtained during preload alteration (Trendelenburg). The end-systolic pressure*volume relation (ESPVR: ESP vs. ESV) and the preload recruitable stroke work relation (PRSWR: SW vs. EDV) quantify systolic ventricular function. In particular, the slope of the ESPVR determines end-systolic elastance Ees, which is generally considered the gold standard index for intrinsic, systolic ventricular function. The end-diastolic pressure-volume relation (EDPVR: EDP vs. EDV) is used to determine diastolic function, quantified by diastolic chamber stiffness and the stiffness constant. Right ventricular afterload is determined by effective arterial elastance Ea, calculated as ESP/SV. Ventricular-arterial coupling is quantified as Ees/Ea [28,37].

Secondary outcome

Analgesia will be assessed bilaterally in the anterior axillary line by pinprick using a short beveled 25-gauge needle and by temperature discrimination using ice blocks. Analgesia is defined as the inability to detect a sharp pinprick. Results from both sides will be averaged. Assessments will be done every 5 minutes after injection of Lidocaine during 15 minutes.

The following parameters will be investigated

Time to initial onset of analgesia at the T3-T4 dermatomes

Time until maximum cephalad spread of analgesia

Time until maximum caudad spread of analgesia

Highest level of analgesia

Maximum numbers of segments blocked

Study description

Background summary

Thoracic epidural anesthesia (TEA) is considered to be the gold standard anesthetic approach in lung surgery and also widely applied in patients undergoing cardiac surgery. TEA provides excellent analgesia, decreases postoperative pulmonary complications [1,2], and may have a positive effect on the immunologic and coagulation system [3,4]. Furthermore, experimental studies have shown that TEA may provide cardiac protection for ischemia-reperfusion injury [5] and avoid vasoconstriction of atherosclerotic coronary arteries and plaque rupture [6,7]. Especially in the elderly population these risk reductions are highly relevant. Regional anesthesia, in particular TEA, was shown to be associated with reduced postoperative morbidity and mortality compared with general anesthesia [8,9,10]. The reduced cardiac morbidity and mortality is presumably related to the fact that stress following surgical trauma typically increases adrenergic nervous activity and catecholamine levels, which puts patients with coronary heart disease at increased risk for

ischemia and myocardial infarction.

However, blockade of the cardiac sympathetic fibres by TEA may affect right ventricular function and interfere with the coupling between the right ventricular function and right ventricular afterload. A possible negative effect of TEA on the regulation of right ventricular contractility could be highly relevant in surgical patients, particularly those with already depressed right ventricular function and in conditions of pulmonary hypertension. The interaction between TEA and the regulation of right ventricular function has been investigated in experimental animal studies but data are partly conflicting [11-16]. Studies investigating this effect in humans are not yet performed.

Experimental studies have shown that increased afterload leads to enhanced right ventricular systolic function which enables the right ventricle to maintain stroke volume without having to invoke the Frank-Starling mechanism [17-19]. This reflex mechanism is referred to as homeometric autoregulation and was suggested to result from stimulation of stretch-activated calcium channels [20], release of positive inotropic substances from the endocardial endothelium [21] and/or from an elevated sympathetic tone [8,22].

Recently, Rex and colleagues [8] demonstrated that in pigs TEA strongly inhibited the positive inotropic response to acute pulmonary hypertension, suggesting an important role for sympathetic nervous system. If this phenomenon is confirmed in humans, it is highly relevant for daily practice in cardiothoracic surgery because pulmonary hypertension is frequently encountered and right ventricular function is an important determinant of early and late outcome [23-25].

Therefore, we aim to investigate this mechanism in patients subjected to lung resection surgery. This intervention, obviously, increases right ventricular afterload and cardiac function was previously shown to be a determinant of outcome [26].

Right ventricular function will be assessed by invasive pressure-volume loop analysis using combined pressure-conductance catheters [27,28]. The response of right ventricular function to increased afterload, induced by brief, partial clamping of the pulmonary artery, will be tested before and after induction of TEA.

Study objective

Right ventricular function will be assessed by invasive pressure-volume loop analysis using combined pressure-conductance catheters [27,28]. The response of right ventricular function to increased afterload, induced by brief, partial clamping of the pulmonary artery, will be tested before and after induction of

TEA

Study design

3.1 Overall study design and flow chart

Ten (10) patients will be included in this open, single-centre study. Before inclusion, the patients will be screened for eligibility according to the inclusion and exclusion criteria and give their signed informed consent before start of the study.
At the screening visit, a routine physical examination will be performed. An ECG will be done and pulse and blood pressure will be measured for baseline registrations.

On the day before surgery, a pregnancy test will be performed in women of childbearing age. Patients will receive premedication and an epidural catheter. A test dose of 3 ml lidocaine 2% will be injected through the catheter. Correct position of the catheter is verified by assessment of sensory blockade. Lack of sensory blockade 15 minutes after injection of the test dose will results in exclusion of the patient from the trial. On completion of the epidural procedure patients will return to the ward.
On the day of surgery, patients will receive standardized premedication and standardized anesthesia induction. After induction of anesthesia a Swan-Ganz pacing Pulmonary Artery Catheter (PAC) and a Pressure-Volume catheter (PV catheter) will be inserted in the internal.jugular vein. Correct position of the PV catheter in the right ventricle will be guided by online pressure and volume signals and confirmed by transoesophageal echo (TEE). The insertion of the PAC and the PV catheter will be performed by an experiences anesthesiologist who works as a cardiothoracic anesthesiologist.

Starting at induction of anesthesia an electrolyte solution (NaCl 0.9%) will be administered at a rate of 5 ml.kg-1.hr-1. and maintained until the end of this study. Lungs will be ventilated with an FiO2 of 0.40 and ventilation will be adjusted to maintain normocapnia and normoxia. After achievement of hemodynamic (HD) steady state, measurements will be performed in baseline with the ventilation temporarily (~15 sec) suspended at end expiration. The left or right pulmonary artery will be briefly clamped for 2-3 minutes. After unclamping the pulmonary artery and achievement of hemodynamic (HD) steady state, 9 mL of lidocaine 2% will be injected through the epidural catheter. A second set of hemodynamic measurements will start 15 minutes after epidural injection and will follow the same protocol as the baseline measurements. After completing the measurements, surgery will continue and anesthetic management will be according to the judgment of the responsible anesthesiologist.

Adverse events (AE) will be recorded from the injection of the epidural test dose until patient is dismissed from the post anesthesia care unit (PACU).

Study Design:

- Premedication & induction anesthesia
- Instrumentation under TEE guidance
PAC
PV catheter, tip in RV apex
Check signals (PAC, PV, pacing)
- Reposition patient
- Check signals
- Thoracotomy and isolation/preparation of left/right PA
- Hemodynamic measurements at baseline and during epidural block
(Semi) continuous display and recording of :
- CO (FlowTrac), RV PV-loops, ECG, PA pressure, arterial pressure
Time line of study design is presented in appendix 1.
Time line of measurements is presented in appendix 2..

Measurement protocol:

Baseline:
- start RA pacing at 80 bpm (or 10 bpm above SR)
- record stable CO reading, with single bolus thermodilution measurement
- record steady state PV loops during 15 s suspected respiration
- record PV loops during positive/negative Trendelenburg maneuver (during suspended respiration)
- back to normal position
- record steady state PV loops during 15 s suspected respiration
- (partial) clamping of pulmonary artery aimed at increase in RV pressure > 20 mmHg (during continuous recording of PV loops
- record steady state PV loops (at increased afterload) during 15 s suspected respiration
- record PV loops during positive/negative Trendelenburg maneuver (during suspended respiration)
- back to normal position
- unclamp pulmonary artery
- record stable CO reading with single bolus thermodilution measurement
- record PV loops during hypertonic saline injection (10% saline, 5 ml bolus, proximal injection port PAC), repeat 3x (preferably during suspended respiration) to determine parallel conductance [29]

TEA
- epidural injection (9 ml, 2% lidocaine):
- wait 15 min to reach sensory blockade and stable hemodynamics
- repeat all measurements (except for hypertonic saline injections)
- remove PV catheter
- PAC will be left in place and used as a central line, which is normal routine

Time schedule (specific for *additional* time):

- Instrumentation of the catheters: 20 min ?
- Surgical preparation: 5 min
- Baseline measurements: 12 min
- Start epidural: 15 min
- Blocked measurements: 8 min

3.2 Discussion of study design, including choice of control groups

The primary objective of this study is to evaluate the inhibitory effect of thoracic epidural anesthesia (TEA) on the native positive inotropic response of the right ventricle to increased afterload. To increase statistical power and for ethical reasons (and to limits costs) we have chosen for a study design in which each individual serves as his or her own control (comparing baseline vs. blocked condition) rather than a placebo-controlled design.

Patients receive their epidural catheter the day before surgery to make sure it is positioned well without the consequence of a test dose having influence on measurements. In our clinic we are familiar with the routine of giving an epidural catheter to patients one day before surgery, as is the case with patients for isolated lung perfusion.

Study burden and risks

8.1 RISKS AND ALTERATIONS VS. ROUTINE

- Additional instrumentation (PAC, PV catheter): The acquisition of venous access for both the central venous catheter and the PAC is associated with similar complications (id est arterial puncture, bleeding at the injection site, pneumothorax, air- or thrombo-embolism, arrhythmias, infections[30]. Catheterization with a PAC may lead to more specific complications like mild tricuspid insufficiency, pulmonary artery rupture and pulmonary infarction[30]. In a general ICU population the beneficial effects of the monitoring characteristics of the PAC is upset by its complications. Several subpopulations, however, have shown to have improved survival due to the monitoring capabilities of the PAC, for example high-risk cardiac surgery [31]. A recent studies by Ranu et al. [32] and Hoeper et al. [33] showed that insertion of a PAC is quick, safe and well-tolerated. PAC-insertion is not associated with an increased risk of pneumothorax or other complications when performed by an experienced operator.

- Longer procedure (20 min instrumentation before surgery, 35 min measurements during surgery
- Hypertonic saline (10%) injections: 3x 5 ml bolus.
- (Partial) PA clamping (2x ~2 minutes)
- Epidural line will not be positioned on the day of surgery but the day before surgery. This way there will not be interference of the epidural test dose with the studt measurements

- Start surgery without use of epidural analgesia. Patients receive iv opiods as analgesic regimen until the study is finished, where after the epidural catheter can be used according to the normal routine. For postoperative analgesia patients receive a patient controlled epidural analgesia system according to the daily routine

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients undergoing lung resection under thoracic epidural anesthesia

Exclusion criteria

Contra-indications for thoracic epidural:
History of lung resection surgery
Pregnancy or lactation
Participation in a trial on investigational drugs within 3 months prior to the study

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-01-2012
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO

Date:	11-02-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL34361.058.10