THE PROTHOR TRIAL

PROtective ventilation with high versus low PEEP during one-lung ventilation for THORacic surgery

PROTHOR Newsletter February/2021

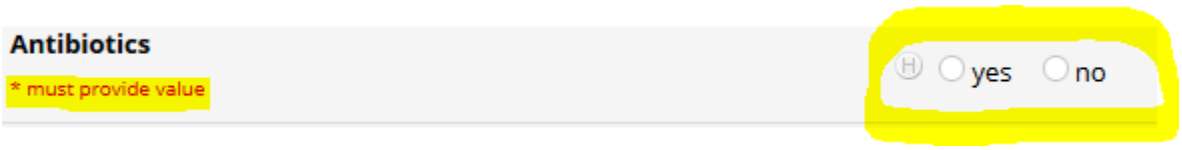
Dresden, February 2021

Dear National Coordinators and Local Investigators of PROTHOR,

Covid continues to keep us on our toes, unfortunately. Nevertheless, the number of patients enrolled is growing continuously. At the time of this report, PROTHOR has randomized 1364 patients. Many thanks for that. We are approaching the next major milestone of the third interim analysis. Therefore, we have sent out monitoring reports in the last weeks. In order to simplify data entry and avoid difficulties, we have summarized the most important general information below.

1. General Information:

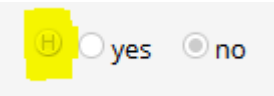
1.1 Mandatory („*must provide value“) Fields:



Fields, which are marked as mandatory, always require an entry. If the required value is not available for whatever reason please leave a short comment (e.g. not available, not done, unknown, etc.). An exception from this can be found under 4.3.

1.2 Comments:

Just click on the “H”-marked button next to a data-entry field to open a text box to leave a comment:

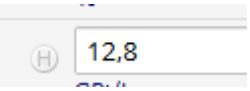


The audit-trial (history of change) is visible in this text box as well.

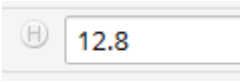
1.3 Laboratory Values:

Please always use a dot (.) for decimal numbers and no commas (,):

wrong format



correct format



1.4 AE-Documentation:

“An Adverse Event (AE) is generally defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during the study, having been absent at baseline or if present at baseline, appears to worsen. Adverse Events are to be recorded regardless of their relationship to the study intervention.”

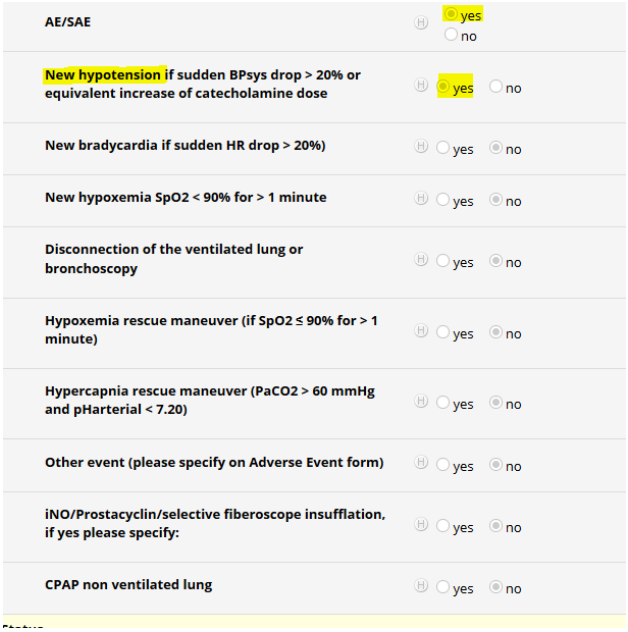
- ➔ In the study protocol, no exceptions from reporting are defined

If the CRF asks whether an AE has occurred, please do not leave these fields blank, even if they are not marked as mandatory. The study monitoring will require you to make an entry.

During the intraoperative visit:

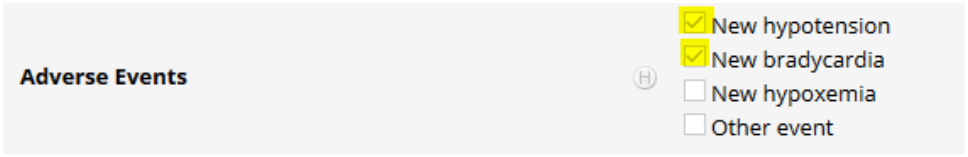
Every unfavorable event from the beginning of the induction of anesthesia to the end of the surgery should be documented as an AE. It is not sufficient to mark the event only in the Intra-OP Variables or Recruitment Maneuvers. All of them have to be reported as an AE separately in the Intra-OP AE-CRF.

Intra-Operative Variables:



→ An AE “Hypotension” has to be created in the AE-tab of the Intra-OP Visit.

Recruitment Maneuvers:



➔ AE “Hypotension” and “Bradycardia” have to be created in the AE-tab of the Intra-OP Visit.

Postoperative AEs:

➔ Every unfavorable Event during the post-operative course of the patient has to be documented according to “Common Terminology Criteria for Adverse Events” Classification (CTCAE) as an AE/SAE (e.g. Fever or unexpected severe postoperative pain). Even if the event is already mentioned in Post-OP Pulmonary Complications (e.g. Pulmonary Infection) or Extrapulmonary Complications (e.g. renal failure), it must be documented as an AE.

1.5 Laboratory Values conversion factors:

Unfortunately, it is not possible to enter every laboratory value as it is into the CRF since only defined units are allowed. An easy conversion can be found on the following website: http://unitslab.com/

2. Pre-OP

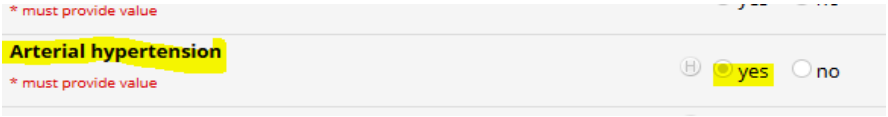
2.1 STOP-BANG-Score:

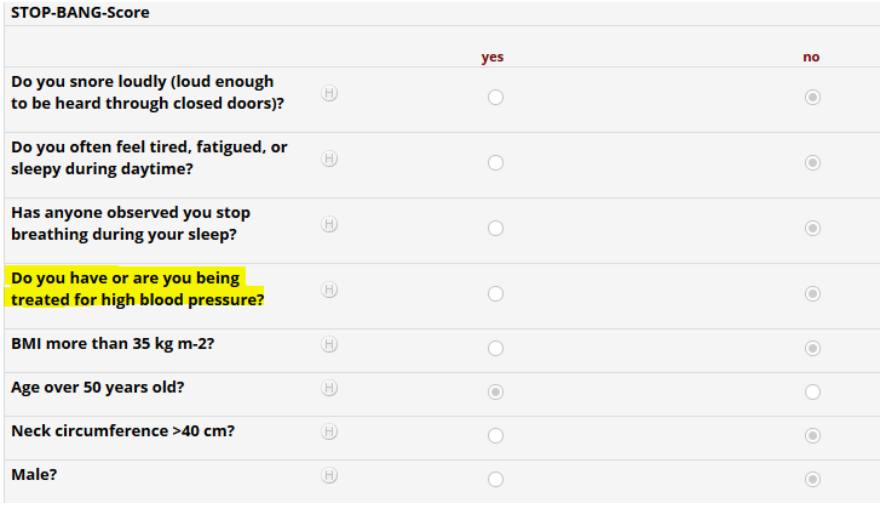
All information given in STOP-BANG-Score should be identical to the information which you can find somewhere else in the CRF since some of the questions in this Score are answered in other CRF-parts as well: e.g.

- ➔ Age: see Patient Details
- ➔ BMI: see Patient Details

Treatment for Hypertension:

If the question “Arterial hypertension” (below the STOP-BANG-Score) is answered with “yes” and the question for the treatment of high blood pressure in STOP-BANG-Score is answered with “no” it will always raise a query if the information is correct.





You may leave a comment to explain the situation in advance to avoid unnecessary queries from the monitoring team.

2.2 ARISCAT-Score:

Age * must provide value	≤ 50 ● 51-80 > 80
Preoperative SpO2 [%] 10 min in room air, beach chair position * must provide value	● ≥ 96 91-95 ≤ 90
Respiratory Infection (last month) * must provide value	● No Yes
Preoperative Anemia (Hb ≤ 6,2 mmol/l or ≤10 g/dl) * must provide value	● No Yes
Emergency procedure * must provide value	● No Yes
Surgical Incision * must provide value	peripheral upper abdominal ● thoracic
Planned duration of surgery [hrs] * must provide value	< 2 ● > 2-3 > 3
Total Risk Score * must provide value	43 View equation

Several questions here are answered in other parts of the CRF: e. g.

- ➔ Age: see Patient Details
- ➔ Pre-OP O2-Saturation: see Pre-OP Organ Function
- ➔ Pre-existing Respiratory Infection: see History of previous disease
- ➔ Pre-OP Anemia: see Pre-OP Non-Mandatory Measurements

All information given in ARISCAT-Score should be identical to the information which you can find somewhere else in the CRF!

Kindly note that, Emergency Procedure is always “no” since only elective surgery is eligible for this study and the surgical Incision should always be “thoracic”.

3. Intra-OP:

3.1 Recruitment Maneuvers performed as Rescue Maneuver:

Rescue Maneuvers may be necessary for both treatment groups. If a rescue maneuver is performed, it is NOT necessary to enter an indication; “rescue” is the indication: see example below:

Purpose for Recruitment Maneuver:	○ Routine ◉ Rescue
Indication for RM (tick one)	○ bronchoscopy / disconnection ○ after begin of OLV ○ every one hour during OLV ○ after lung re-expansion, measure in TLV ○ at end of surgery(supine)

3.2 Duration of Anesthesia:

The total duration of the anesthesia should be as long as the sum of the time of two and one-lung ventilation. If this is not the case for whatever reason, please leave a comment explaining this circumstance.

Duration of anesthesia * must provide value	217 [min] from intubation to extubation (or exit from OR if on mechanical ventilation)
Duration of OLV * must provide value	164 [min]
Duration of TLV * must provide value	33 [min]

197 minutes

→ *What happened with the patient in the 20 minutes without documented ventilation?*

3.3 Intra-OP Variables:

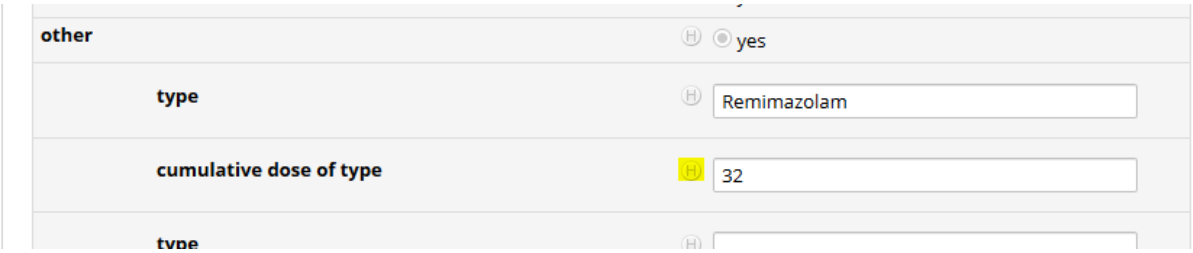
Please give as much information here as possible (especially Ppeak, Pplat, PEEP, VT) and answer the questions at the end of each measurement (AE/SAE, iNO/Prostacyclin/…, CPAP non-ventilated lung), see example below.

AE/SAE	○ yes ○ no
iNO/Prostacyclin/selective fiberoscope insufflation, if yes please specify:	○ yes ○ no
CPAP non ventilated lung	○ yes ○ no

Should some information concerning Ppeak, Pplat, PEEP, and VT not be available, please leave a comment.

3.4 Unit of “other” Anesthetic agents:

If you use an “other” anesthetic then the given presets (e.g. Propofol, Midazolam, etc.) please use the comment-function to amend the unit of the cumulative dose of the anesthetic.

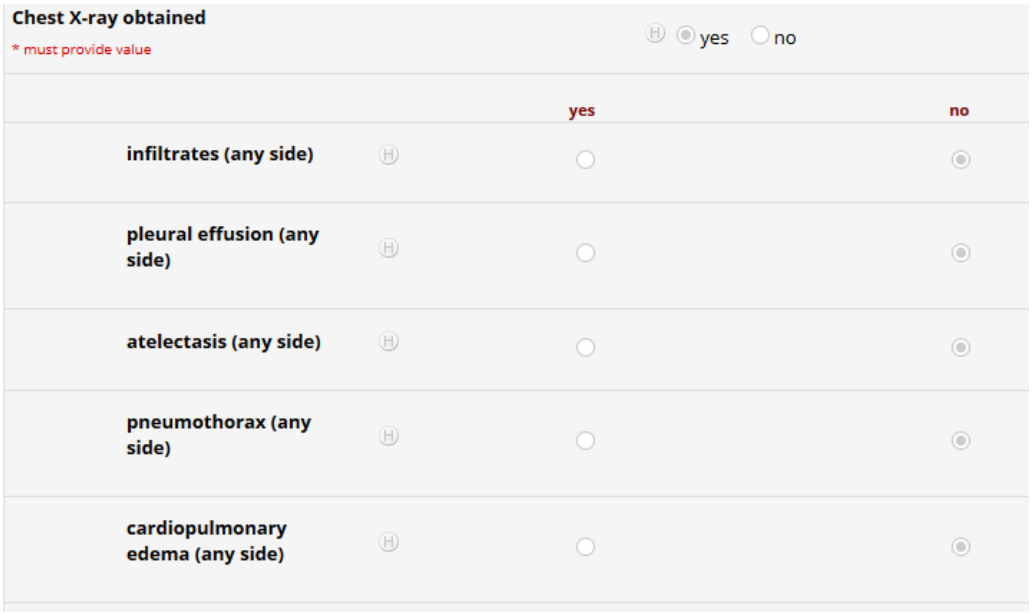


4. Post-OP

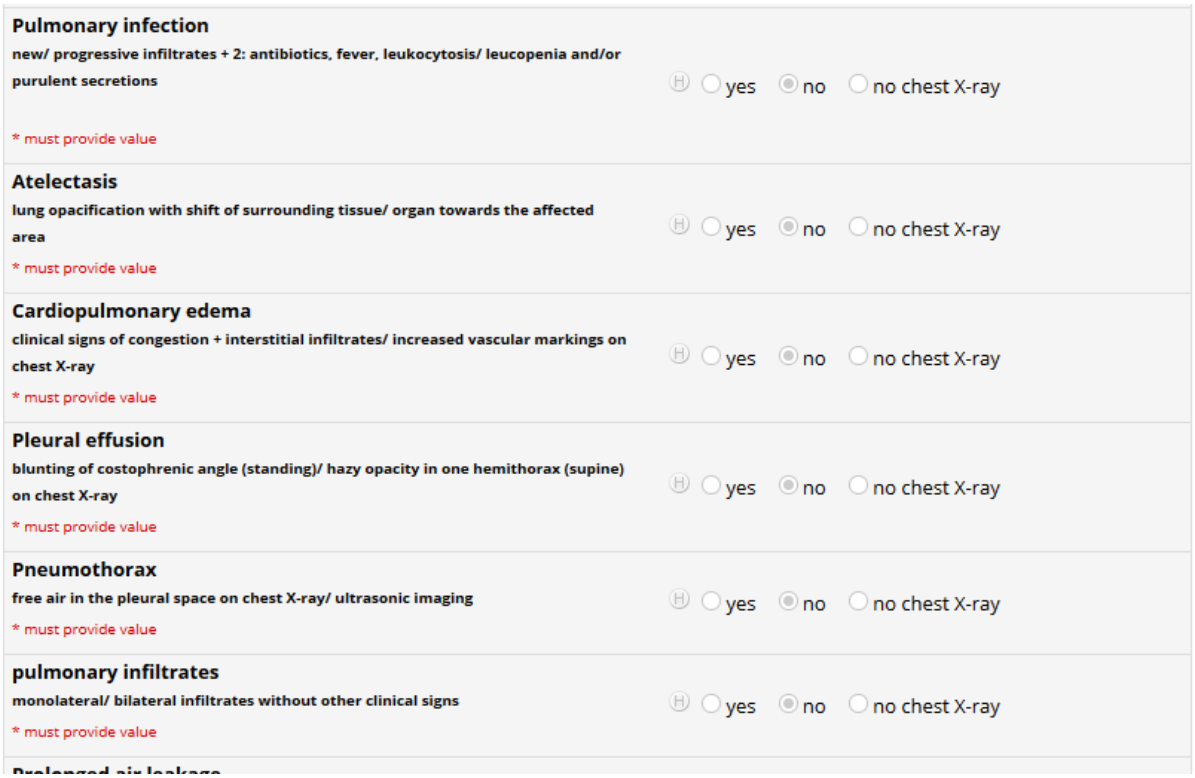
4.1 Post-OP X-ray diagnostic:

The information on chest X-ray diagnostic is documented twice!

1. Post-OP Non-Mandatory Measurements



2. Post-OP Pulmonary Complications



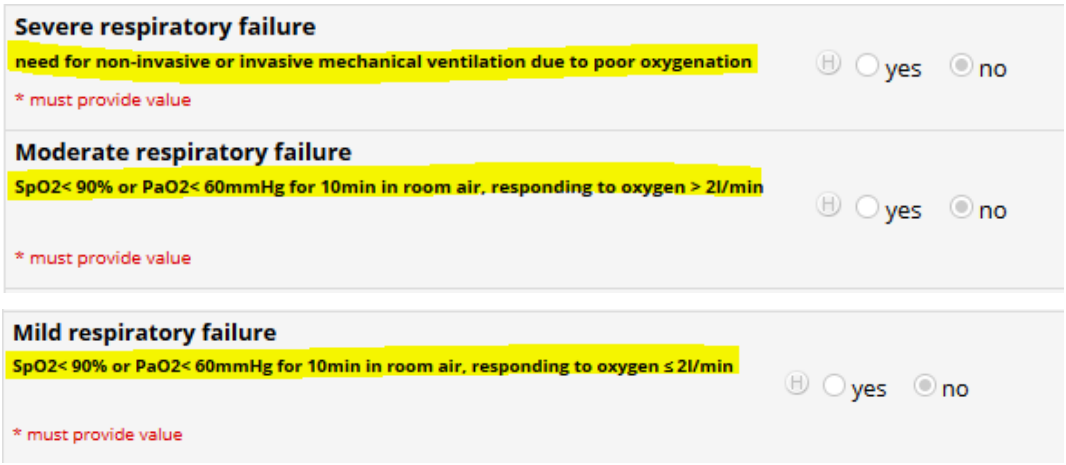
Answers between Non-Mandatory Measurements and Pulmonary Complications must be identical!

When in Non-Mandatory Measurements is stated that no chest X-ray was obtained all questions regarding X-ray-diagnostic in Pulmonary Complications should be answered with "no chest X-ray".

4.2 Post-OP respiratory failure:

Postoperative respiratory failure must be assessed based on the measured value documented in Post-OP Organ Function. If no SpO_2 is available (e.g. not done) respiratory failure cannot be evaluated and answers are always "no".

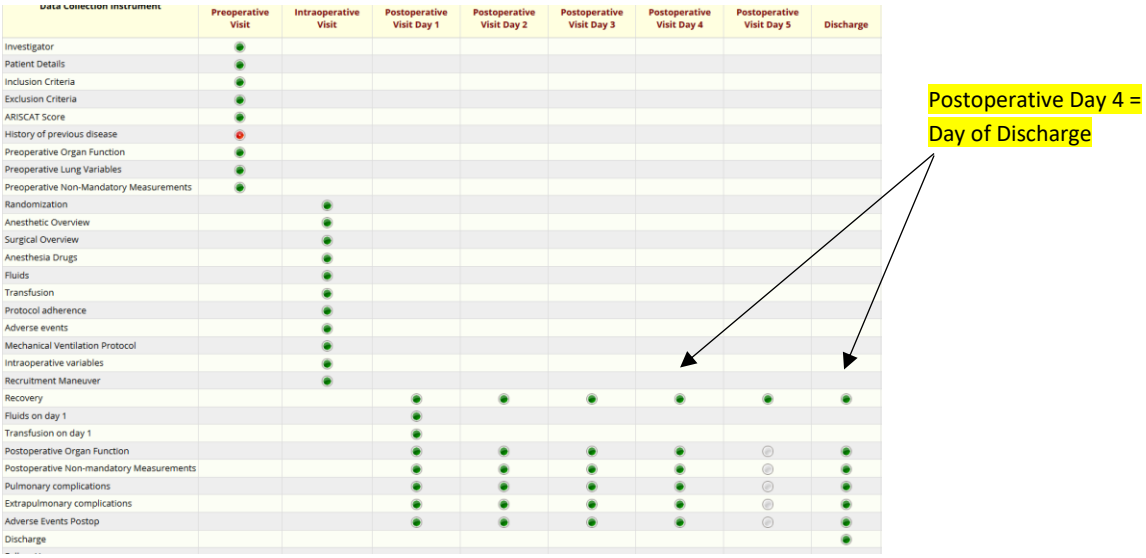
If the patient needs additional oxygen (FiO_2>21%, e.g. continuous O_2-administration via a nasal probe) to maintain adequate SpO_2 respiratory failure is present and has to be documented according to the definition (mild to severe), see example below!



4.3 Discharge of Patient within the postoperative observational phase (POD1-5):

To the extent that a patient is discharged from the hospital within the 5-day follow-up period, the day of discharge must be documented as a regular postoperative visit (postoperative visits 1-5), but also as the discharge visit:

Example: Patient is discharged on day 4 after the surgery:



Please document all visits as usual up to and including postoperative day 4. Please also document postoperative day 4 (day of discharge) as the discharge visit.

Best regards and stay safe,

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