iPROVE-EAL

Individualized **P**eriope**R**ative **O**pen lung **VE**ntilatory approach in **E**mergency **A**bdominal **L**aparo-tomy/scopy. A prospective multicenter randomized controlled trial

Investigator Information Brochure iPROVE-EAL

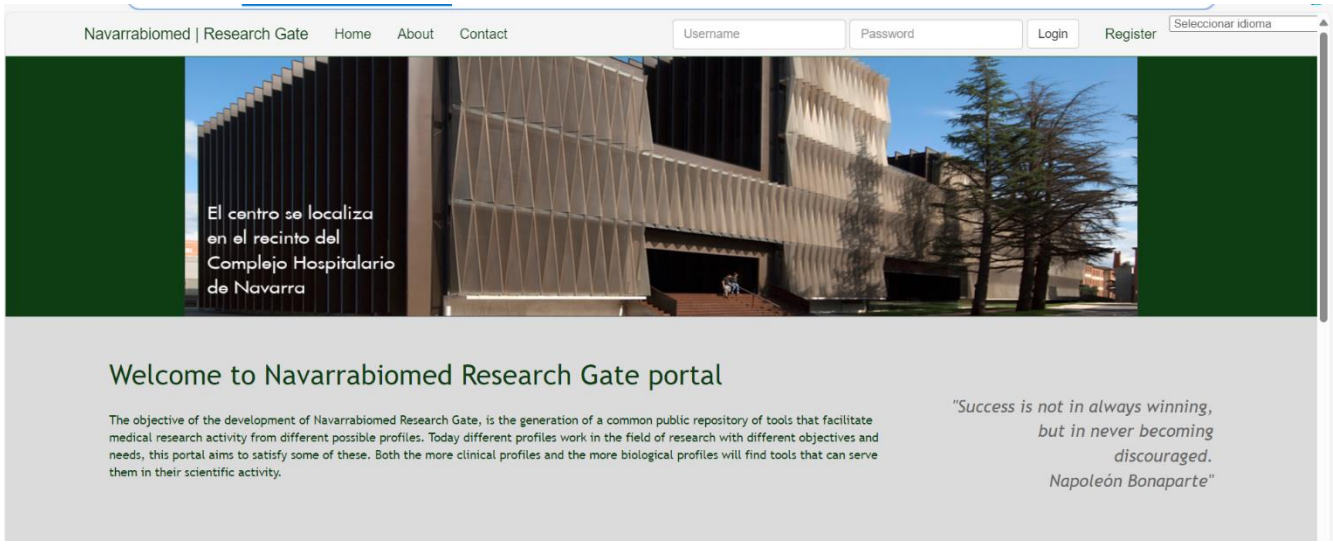
A) Dissemination of research results and sub-studies

The Scientific Committee will appoint a Drafting Committee to draft the scientific report (s) of this research, which will be disseminated in a timely manner. It is expected that a series of secondary analyzes will be carried out. Researchers will have priority to direct this type of analysis and are encouraged to do so. Participation will be based on the contribution to the study in its two phases. The Steering Committee will take into account the scientific validity and the possible effect on the anonymity of the participating centers before the granting of any of these applications. If necessary, a prior written agreement will establish the terms of this type of collaboration. The Scientific Committee must approve the final version of all manuscripts, before submission. In case of disagreement within the Steering Committee, the head of the investigation will make a decision. Any data from the PEAL and iPROVE-EAL analysis with the incorporation of two or more study sites will be taken into account for possible secondary analyzes and will be subject to predefined rules.

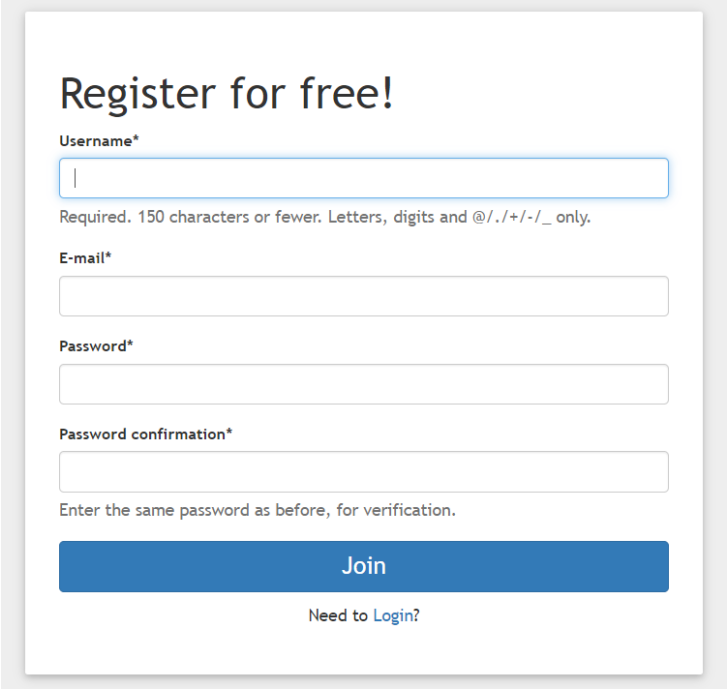
All participants in the study will be included as co-authors under the iPROVE Research Network Group.

Register as a center in eCRF

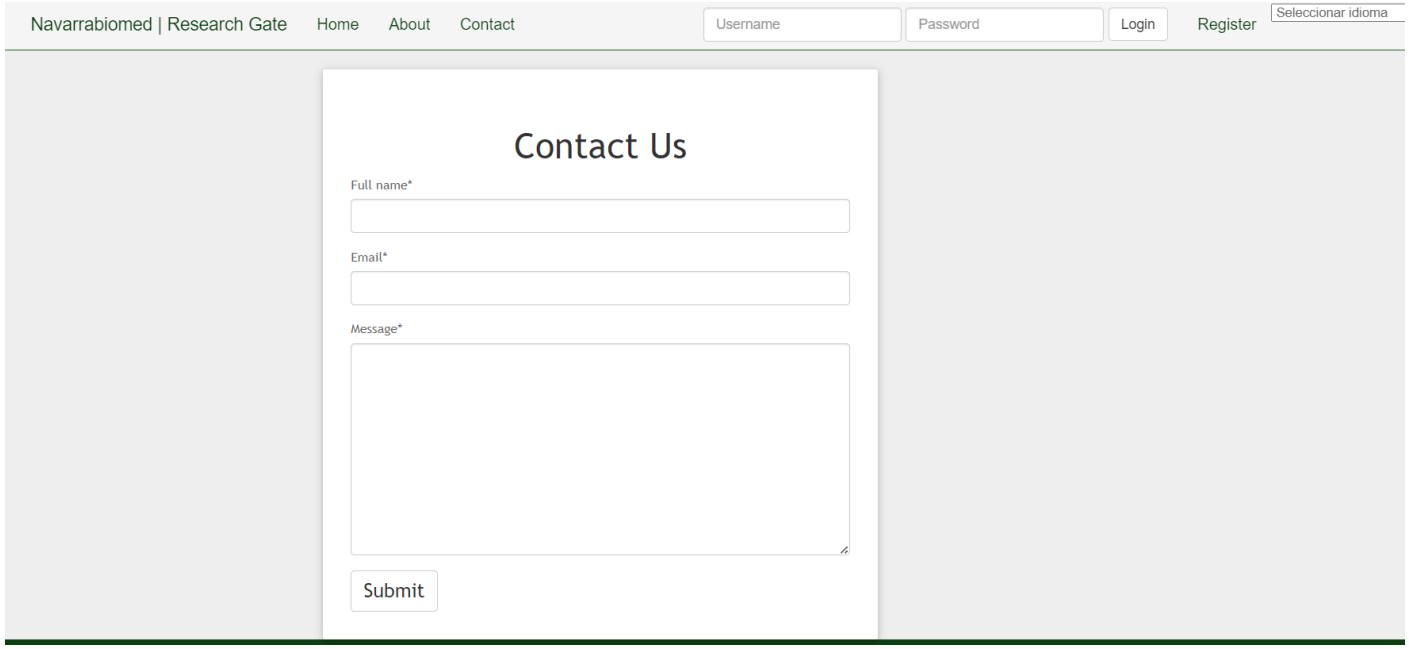
1. First of all, you must register in Navarrabiomed website (http://www.navarrabiomed-researchgate.com/) by clicking in the button “Register”.



2. You must complete the registration form in order to create an account in the website.

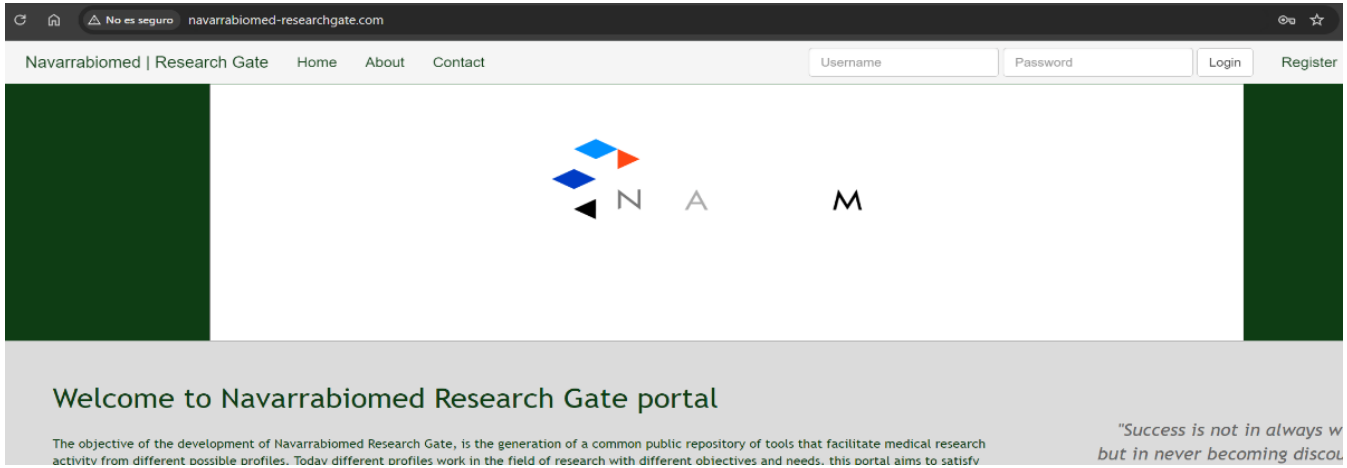


3. Once the registration form is completed you will receive a confirmation email in the address used, you must open this email and click in the verification link to complete registration.
4. After that you must enter again in Navarrabiomed website and click in the “Contact” button.



5. Once the contact form is open you must fill it with your full name and the mail used to create the account. In the “Message” box you must indicate the complete name of your hospital and the complet name of the study (iPROVE-EAL) so that you can get access to the eCRF of the study in Navarrabiomed. You will the receive a confirmation email verifying you have access to the eCRF study in the next hours.

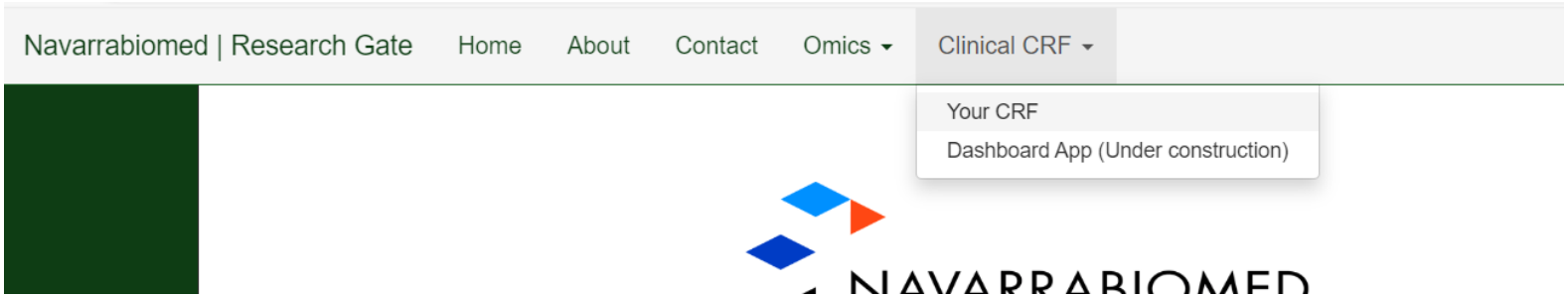
If you do not receive a response, please contact to iprove.eal@gmail.com or the corresponding managers listed on the contact page that we can find on the website http://www.iprove-network.es in the "PEAL" section.



Enter or modify data in eCRF

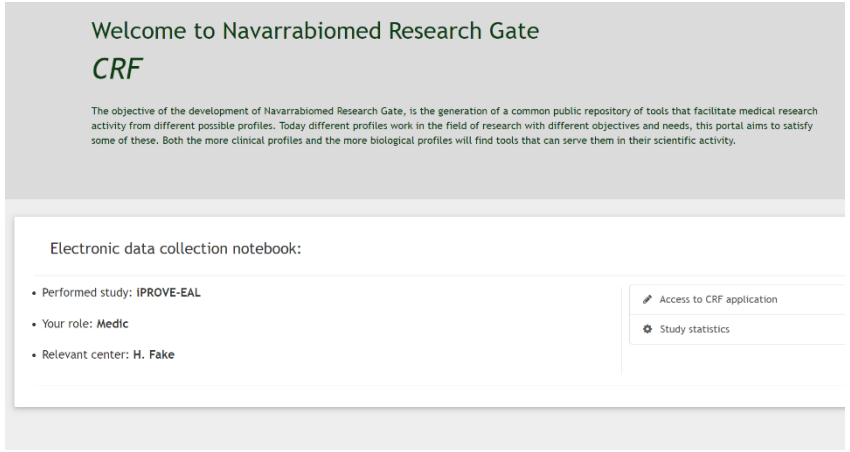
At this point we will find ourselves inside the data collection notebook. To access it, we must click on " Clinical CRF", and then in “Your CRF”. There we will see the iPROVE-EAL study, we must click in “Access to CRF application”.

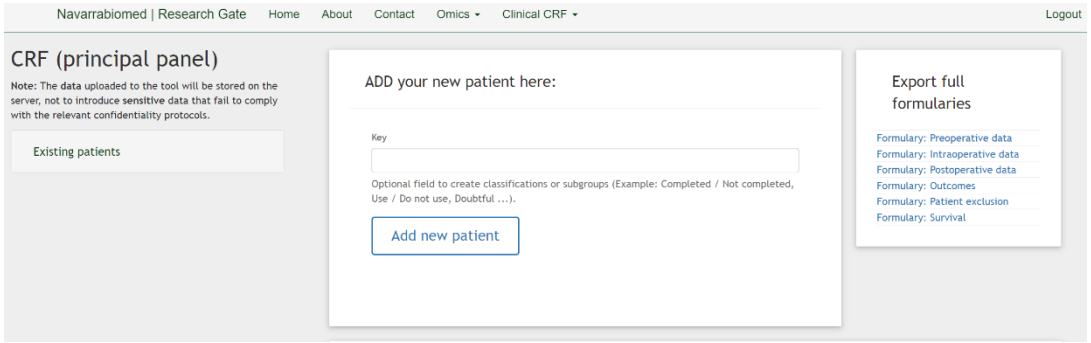
This access will take us to the main panel where we will have two options: Consult a previously entered patient, by clicking on "Existing patients" or add a new patient, pressing "Add new patient".

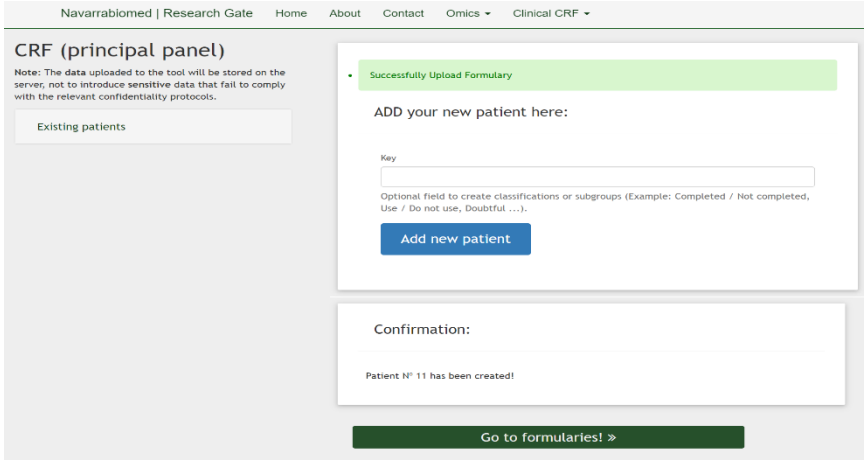


If we enter add new patient, it will inform us that it has been created correctly and will allow us to enter its eCRF through the "Go to formularies!" button.

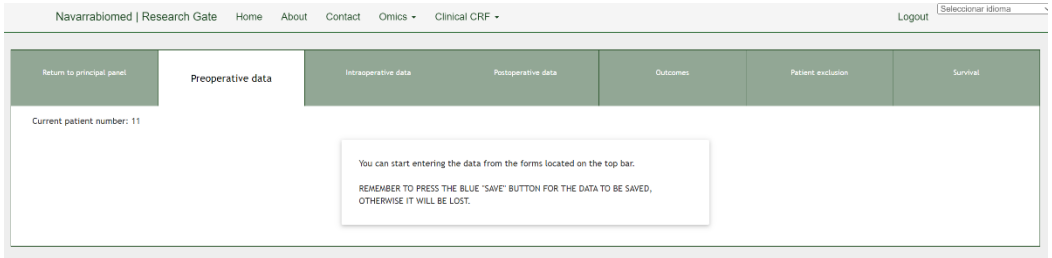
Once the eCRF has been created, we can first randomize it and then enter data, which can be done in a second time.







Patient Randomization with the eCRF



In order to proceed with the randomization, we must access the "Preoperative data" tab and first fill in the inclusion and exclusion criteria in the "Consent based on selection criteria" section. After this, we will be able to access the "Randomization" tab.

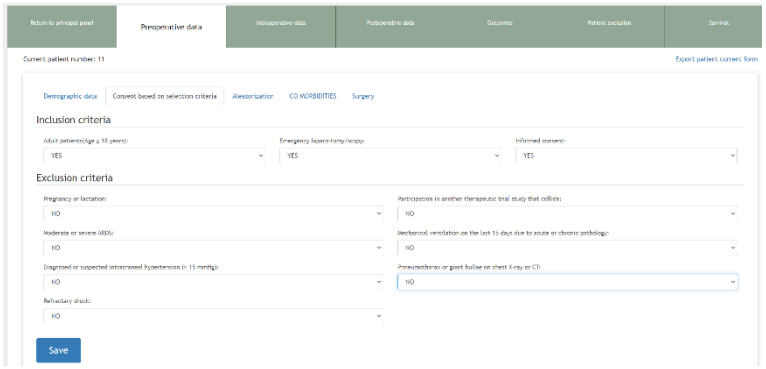
NOTE: If the inclusion and exclusion criteria data have not been filled in, it will not allow the form to be saved and it will not be possible to randomize it

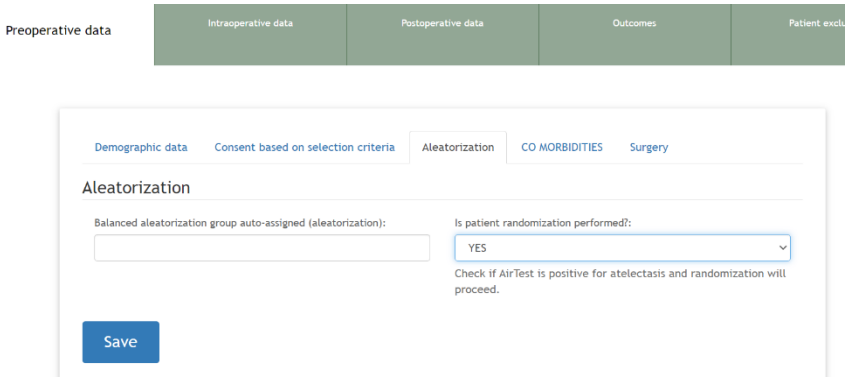
In case the AirTest has been positive, "YES" will be marked in the question "Is patient randomization performed?" and the document will be saved by pressing "Save", after which the randomization will be generated in the label under "Balanced randomization group auto-assigned"

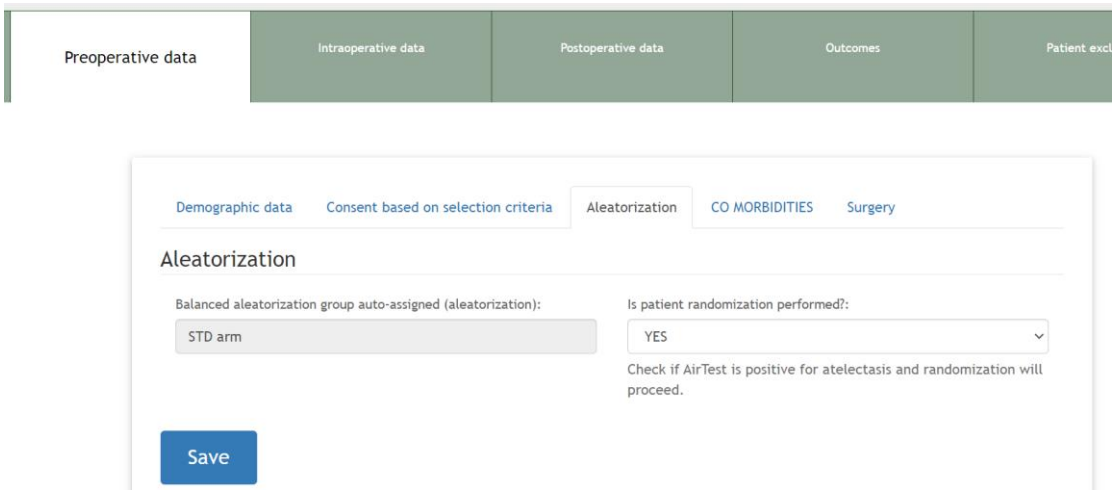
In case the randomization result does not appear, we recommend exiting and re-entering the patient's eCRF as shown above to solve problems reloading the information.

The randomization will be marked as "STD_arm" as the control arm or "OLA_arm" as the experimental arm.

We recommend saving the Patient ID of the patients entered in case you need to recover or modify the previous ones.







B) Definition of complications

Pulmonary Complications	PEAL + iPROVE-EAL
Atelectasis	Combination of $SpO_2 \leq 96\%$ during the air test and chest radiography with lung opacification with shift of the mediastinum, hilum, or hemidiaphragm towards the affected area, and compensatory overinflation in the adjacent non-atelectatic lung
Hypoxemia or Mild respiratory failure	$SpO_2 < 92\%$ or $PaO_2 < 300$mmHg with FiO_2 of 0.21
Severe respiratory failure	Increased FiO_2, increased requirement for CPAP, or the need for noninvasive or invasive ventilation
Weaning failure	Reintubation within the first 48h after postoperative extubation.
ARDS	● **Mild**: $PaO_2/FiO_2 < 300$ mmHg with CPAP ≥ 5 cmH_2O y $FiO_2 \geq 0.5$. ● **Moderate:** $PaO_2/FiO_2 < 200$ mmHg with PEEP ≥ 5 cmH_2O y $FiO_2 \geq 0.5$. ● **Severe**: $PaO_2/FiO_2 < 100$ mmHg with PEEP ≥ 5 cmH_2O y $FiO_2 \geq 0.5$. Acute (within one week) symptoms with bilateral pulmonary opacities
Pulmonary infection	Presence of a new pulmonary infiltrate and/or progression of previous pulmonary infiltrates on a chest radiograph plus at least two of the following criteria: (a) leukocytosis with > 12,000 WBC/mm^3 or leukopenia with < 4000 WBC/mm^3, (b) fever > 38.5°C or hypothermia < 36°C, and (c) increased secretions with purulent sputum and a positive bronchial aspirate
Pleural effusion	Chest radiography with the presence of costophrenic angle blunting, displacement of adjacent anatomical structures, and blunting of the hemidiaphragmatic silhouette in the supine position
Pneumothorax	Chest radiography with air in the pleural space with no vascular bed surrounding the visceral pleura
Bronchospasm	Presence of expiratory wheezing treated with bronchodilator
Aspiration pneumonitis	Respiratory failure after the inhalation of regurgitated gastric contents
Pulmonary edema	Fluid accumulation in the alveoli due to poor cardiac function diagnosed with chest radiography of lung ultrasound.
Pulmonary embolism	A new blood clot or thrombus within the pulmonary arterial system.

Systemic Complications	**PEAL + iPROVE-EAL**
Severe sepsis	Infectious focus identified plus organ dysfunction (defined as an increase in SOFA ≥2).
Septic shock	Severe sepsis with hypotension and hypoperfusion that is unresponsive to fluids.
Surgical site infection	The CDC defines a superficial incisional surgical site infection as one which meets the following criteria. (1) Infection occurs within 30 days after surgery and (2) Involves only skin and subcutaneous tissue of the incision and (3) The patient has at least one of the following: (a) purulent drainage from the superficial incision (b) organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision (c) at least one of the following symptoms or signs of infection: pain or tenderness, localised swelling, redness or heat, and superficial incision is deliberately opened by surgeon and is culture positive or not cultured. A culture negative finding does not meet this criterion. (d) diagnosis of an incisional surgical site infection by a surgeon or attending physician.
Urinary tract infection	A simplified version of the CDC recommendations defines a urinary tract infection as follows: a positive urine culture of 105 colony forming units ml1 with no more than two species of microorganisms, and with at least one of the following symptoms or signs: fever (> 38.8ºC), urgency, frequency, dysuria, suprapubic tenderness, costovertebral angle pain or tenderness with no other recognised cause.
Arrhythmia	ECG evidence of cardiac rhythm disturbance.
Myocardial infarction	Increase in serum cardiac biomarker values (preferably cardiac troponin) with at least one value above the 99th percentile upper reference limit and at least one of the following criteria:10 symptoms of ischaemia; new or presumed new significant ST segment or T wave ECG changes or new left bundle branch block; development of pathological Q waves on ECG; radiological or echocardiographic evidence of new loss of viable myocardium or new regional wall motion abnormality; identification of an intracoronary thrombus at angiography or autopsy
Heart failure	Cardiac index <2.5 ml/min/m^2 or >2.5 when ≥5 µg/kg/min dobutamine is required. Clinical signs (hypotension, oliguria, pulmonary edema) together with NT-proBNP >13 pg/ml or echocardiographic diagnosis.
Acute kidney injury	AKIN scale: ● **Stage I**: Diuresis < 0,5 mg/Kg (6h) or increase in serum Cr > 0,3 mg/dl. ● **Stage II**: Diuresis < 0,5 mg/Kg (12h) or basal Cr x 2 mg/dL. ● **Stage III**: Diuresis < 0,3 mg/Kg (24h) o anuria (12h) or basal Cr x 3 mg/dL, or Cr > 4 mg/dL or renal replacement

	therapy.
Delirium	Positive Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (see information brochure)
Paralytic ileus	Failure to tolerate solid food or defecate for three or more days after surgery
Postoperative hemorraghe	blood loss within 72 h after the start of surgery which result in transfusion of blood or a drop in hemoglobin > 7gr/dL
Anastomotic breakdown	Leak of luminal contents from a surgical connection between two hollow viscera. The luminal contents may emerge either through the wound or at the drain site, or they may collect near the anastomosis, causing fever, abscess, septicemia, metabolic disturbance and/or multiple organ failure. The escape of luminal contents from the site of the anastomosis into an adjacent localized area, detected by imaging, in the absence of clinical symptoms and signs should be recorded as a subclinical leak.

C) Scales and calculations

ASA physical status classification system

ASA I	**A normal healthy patient.** Healthy, non-smoking, no or minimal alcohol use
ASA II	**A patient with mild systemic disease.** Only mild diseases without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled DM/HTN, mild lung disease
ASA III	**A patient with severe systemic disease.** Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	**A patient with severe systemic disease that is a constant threat to his life.** Examples include (but not limited to): recent (< 3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis

Body mass index (BMI): Kg/m^2

Predicted body weight (PBW):

men: PBW (kg) = 50 + 0.91 (height in cm-152)

women: PBW (kg) = 45.5 + 0.91 (height in cm-152)

8 ml/kg PBW in men				8 ml/kg PBW in women		
162 cm 470 ml	164 cm 485 ml	166 cm 500 ml		153 cm 370 ml	155 cm 385 ml	157 cm 400 ml
168 cm 515 ml	170 cm 530 ml	171 cm 535 ml		159 cm 415 ml	160 cm 420 ml	161 cm 425 ml
172 cm 540 ml	173 cm 550 ml	174 cm 560 ml		162 cm 435 ml	163 cm 440 ml	164 cm 450 ml
175 cm 565 ml	176 cm 570 ml	177 cm 580 ml		165 cm 455 ml	166 cm 465 ml	167 cm 470 ml
178 cm 585 ml	179 cm 595 ml	180 cm 600 ml		168 cm 475 ml	169 cm 485 ml	170 cm 490 ml
182 cm 615 ml	184 cm 630 ml	186 cm 645 ml		171 cm 500 ml	172 cm 505 ml	174 cm 520 ml
188 cm 660ml	190 cm 670 ml	192 cm 685 ml		176 cm 530 ml	178 cm 550 ml	180 cm 565 ml

Visual Analog Scale (VAS)

The VAS scale allows to measure the pain intensity that the patient describes with the maximum reproducibility among the observers. It consists of a horizontal line of 10 centimeters, at the ends of which are the extreme expressions of a symptom. On the left is the absence of pain or less intensity. The patient is asked to mark the point indicating the intensity on the line and it is measured with a millimeter ruler. The intensity is expressed in centimeters or millimeters.

Charlson comorbidity index

Clinical condition	Weight
- Myocardial infarct, Congestive cardiac insufficiency, peripheral vascular disease, cerebrovascular disease. - Dementia - COPD - Ulcers - Conjunctive tissue disease - Cirrhosis or chronic disease of the liver - Diabetes	**1**
- Hemiplegia - Moderate or severe kidney disease - Diabetes with organ complication - Tumor/Leukemia/Lymphoma	**2**
- Moderate or severe liver disease	**3**
- Malignant tumor, metastasis, AIDS	**6**

Apfel score for PONV

Risk factors	Points	Risk factors	Points
Female gender	1	**Postoperative Opioids**	1
Non-smoker	1	**Sum=**	0.....4
History PONV	1		

SOFA (Sequential Organ Failure Assessment) SCORE

System					
	0	**1**	**2**	**3**	**4**
Cardiovascular	MAP > 70 mmHg	MAP < 70 mmHg	Dopamine≤5 µg/kg/min or dobutamine (any dose)	Dopamine>5 or epinephrine≤0.1 or norepinephrine ≤0.1	Dopamine>5 or epinephrine >0.1 or norepinephrine >0.1
Respiratory (PaO_2/FiO_2)	>400	301-400	201-300	101-200	≤ 100
Hepatic (bilirrubin,µmol/l mg/dl	≤ 20 <1.2	20-32 1.1-1.9	33-101 2.0-5.9	102-204 6.0-11.9	>204 >12.0
Kidney (creatinine, µmol/l) mg/dl	≤ 110 <1.2	110-170 1.2-1.9	171-299 2.0-3.4	300-440; 3.5-4.9; or urine output ≤500 ml/d	>440; >5.0; or urine output <200 ml/d
Coagulation (platelets, x 10^3/microL)	>150	≤150	≤100	≤50	≤20
SNC (Glasgow Coma Scale)	15	13-14	10-12	6-9	<6

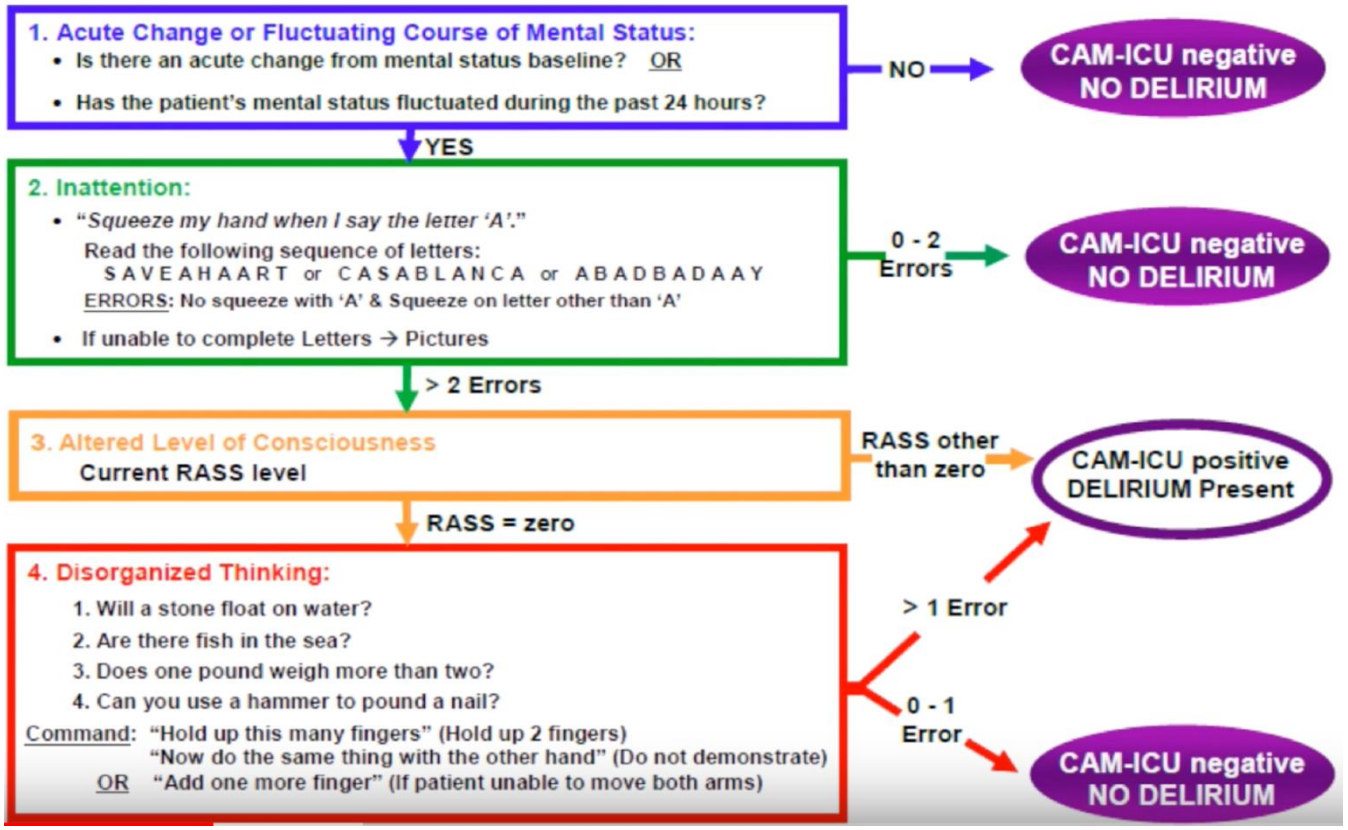
ARISCAT Score

Age	≤ 50	0
	51-80	3
	≥ 80	16
Preoperative SpO_2	≥ 96	0
	91- 95	8
	≥ 90	24
Respiratory infection (last month)		17
Preoperative hemoglobin (≥ 10 g/dl)		11
Surgical incision	Peripherical	0
	Abdominal	15
	Intrathoracic	24
Duration of surgery (h)	≤ 2	0
	> 2 a 3	16
	> 3	23
Emergency surgery		8

Richmond Agitation Sedation Scale (RASS)

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger for the staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior towards staff
+2	Agited	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive movements but not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

CAM-ICU scale



Clinical Fraily Scale

CLINCAL FRAILTY SCALE		
Very fit	Robust, active, energetic, motivated. Exercise regularly.	**1.** ☐
Well	No active disease symptoms. Exercise or very active occasionally.	**2.** ☐
Managing well	Well controlled medical problems. Not regularly active (walking).	**3.** ☐
Vulnerable	Symptoms limit activities, but not dependent on others for daily help.	**4.** ☐
Mildly frail	Evident slowing and need help in instrumental activities of daily living (controlling medication, finances, transportation, heavy housework). Typically impairs shopping, walking outside alone, meal preparation and housework.	**5.** ☐
Moderately frail	Need help with all outside activities and housekeeping. Often have problems with stairs and need help with bathing and getting dressed.	**6.** ☐
Severely frail	Completely dependent for personal care, any physical or cognitive activity. Stable, not at high risk of dying within 6 months.	**7.** ☐
Very severely frail	Completely dependent, approaching the end of life. Typically, they could not recover from a minor illness.	**8.** ☐
Terminally ill	Approaching the end of life. Life expectancy < 6 months.	**9.** ☐