COMPARISON OF THREE CENTRAL VENOUS CATHETERIZATION TECHNIQUES IN TERM AND PRETERM NEONATES

A randomised, parallel-group, multicentre, non-inferiority, and open-labelled clinical trial

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1. ABBREVIATIONS

NICU = Neonatology intensive care unit

NN = Neonates

IJV = Internal Jugular Vein

SCV = Subclavian Vein

BCV = Brachiocephalic vein

CVC = Central Venous Catheter

CVA = Central Venous Access

UVC = Umbilical Venous Catheter

PICC = Peripherally Inserted Central Catheter

VAD = Vascular Access Device

2. ABSTRACT

Background: Central venous catheterizations in term and preterm neonates can be challenging, even in experienced hands. The use of US guidance for its placement increases the success rate and decreases complications. There are different techniques, the most used nowadays is through the internal jugular vein access; however, this approach is difficult in this population, and there are others, such as the supraclavicular and brachiocephalic vein', that must be considered in clinical practice.

Objective: To compare the efficacy between BCV, SCV and IJV catheterizations in term and preterm neonates.

Design: This study will be a randomised, parallel-group, multicentre, non-inferiority, and open-labelled clinical trial.

Participants: Every preterm or term neonate admitted in NICU that requires a central venous catheter. We will enrol 114 patients during 1 year from 3 Spanish hospitals. These patients will be randomised into three groups, one for each technique of catheterization.

Keywords: neonates, catheterization, central venous catheter, brachiocephalic.

3. DEFINITIONS (1)

Table 1. VAD and infusion catheter types. Adapted from (1).

Intraosseous catheter	Catheter inserted into the spongy, cancellous bone of the epiphysis and the medullary cavity of the diaphysis.
Peripheral device	
Peripheral intravenous catheter	A catheter that enters and terminates into the peripheral veins.
Midline catheter	A catheter inserted into a peripheral vein (basilic, cephalic and brachial vein) and threaded to a greater blood flow in the proximal portion of the extremity (the tip is located near the axilla and distal to the shoulder).
Central device	
Umbilical catheter	A catheter inserted into the vein of the umbilical cord, available only immediately after birth.
PICC	Inserted through superficial veins of the extremity or the scalp, and threated proximally, locating its tip in the superior or inferior vena cava, preferably at its junction with the right atrium.
Tunneled CVAD	A segment of the catheter remains in a subcutaneous tunnel. The subcutaneous tissue grows to offer security for the catheter, and it deters the translocation of bacteria along the catheter to bloodstream. They are very invasive, non-tunneled are preferred in NICU.
Non-tunneled CVAD	Also known as “acute”, “short-term” or “percutaneous” device. No segment remains in the subcutaneous tract.
Total implanted venous device	Also known as “port” or “mediport”. A device implanted in the subcutaneous tissue of the chest or abdominal wall. It is a reservoir for injection or aspiration. It is connected to a catheter that communicates from the reservoir to a deep vein.

See Figure 1 (1).

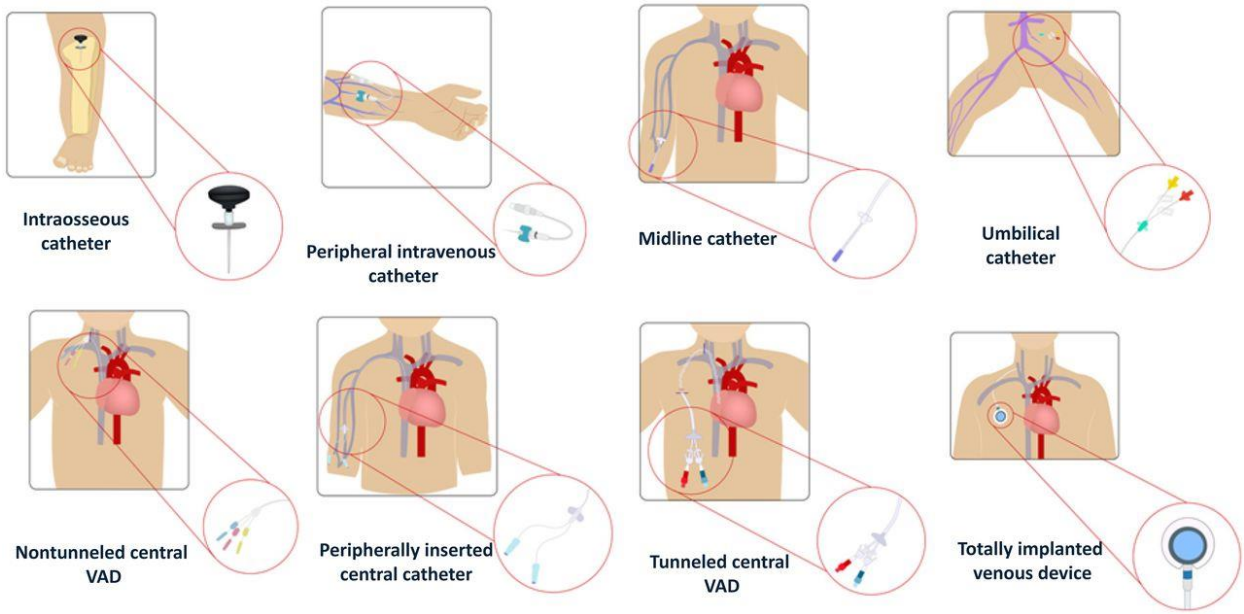


Figure 1. Vascular access devices and infusion catheter types.

4. INTRODUCTION

Intravenous catheters are frequently required in preterm and compromised term neonates. They have become part of the daily routine in the neonatal intensive care units (NICU), as they are essential to monitor constants, provide fluids, medication, total parenteral nutrition, hyperosmolar solutions, vasoactive drugs and take blood samples to analyse.

Intravenous lines can be defined as flexible and large tubes which are introduced through the skin to the vein. Depending on the tip's location, they are divided into two categories (1):

1. Peripheral catheter

The tip is located in a peripheral vein. These lines are associated with multiple complications, none of them related with high morbidity, such as thrombophlebitis, and they also have a low rate of infusion. However, if an intravenous access is needed for more than 5 days, is recommended to use another type of catheter, such as a midline or a PICC, in case that is only required to administrate medication.

2. Central venous access

Central venous access is defined as placement of a catheter with its tip in a venous great vessel (superior or inferior vena cava, brachiocephalic, internal jugular, subclavian, iliac, and common femoral veins). In neonates, there are three types of central catheters: central venous catheters (CVCs), umbilical venous catheters (UVCs) and peripherally inserted central catheters (PICCs) (2).

CENTRAL VENOUS ACCESS

The main devices used in NICU are: UVC, PICC and CVC catheters (non-tunneled type).

UVCs are the most used in preterm neonates, while the calibre of their peripheral veins is small, but it is only available during the first's days of life. It has been reported that premature neonates receiving parenteral nutrition via UVC have a higher weight gain and lower infection rates, compared with those with multiple peripheral lines (3).

As UVC are associated with a high infection risk when they are used for long periods, these lines are removed or exchanged for another central access between days 5 to 7 (4).

There is evidence which demonstrate that a serial usage of UVC followed by PICC in low birth weight neonates is better compared with only PICC access. Nevertheless, clinical practice guidelines recommend UVCs placement only for as long as clinically necessary, or ≤ 7 days (5). When UVC is not available or need to be exchanged, the election of PICC or CVC is ambiguous, it depends mainly on unit protocols and operator preferences, also, there are indications that only a CVC could do. In NICU, CVCs are less preferred, because of its procedural difficulty, higher complication rate and user preferences.

PICCs are the most commonly used for central venous access in neonates in NICU, the catheterization procedure is simpler to perform, relatively rapid, less expensive and requires only mild sedation or pain relief. Although PICCs can be used for administration of vasoactive medication and even parenteral nutrition, their small lumen often makes them uncapable for blood sampling or hemodynamic monitoring. Also, for this small lumen and their length, they are inadequate for bolus administration of fluids. In paediatrics, PICCs are used between 2 to 4 weeks to prevent infections (6).

CVCs are placed directly into central veins with Seldinger's technique, and they are indicated when there is a need of monitorization, quick fluid administration or frequent blood sampling. Although PICC and UVC are preferred in NICU, many studies of ultrasound-guided placement of CVCs reported a high success rates (7,8).

The main central veins where CVCs are placed are the internal jugular vein (IJV), subclavian vein (SCV) and brachiocephalic vein (BVC).

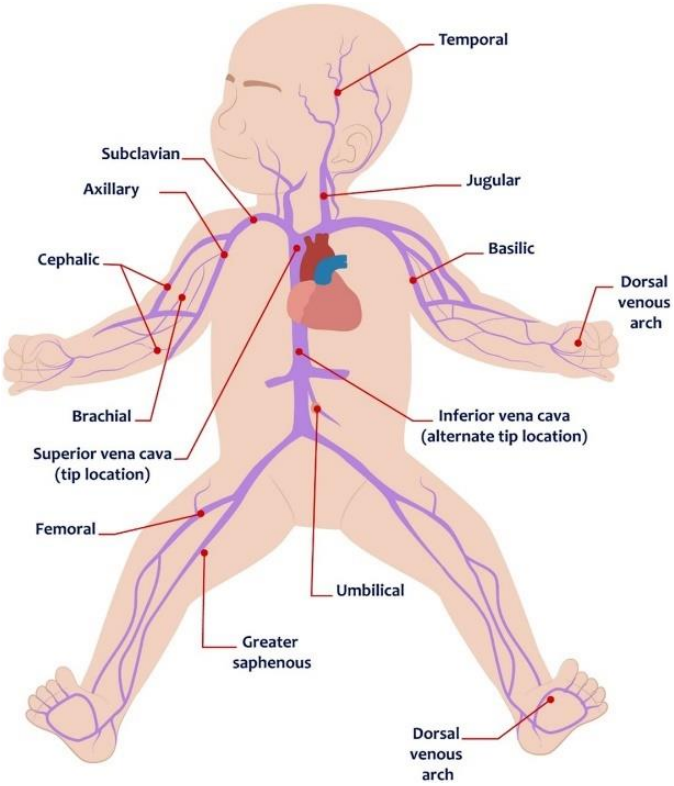


Figure 2. Common vessels used for vascular access devices

Anatomy:

The axillary vein courses medially and becomes the SCV at the lateral border of the first rib. It continues its path under the clavicle, and then inclines medially, downwards, after which, it enters the thorax as it unites with the IJV behind the sternoclavicular joint to become the BCV (9). Then, the pair of BCVs merge into the superior vena cava (See Figure 2 (1)).

1. Internal jugular vein (IJV)

It has been the most used to date due to its ease to be catheterized; with the evolution of the US, this tendency is changing. Some of the disadvantages found during its catheterization are:

- Tends to collapse under pressure.
- Is uncomfortable to patients as it is introduced through the neck.
- Neck movements disrupts the integrity of the catheter dressing and allow the translocation of bacteria inside the bloodstream (10).
- Smaller neonates have short and lax necks in whom the transducer may not fit if placed longitudinally (11). Therefore, their anatomy makes this approach complicated.

2. Subclavian vein (SCV)

Since the ultrasound assisted placement development, SCV cannulation using US have demonstrated a high overall success rate and lower risk of complications. More than 1,250 catheters have been reported inserted un children and neonates for a cumulated success rate of 98,4% (11).

Ultrasounds allow the visualization of the longitudinal route of the SCV, the needle in plane and the pulmonary pleurae (see Figure 3 (12)). With this view, the risk of accidental puncture of the subclavian artery or the pleura is clearly reduced.

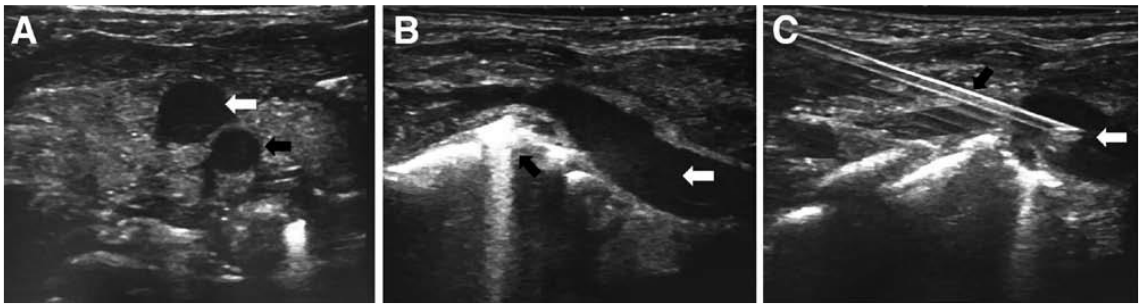


Figure 3. SCV catheterization with US

A) The internal jugular vein (*white arrow*) and the carotid artery (*black arrow*) out of plane. The nature of the vessels can be identified by the relative compression of the vein and by pulsed Doppler control of vascular flux. **B)** the pleura (*black arrow*) overlying the lung and the subclavian vein (SCV) in plane (*white arrow*). The pleura and the lung are easily identified. **C)** Needle (*black arrow*) with the tip placed (*white arrow*) in the SCV. The correct position of the catheter is verified by aspiration of blood.

The SCV approach has the following advantages: its diameter remains large regardless of haemodynamic and respiratory status (13), and the insertion site is at a distance from nasobucal area, reducing oropharyngeal flora contamination (14).

Besides its advantages, in NICU, most nurses and neonatologists prefer the IJV over the SCV, because they feel more comfortable with IJV due to their experience. Moreover, SCV cannulation is a complex technique and the ones who perform it need to be trained. One of the main difficulties during the catheterization is that there is a part of the line's path where the clavicle is overlying the vein, so the performer is temporarily "blind". However, studies have reported a fast learning curve (13).

3. Brachiocephalic vein (BCV)

Historically, some authors called it “the forgotten central line”, as it loses popularity because of a study where BCV approach was related with pneumothoraxes in 1969 (15).

Nowadays, with the introduction of ultrasound into routine clinical practice, it has regained interest because of its superficial location and lack of bone overlying the vein (see Figure 4 (10)), which makes possible to visualize the entire path of the needle during catheterization.

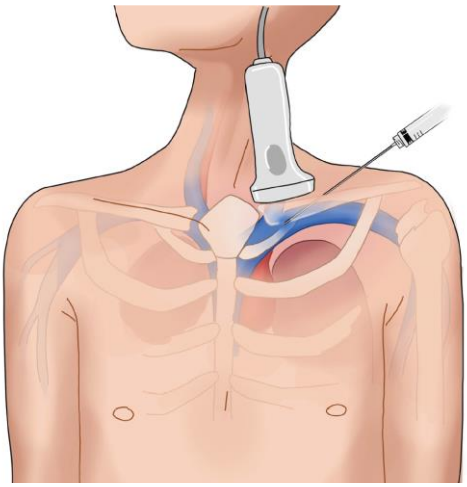


Figure 4. Supraclavicular position of US probe and needle

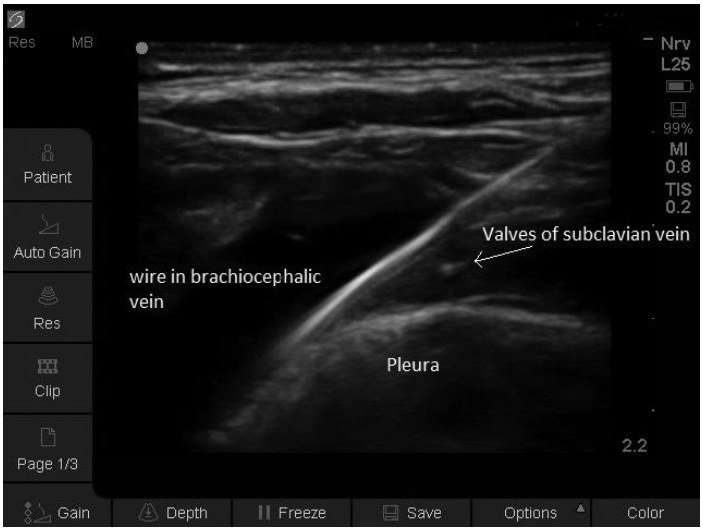


Figure 5. US image of wire entry at the confluence and extending down into BCV

Between the advantages of this approach, we find the following:

- Complete visualization of the needle during the entire path (see Figure 5 (10)).
- Patient comfort when the catheter is secured over the shoulder, allowing arm or neck motion.
- As the patient is comfortable, the risk of early removal and contamination due to the loss of integrity of the skin’s zone of insertion for patient’s movement is reduced.
- It has been promoted to have a lower potential of contamination, compared to IJV, subclavian or femoral central lines (10).
- The vein distance of BCV is slightly longer than SCV, which allows real-time adjustment of the needle position as it makes toward to the vessel (11).
- BCV is located further away from the pleural dome than the SCV, so it has a lower risk of accidental pneumothorax (11).

PLACEMENT

The technique for CVC placement has changed with the use of ultrasound guidance to minimize complications. With PICC, they are still introduced blindly, inserted to a predetermined length by estimating the catheter pathway with previous external anatomic measurements (16).

ULTRASOUND GUIDANCE

Almost 40 years ago, ultrasounds were used for the first time to facilitate intravascular catheterization. For the last 10 years, ultrasound machines have evolved to mobile US devices which could be used bedside, and for this reason, they have become a valuable tool for establishing vascular access in the daily usage (17).

US allows an optimal visualization of the needle entering the vein, as well as the relationship between the surrounding structures. This leads to a reduction of failure rates in first and total attempts at placement, and lower complication rates.

Evidence recommend the use of US over anatomical landmarks in adults for CVA. In neonates and preterm infants, the superiority of US for CVA placement is demonstrated too (18). Thus, a prospective trial comparing the ultrasound-guided placement of IJV vs PICC standard placement in preterm infants found increased success rates, decreased number of attempts, and decreased procedure duration with the use of ultrasound (19). In this study, they also noted that the learning curve for an adequate use of the ultrasound is short, whereas the number of attempts required for PICC placement remained higher.

A novel technique using ultrasound guidance is the supraclavicular CVC placement in SVC and BCV, which has a better overall success rate, decreased cannulation time and lower number of attempts than the infraclavicular one.

Apart from its usage during the procedure itself, US is also useful after the catheterization, to determine the catheter and tip position. Furthermore, it can substitute the radiograph to diagnose catheter malposition and procedure-related complications.

ANATOMICAL LANDMARKS

This technique is based in the identification of anatomical landmarks to guide venipuncture.

METHOD OF VERIFICATION FOR THE CATHETER'S PLACEMENT

Thoracoabdominal radiograph is the most common method used to confirm the catheter tip position. Recently, there has been an increased use of US to locate catheter's tips, as they provide real time assessment and there is no need to expose the patients to radiation (20).

Moreover, some studies confirm that RTUS can be used in neonates to find the PICC tips, and many others strongly suggest that RTUS should be considered the gold standard to confirm UVC placement (21,22).

COMPLICATIONS OF CVC

Despite the routine of placing CVCs in NICU, studies which compare complications from CVC devices have identified that most of the complications occur with PICCs (51%) and non-tunneled CVCs (34,4%), followed by tunneled CVCs (6,3%), totally implantable venous access devices (5,2%) and umbilical vein catheters (1,6%) (23).

CVC related complications are divided into early, or insertion-related, and late complications.

Table 2. Complications of catheterization

EARLY COMPLICATIONS	LATE COMPLICATIONS
1. Pneumothorax 2. Haemothorax 3. Accidental arterial puncture 4. Hematoma 5. Arrythmias 6. Arteriovenous fistula 7. Infiltration into adjacent tissues, including pericardial and pleural spaces. 8. Malpositioning	1. Catheter rupture 2. Erosion 3. Occlusion 4. Dislodgement 5. Migration 6. Local and bloodstream infection 7. Thrombosis

Central line associated bloodstream infections (CLABSIs) are the most common nosocomial infections in paediatric population, leading to an increased length of hospital stay for about 19 days, increased healthcare costs estimated as 45.000 euros per infection (24), and increased mortality rates. Overall, 25% of these catheters need to be removed or exchanged before the therapy has ended (6). Reinsertions are costly, requiring highly skilled staff, large amounts of sterile equipment, monitoring devices, and radiologic confirmation of placement (25).

5. JUSTIFICATION

Intravenous catheterization is the most common invasive procedure in NICU. Therefore, is important to know the best approach and the best vein to use in each situation. Referring to central venous catheterizations, it is a difficult procedure to carry out in preterm and term neonates, for this reason, is essential for the professionals to be trained.

Ultrasounds have become an important tool in NICU to diagnose and treat, furthermore, it facilitates difficult approaches that were not contemplated before, such as using the SCV or BCV vein. However, although studies have demonstrated that BCV cannulation with RTUS has a lower infection rate and an anatomy which facilitates the visualization of the needle's path, this type of catheterization is not the first, or even the second choice when CVA is required.

With this study, we want to prove that BCV catheterization with US assisted placement has a higher efficacy compared with the other CVC techniques. Thus, it is important to add US training for catheterizations to the clinical practice of neonatologists to be allowed to take advantage of new technological advances to improve the patient's condition. In this way, if results are positive and relevant, BCV catheterization and its training will be introduced to clinical practice.

This study is also relevant as there are many studies of catheterization with ultrasound placement in adult and paediatric population, but in neonates, there is fewer literature, focused in comparing different approaches to do catheterizations in a same vein, whether than wonder the best vein to do it. Considering this, we think that is important to know and implement a new protocol of catheterization in NN, based on both, the best location, and the best procedure.

6. HYPOTHESIS AND OBJECTIVES

- **Hypothesis**

BCV catheterizations with real-time ultrasound guidance are more effective than the SCV and IJV's ones.

- **Objective**

To compare the efficacy between BCV, SCV and IJV catheterizations in term and preterm neonates.

Definition of efficacy: success at introducing the catheter at 1st attempt.

7. METHODS

STUDY DESIGN

This study will be a randomised, parallel-group, multicentre, non-inferiority, and open-labelled clinical trial.

STUDY POPULATION

Inclusion criteria

- Every preterm and term neonate admitted in NICU.
- Must require a central venous catheter (based on clinical judgement and protocol unit), independently of the admission diagnosis.
    - Parenteral nutrition, hyperosmolar solutions, apheresis, chemotherapy, consecutive blood samples, medication, vasoactive drugs, monitorization.
- Informed consent signed.

Exclusion criteria

- Any congenital malformation which difficulties the intervention: vascular or cutaneous in the zone of catheters' insertion.
- Weight below 1,000g.

- Emergent catheterization: the intervention must be carried out, precluding the possibility of randomization.

SAMPLE SIZE

We estimated the sample size using the free online software GRANMO, and the setting for two independent proportions.

We have assumed an alpha risk of 0.025 and a beta risk of 0.2 in a two-sided test. Estimated loss at follow up was 0. For these numbers, GRANMO recommended 38 subjects for each group of intervention to be sure that there is a significant difference (>5%) between one group and the other.

Our study has 3 groups of intervention, that is a total of 114 study participants.

If we suppose that differences between techniques is median, the statistical potency is 89.30%. Computations were carried out with Prof. Marc Saez' software, based on the package 'pwr' of the free statistical environment R (version 4.0.2).

ESTIMATED TIME OF RECRUITMENT.

It is a difficult procedure to know how many neonates used an intravenous central catheter in different NICU from Catalonia. However, we can know these data from Hospital Universitari Josep Trueta, and then, extrapolate it to the other hospitals.

According to annual data, the admissions in the NICU of Hospital Universitari Josep Trueta are about 200 patients/ year, 20% of whom are preterm, weighing <1500g. From these 200, the 80%, 160 neonates need a central venous catheter.

To realize our study, we need 114 patients. If we assume that the 50% will be excluded from our sample, and we want to collect the required data in one year, we have to design a multicentre study with the participation of hospitals with level IIIB NICU from Catalonia. With the appropriate collaboration and coordination, we will enrol the 114 participants in 1 year.

We have estimated a high percentage of loss, considering that the studied population are neonates, they are vulnerable, and parents or tutors will be hesitant to enrol them in our study.

The hospitals participating in the study will be: Hospital Universitari Josep Trueta, H. Universitari Vall d'Hebron, H. Sant Joan de Déu.

STUDY INTERVENTION

We have three techniques of central intravenous catheterization that we want to perform in our study: IJV, SCV and BCV. They will be performed by neonatologists or residents from the neonatal intensive care unit.

First of all, it is necessary to define the investigators. The difference between the neonatologist and the resident are the years of clinical practice.

The resident is whoever doing the paediatric specialty after finishing the medical degree. It is a four year's period where she/he take turns into the different areas from paediatrics, gaining clinical practice skills. For the complexity of the intervention, the resident must be in the 3rd or 4th year and have more than 6 months of experience in the neonatology department.

The neonatologist is a specialist in neonatology, a resident that has finished the four year's program and has specialized in this area.

TRAINING

All residents from paediatrics and neonatologists from NICU participating in this trial must be trained before the study begins to know how to use ultrasounds, and how to combine it with the catheter's introduction into each vein. The training will be directed just to neonatal population.

This training will have four stages: (1) theorical learning, (2) observation, (3) practice with mannequins, (4) performing the procedure in real life.

- Theorical learning: this stage will consist in remembering the anatomy basics needed to consider during the catheterization (vessels, surrounding structures),

and an accurate description of the catheterization procedure of each central vein.

- Observation: this stage will consist in observational learning, watching several auto-explained videos about the three techniques of catheterization, performed by a specialist.
- Practice: use the acquired knowledge to practice in mannequins, through a simulation course of 8 hours duration.
- Performing in real life: once learned and practice the different techniques, the residents and neonatologists must demonstrate their skills in real situations. This stage will be considered as part of the clinical trial.

All residents and specialists included in the trial must have successfully passed all the previous stages.

RANDOMIZATION

Every term or preterm neonate admitted in NICU which need a CVC and meet the inclusion criteria to enter in this study, has to be randomized into one of the three intervention groups: a) IJV, b) SCV, c) BCV. All consents must be signed first.

The study biostatistician will prepare the randomised allocation, and then, it will be revealed by a researcher not involved in outcome assessment or interventions to the randomly assigned neonatologists or resident.

MASKING TECHNIQUES

Due to inherent limitations of an intervention procedure, there is no option to do a triple blinded study. The neonatologist will be aware of the catheterisation procedure assigned to every case.

Therefore, the only possibility to reduce the bias of the study is to blind the person who will analyse the statistics. To do it, ID codes will be used to conceal participant's name, and another code will be created to indicate the intervention performed.

CATHETERIZATION PROCEDURE

1. **<u>BCV catheterization's procedure</u>** (26)

With the patient sedated, we will perform the catheterization of the BCV with the Seldinguer technique, under sterile conditions.

1. Place the NN on the back, in a slightly Trendelenburg position with the arms toward the feet and the head turned 30-45º to the opposite side of the puncture site. Place a cushion under the shoulders to lift and expose the site of puncture. The operator stands on the same side as the puncture site.
    - A position more at the child's head, facing the body is preferable for puncture on the right side due to the more descending angle of the vein.
    - If the operator is positioned in the left side, she/he must position himself next to the neonate's body, while facing the head of the patient to cannulate left BCV.
2. The US image has to be positioned to enable the operator to see both, the US pictures, and patient's landmarks. Use a mobile ultrasound, equipped with 12 Hz linear probe and 8 Hz microconvex, to realize a 2D exploration and Doppler-colour of the jugular, subclavian and brachiocephalic veins, to value its anatomy, calibre, and permeability.
3. To obtain an adequate view of the BCV, first, we must obtain a transversal view of the intern jugular and carotid, by placing the US probe perpendicular to the neck's skin, lateral to the cricothyroid membrane area. Then, we must slide the transducer caudally, following the IJV, until the junction of the SCV and IJV in the supraclavicular fossa is reached. After that, turn the probe slightly medial and caudal, until a good longitudinal view of the beginning of the BCV is obtained.

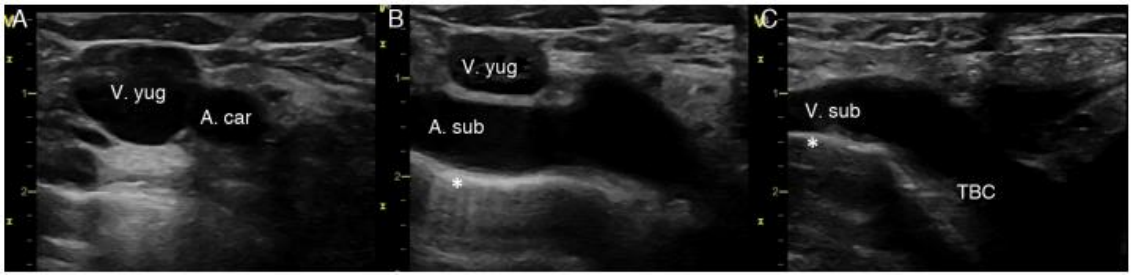


Figure 6. US exploration of the right BCV

4. To realize a safe insertion of the needle, first, by swinging the transducer, we must identify the subclavian artery, and then, the subclavian vein and the BCV. Otherwise, we must identify the pleura, or, if it is the left BCV, the aortic arch (see Figure 6 (26)).
5. Thus, proceed with needle's insertion into the BCV, under the direct US vision from the lateral supraclavicular fossa.
6. Once the blood flow has a spontaneous return via the needle, the US probe can be withdrawn, and a guidewire can be introduced into the vein.
7. Finally, after dilatation, thread the catheter over the guidewire into the vein. Use aspiration of blood and US to confirm the correct position of the catheter.
8. The position of the guide and catheter can be checked with ultrasounds during the entire procedure.
9. The catheter's size is selected in function of the vein's calibre. The external diameter of the catheter cannot exceed a third of the vein's lumen.

We must consider the following considerations:

- If according to the US image the tip of the needle is inside the vein, but it has not a spontaneous return of blood flow, use a syringe to try blood aspiration while slowly withdrawing of the needle.
- If blood flow could not be aspirated, try to redirect the needle into the vein using direct US vision.
- If the guidewire cannot advance successfully, remove the guidewire and the needle, and repeat the whole procedure.

2. SCV catheterization's procedure

It follows the same dynamic as the BCV catheterization. After identifying the anatomical landmarks with the US and confirmed systematically through Doppler colour of vascular flux, by moving the probe caudally, the IJV and the SCV will merge along with the clavicle and the pleural line (see Figure 3 (12)).

The probe must rest un the supraclavicular fossa and if we move it slightly to posteroanterior, an ideal view of the SCV in plane will be obtained. Then, follow the

same steps as the BCV catheterization procedure (from step 5) to complete the intervention.

3. IJV catheterization's procedure

It also follows the steps of the previous interventions, however, for IJV cannulation, a standard transverse out of plane approach is used, also supported by US image (27) (See Figure 7 (28)). See Figure 8 (27) to understand the basic axial planes obtained with the orientation of the transducer.

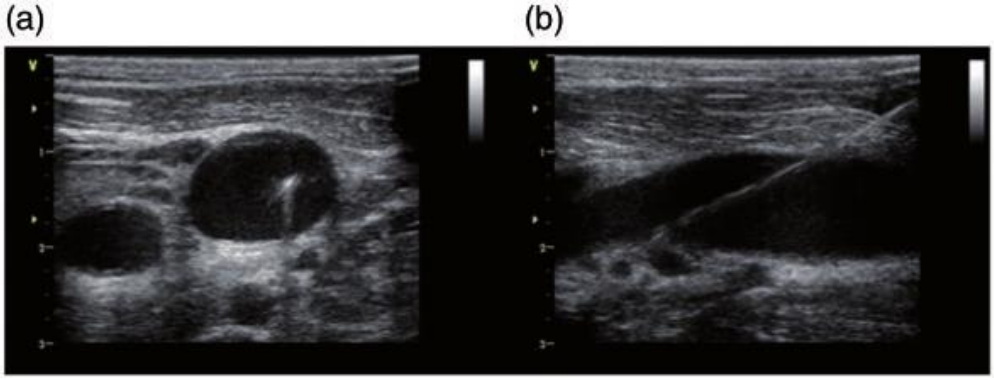


Figure 7. Guidewire in the right internal jugular vein.
(a) Out-of-plane view, transverse view, and (b) In-plane view, longitudinal view

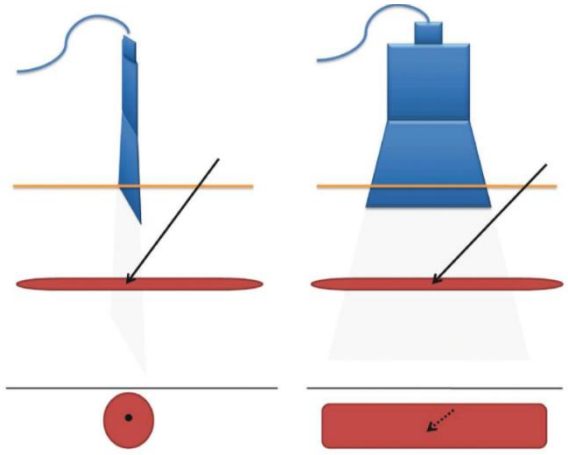


Figure 8. Transducer orientation with basic axial planes

CONFIRMATION OF CATHETER'S LOCATION

Once done the catheterization, we need to check if the catheter is placed suitably or not, by a chest ray-X or by ultrasounds.

We will do it with ultrasounds to avoid unnecessary radiation to the patient, and if the results are not conclusive, then, the catheter's location will be revaluated with a chest-ray-X.

VARIABLES

1. INDEPENDENT VARIABLE

The independent variable will be the location where the central catheter is inserted: the internal jugular vein, the subclavian or the brachiocephalic vein. It will be measured as a nominal qualitative variable (IJV/SCV/BCV).

For further information of the different catheterization' techniques, see page 21.

2. MAIN DEPENDENT VARIABLE

The primary outcome variable will be the success at 1st attempt. This variable will be measured as a dichotomous qualitative variable (1 Success, 0 otherwise). It will be not considered success, if after the US verification of the catheter's location, specialists consider that the catheter should be removed.

3. SECONDARY DEPENDENT VARIABLES

- Number of attempts

It is a quantitative discrete variable. The importance of this variable lies on the complexity of the catheterization's technique or the disadvantages of the vein elected to insert the line.

- The duration of the procedure

It is a quantitative continuous variable, calculated in minutes. It will measure the time since the beginning of the catheterization, until the end of the line's placement.

- Pain

It will be measured before and during the catheterization using the Neonatal Pain, Agitation and Sedation Scale (N-PASS) (see Annex 1). The N-PASS is based on several criteria: crying/irritability, behaviour/state, facial expression, extremities/tone, and vital signs. Pain score difference was calculated by subtracting the score during the procedure from the pain score before the procedure. It is a quantitative discrete variable.

- Complications

This variable will be measured as a dichotomous categorical qualitative variable (yes or no). It will express the existence of any of the adverse effects due to the process of catheterization, mentioned in the table above, which can appear since the moment of insertion until the catheter's removal.

- Short-term complications: pneumothorax, haemothorax, accidental arterial puncture, hematoma, arrythmias, arteriovenous fistula, infiltration into adjacent tissues, catheter malpositioning.
- Long-term complications: catheter's rupture, erosion, occlusion, dislodgement, migration, local bloodstream infection, thrombosis.

- Duration of the catheter in place

Defined as the length of the catheter remaining in the vein, before removing it for any reason. Measured as a quantitative discrete variable, from the day of catheter's insertion (day 1) to its removal (also included).

- Mortality

Death after being admitted in NICUs and before to hospital discharge. Measured as a categorical dichotomous variable (yes/no).

- Length of the stay

Defined as the number of days in the calendar from the day of admission (day 1) until the day of discharge (included). Measured as a discrete quantitative variable.

4. CO-VARIABLES

- Gestational age

It will be calculated in early prenatal ultrasound and obstetric examination. Is defined as the time elapsed between the first day of the last normal period and the day of delivery. It is measured as a discrete quantitative variable (weeks + days).

- Preterm

Measured as a dichotomous qualitative variable (1 preterm, 0 otherwise).

- Birth weight

Child's weight at birth in grams (g), measured as a discrete quantitative variable. We will categorize them into two groups: <1500g and >1500g.

- Small for gestational age

Defined as infants with a birth weight below the percentile 10 (for weight of all neonates at the same gestational age). Measured as a categorical dichotomous variable (yes/no).

- Gender

Measured as a categorical dichotomous variable (male/female).

- 5-minute Apgar score

The Apgar score is done to all neonates in the first and fifth minutes of life, immediately after the delivery. It gives us a retrospective idea of the neonate's physical condition after birth, and if there is an immediate need of resuscitation. The Apgar score rates Appearance (skin colour), Pulse (heart rate), Grimace response (reflexes), Activity (muscle tone) and Respiration (breathing rate and effort). Each category is scored with a 0, 1 and 2, from worst to best score respectively (see Annex 2).

This variable is going to be measured as a quantitative discrete variable (0-3, 4-6, 7-10).

DATA COLLECTION

All baseline and outcome data will be prospectively collected using a data form. This data form has been made to gather all the clinical and procedural information (see Annex 3) from the different NICUs participating in our project.

The name of the patient cannot appear, the researcher will use a special ID code to ensure anonymity and another code to describe the catheterization technique performed (i.e. 1 for IJV, 2 for SCV, and 3 for BCV), in order to keep blind the person who analyse the data.

Once a week, the neonatologist expert from each hospital must collect all the files gathered by the neonatologists of his/her hospital and add them to an online database. When the statistical specialist will analyse the database, he/she will not know the name of the infant or the technique performed on him/her.

A data quality control service will be hired to ensure correct data collection and registration.

Period 1: inclusion and baseline measures

Interview. A baseline researcher will contact potential participants to evaluate if they fulfil the study criteria. It will take place in the NICU when researchers consider that a neonate needs a CVC.

Visit 1. Will take place in a general consultation room, with a baseline researcher not involved in outcome assessment. Informed consent will be signed. Then, the researcher must proceed to collect the rest of the baseline data, corresponding to the covariates (section 1 of the data form must be completed).

Period 2: intervention period

Visit 2. A baseline researcher not involved in the outcome assessment will be in charge of assigning the ID code to each participant. In addition, this researcher will distribute to the neonatologist/ resident the randomised allocation prepared by the biostatistician which indicates the technique he/she will perform.

During the intervention, the baseline researcher must ensure that all dependent variables related to the intervention are collected (section 2 of the data form must be completed).

Period 3: follow up

Visit 3. Every day, the baseline researcher not involved in the outcome assessment will evaluate the rest of variables (section 3 of the data form must be completed). This period ends when the neonate is discharged from the NICU.

When the data form is completed, it has to be delivered to the main neonatologist expert, who will add the data to the online general database.

Is difficult to determine with accuracy when these periods will take place. They are distributed by order, in the period that goes from the neonatologists' decision to insert a CVC to a neonate because he/she requires it, until the infant is discharged from the NICU.

8. STATYSTICAL ANALYSIS

Descriptive analysis

First of all, we will summarize all dependent, independent variables and covariables.

- Qualitative variables (dependent and independent variables) will be summarized by mean proportions.
- The rest of covariates, all of them quantitative, will be summarized through means, standard deviations, medians, and interquartile ranges.

The relation between the dependent qualitative variables and each of the techniques will be assessed with crosstables between qualitative dependent variables and each one of the techniques performed.

In the case of the quantitative dependent variables, we will compare the medians in relation to the performed technique (or not performed).

These analyses will be stratified by the categories of the covariates. With the exception of "gestational age", the quantitative covariates will be categorized in quartiles. "Gestational age" will be considered as a discrete variable.

Bivariate inference

The relation between qualitative dependent variables and each technique, we will contrast them with chi-quadrat. If the number expected is lower than 5, test F exact of Fisher will be used instead.

With quantitative dependent variables, we will compare the medians in relation with the use (or not) of each technique. T-Student will be used (if the dependent variable is distributed as a normal), or U de Mann-Whitney (if the dependent variable is not normally distributed).

These analyses will be stratified by the categories of the covariates. With the exception of "gestational age", the quantitative covariates will be categorized in quartiles. "Gestational age" will be considered as a discrete variable.

Multivariate analysis

The relation between the dependent variables' success, complications, preterm or not, and mortality, and the different techniques employed, we will adjust them in logistical regressions, controlling for all the covariates.

The dependent continuous variable "duration of the procedure", it will be adjusted in lineal regressions.

The relation between the dependent discrete variables' number of attempts, pain, duration of catheter in place, length of stay, and the different techniques, we will assess them using regression of Poisson, adjusting for all the covariates.

9. WORK PLAN AND CHRONOGRAM

RESEARCH TEAM MEMBERS

- Study coordinator (SC): his/her function is to supervise all aspects of the study.
- Neonatologist expert (NE): the neonatologist manager of each hospital.
- Resident representative (RR) from each hospital.
- Statistical specialist (SS): to perform the statistical analysis.

STUDY STAGES

The duration of the entire study will be two years, and it will consist in 5 stages.

Stage 0: Preparation

1. **Protocol elaboration**

   Includes the literature review and all practical considerations (available population, location to develop the training…) to elaborate the protocol.

   Estimated period length: 3 months.

   Responsible to carry out this stage: research team members.

2. **Meeting 1: participants recruitment and organisation**

   Includes the selection of the hospitals participating in the study, and its selection of each NE and RR. Neonatologists and residents will evaluate the protocol and decide if they want to participate.

   Place of the meeting: Hospital Josep Trueta.

3. **Ethics committee's authorization**

   Presentation of the protocol to the research ethics committee (CEIC) at Hospital Josep Trueta, H. Vall d'Hebron, H. Sant Joan de Déu. Make any necessary modifications to the protocol if necessary, to achieve CEIC's conditions.

   Estimated period length to receive the CEIC authorization: 1 month.

4. **Management department authorisation**

   From each hospital participating in the study.

   Estimated period length: 1 month.

5. **Authorisation from local government (Generalitat de Catalunya)**

   As it is an invasive procedure in accordance with the Spanish legislation (Law 14/2007), it requires authorization from the autonomous community.

   Estimated period length: 1 month.

6. **Training of the researchers**

   The main researchers involved in the intervention or data collection will receive instructions to ensure the maximal and equal adherence to protocol stipulations.

   Estimated period length: 1 month.

Stage 1: Training

All residents and neonatologists participating in this trial must be trained before the study begins to know how to use ultrasounds, and how to combine it with the catheter's introduction into each vein. The training will be directed just to neonatal population.

This training will have four stages: (1) theorical learning, (2) observation, (3) practice with mannequins, (4) performing the procedure in real life.

- Theorical learning: this stage will consist in remembering the anatomy basics needed to consider during the catheterization (vessels, surrounding structures), and an accurate description of the catheterization procedure of each central vein.
- Observation: this stage will consist in observational learning, watching several auto-explained videos about the three techniques of catheterization, performed by a specialist.
- Practice: use the acquired knowledge to practice in mannequins, through a simulation course of 8 hours duration.
- Performing in real life: once learned and practice the different techniques, the residents and neonatologists must demonstrate their skills in real situations. This stage will be considered as part of the clinical trial.

All residents and specialists included in the trial must have successfully passed all the previous stages.

Stage 2: Intervention

1. **Patients recruitment and randomisation**

   The statistical specialist will design a software for each hospital to carry out the randomisation sampling. It will allocate the technique of catheterization that each participant will perform on each occasion.

2. **Pilot experiment**

   With the aim to detect problems in organisation or data collection that should be corrected.

   Period length: 1 month.

3. **Meeting 2**

   To correct the wrong aspects collected in the previous stage. This meeting is not mandatory if everything is right.

4. **Intervention, data collection and registration in the database**

   It will start once the first patient is recruited and it will end 4 months after the last participant is recruited. In total, we estimated the intervention period to last for about a year.

5. **Meeting 3**

   To evaluate the data collection quality and solve any problem detected. It will be done 4 months after the study begins.

6. **Data monitoring and quality control**

   An external service will monitor and control data quality during the data collection process and the final analysis, to ensure all data is correctly collected and registered in the database.

Stage 3: Data analysis and interpretation

1. **Statistical analysis**

   Performed by the SS. It will begin when data from the infants enrolled is collected. Data from all 114 patients will be analysed.

   Period length: 2 months.

2. **Interpretation and elaboration of final report**

   The final article exposing the results of our clinical trial will be written by the study coordinator, in collaboration with the research teams and supervised by the statistical specialist.

   Period length: 4 months.

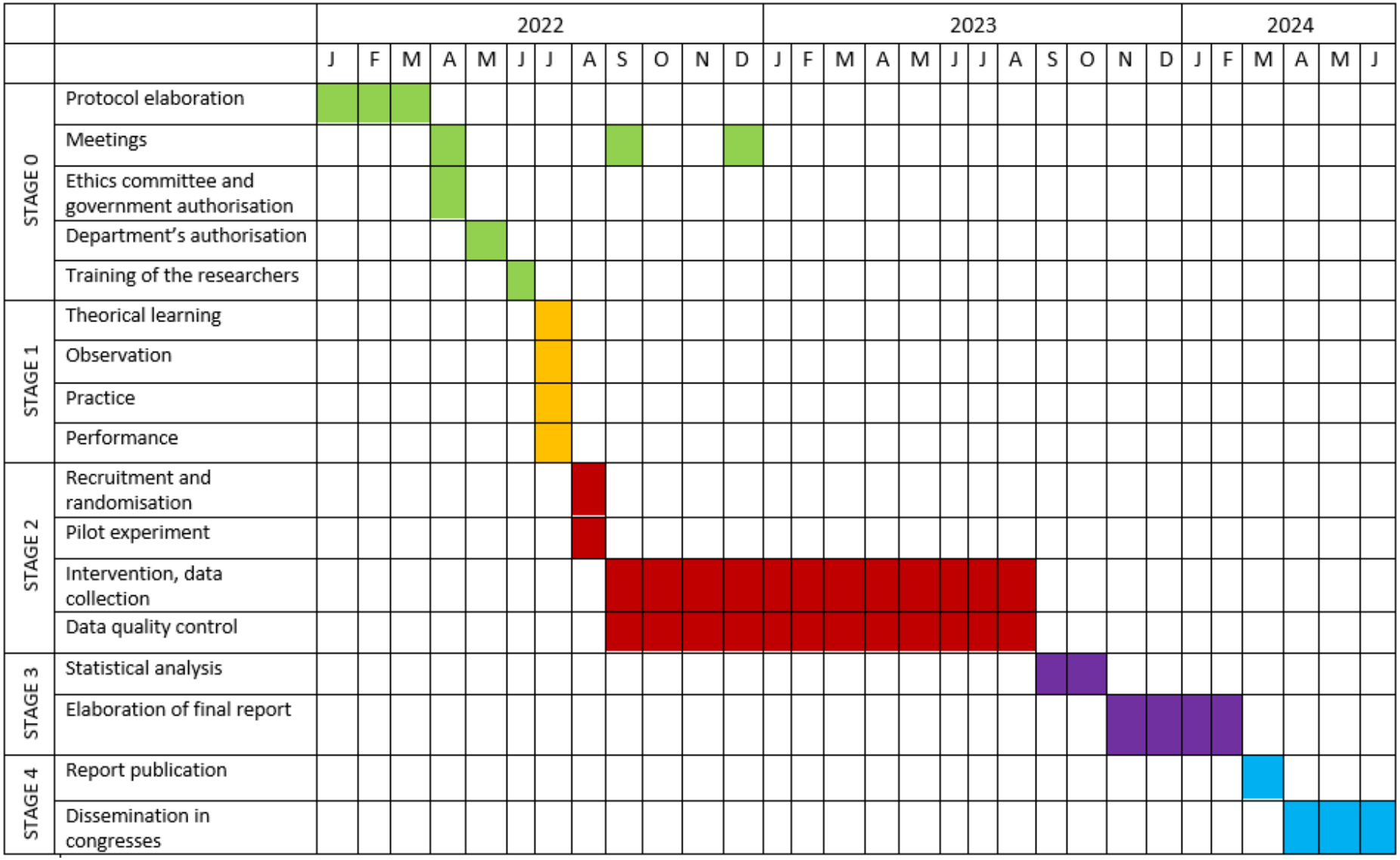
Stage 4: Divulgation

1. **Publication of the results**

   Period length: 1 month.

2. **Dissemination of the results** at national and international congresses.

10. CHRONOGRAM



11. ETHICAL ASPECTS

The study will be performed under the basic ethical principles established by the Helsinki Declaration and the European agreement on Human Rights and Biomedicine (last actualization October 2013) with regards to autonomy, risk-benefit ratio, and protection of vulnerable individuals.

The protocol of the study will be presented to the Clinical Research Ethics Committee (CEIC) of the different centres participating in the study. The committee will ensure that the protocol fits the ethical requirements and any modifications proposed will be implemented into a modified protocol.

The research project will be performed according to the Spanish laws related to clinical trials "Law 14/2007, July 3rd, on biomedical research", which classify our study as an invasive procedure.

As this project involves neonates, parents or legally authorized representatives must sign two reports: the first, giving the authorization to perform any intervention to the infant admitted in NICU (see Annex 4); and the second, allowing the participation in our study, after providing comprehensive information (see Annex 5).

All personal data collected from each patient during the study will be confidential, only for purpose of research and education; moreover, all data will be analysed anonymously, in accordance with the present legislation:

- EU Regulation 2016/679 of the European Parliament and the Council of 27 April 2016, in relation to the protection of natural people about the processing of personal data and on the free movement of such data.
- Spanish data protection legislation: "Organic Law 3/2018, of December 5, on Data Protection and Guarantee of Digital Rights and the royal decree 1720/2007".

All the investigators will have to declare no conflict of interest. They will also have to agree to publish all data and results with total transparency, including unfavourable data or events.

This study will also adhere to the basic bioethical principles stablished in the Belmont report:

- Autonomy: the recognition that people are autonomous and entitled to their own opinion and choices. In our study, as participants are neonates, parents or legal tutors will be informed in detail about the study procedures, how data will be handled, and their right to be informed or to withdraw at any moment will be preserved. To express their agreement to participate in the study, they will sign the informed consent form (see Annex 6). Participant autonomy is regulated through the Spanish legislation: "Law 41/2002, November 14th, regulating patient autonomy and right and obligations of information and clinical documentation".

- Beneficence: is the recognition that people are treated in an ethical manner, respecting their decisions, and protecting them from harm. It is an obligation to secure their well-being. The Belmont report identifies two general rules: do not harm and maximize the benefits. In our study, all participants will be receiving the CVC, because they required it, according to protocol unit bases. Also, specialists will be accurately trained before doing any new technique intervention.

- Justice: everyone ought to receive the benefits of research. To ensure a just selection of the sample, we have created very inclusive and exclusive criteria, while taking a sample which we consider that would most benefit from this intervention. After sampling, we have randomised the technique elected and the researcher responsible of performing it to ensure equal chances for all participants to receive a specific intervention.

12. LIMITATIONS

There are several limitations in our protocol which must be taken into account for future analysis and extrapolation of results.

1. It is a clinical trial that study the performance of three catheterizations' procedures in term and preterm neonates, so it is impossible to be a double-blind design. In order to reduce the detection bias, the statistical specialists will be blinded to the participants' intervention.

2. Another bias is related with the recruitment of the sample. Consecutive sampling will be used, which is a non-probabilistic method; therefore, there is a risk of not obtaining the most representative population. To minimize this selection bias and ensure a good external validity, the designed inclusion criteria are extensive, and exclusion criteria aim to reduce confusing factors. We are aware that the studied population will not be the same as the general population, but we consider it to be closer to the real target population who may benefit from the final outcomes.

3. To reduce the performance bias, intervention researchers will be trained equally to perform the three interventions. However, the previous experience of the researchers is not valued.

4. The study may be an important step to start implementing a training in different NICU to improve the skills of professionals in this field. Even though we have some exclusion criteria that prevent the generalization of our results to all neonates, it is expected that, if the results are satisfactory, a new study could be design, involving neonates weighing <1000g.

5. As we are a multicentre study, it is required a prepared organization. For this reason, is important to have a person analysing the data collection while it updates, ensuring a good quality of the gathered information. Communication between different hospitals needs to be flexible to facilitate the identification of any problem.

6. The final limitation is participant loss before randomization, which we have estimated to be a 50%. We consider that mostly will be because parents/tutors will not sign the informed consent, while they will be worried as neonates are a vulnerable population. We will try to minimize this loss by giving the tutors widely information with patience and answering their questions as much as necessary.

7. Attrition bias occurs when participants leave the study. In our study, the follow-up of the participants is very short, it ends when they abandon the NICU. Considering this aspect, we consider that this bias will be regrettable, since we will achieve the required outcomes from almost 100% of patients.

13. BUDGET

The estimated investment needed to realize our study is 35,400€.

Table 3. Budget

STAFF	
Qualified Statistician: 40€/hour, 70h	2,800€
Study Coordinator: 500€/ year, 2 years	1,000€
Data monitoring and quality control	15,000€
	Subtotal: 18,800€
MEETINGS	
Organization meeting: 50€/person. 8 participants. 1 meeting.	400€
Analyse meeting: 50€/person. 8 participants. 2 meetings.	800€
	Subtotal: 1,200€
TRAINING	
Videos and workshops with qualified staff	2,500€
	Subtotal: 2,500€
PUBLICATION	
Paper revision	500€
Paper publication	2,500€
	Subtotal: 3,000€
DISSEMINATION	
Inscription to national congress	300€
Inscription to international congress	500€
Travel accommodation and food, 1700€/participant, 2 participants	3,400€
	Subtotal: 4,200€
INSURANCE	Subtotal: 5,700€
TOTAL	35,400€

We will hire a biostatistician to perform initial randomisation and the statistical analysis of results. Initially, we have estimated 70h of work, with a salary of 40 euros per hour. It would cost 2,800€.

We will need to hire a data monitoring service to ensure data collection. Thus, we will hire a study coordinator to give assessment and coordinate the medical staff. Both would cost 3,800€.

For the publication in nation and international journals, we have assigned 2,500€. For the dissemination at congresses, one national and the other international, two researchers will attend with the travel and food included, it corresponds to a total of 4,200€.

We will hire specialists in these catheterization's technique to train our researchers. We estimate a total of 2,500€ for material and personal expenses.

Because this study uses a different intervention to current medical practice, and the population involved is very vulnerable, we will hire an additional insurance for participants, aside from the general health coverage. Nonetheless, the CEIC must agree. The estimated cost of the insurance is 5,700€.

Other costs that has not been considered because they are already covered by national health system are salaries of the researchers involved, accommodations used in the hospitals involved (catheter, US, computers…).

14. FEASABILITY

We have considered our study feasible for several reasons.

First of all, the research team, and the other specialists collaborating in the study will be sufficiently qualified for their role. Their salary, as professionals working for the public health system will be covered.

This trial will be carried out in several hospitals, all of them with level IIIB NICU, which can provide the entire infrastructure and materials needed to realize a CVC catheterization.

The recruitment and intervention period are estimated to last a year. With the three hospitals involved, we won't have any problems to obtain the number of participants wished, while we have estimated a high rate of loss, about 50%, and also, because we are studying different techniques of a routinely procedure, considering that 80% neonates admitted in NICU in a year need a CVC.

15. FUTURE RESEARCH

If our clinical trial will carry out and the results are relevant and positive, future research studies could consider comparing the most effective technique of catheterization of this study to the gold standard, the umbilical vein catheter.

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17. ANNEXES

Annex 1: Pain. N-PASS scale

EVALUACIÓN DEL DOLOR NEONATAL N-PASS, ESCALA DE AGITACIÓN Y SEDACIÓN

Table 4. Escala de dolor neonatal N-PASS (29)

Criterio de evaluación	Sedación		Sedación/dolor	Dolor/Agitación	
	-2	-1	0/0	1	2
Llanto Irritabilidad	No llora con estímulos dolorosos.	Gime o llora con pocos estímulos dolorosos.	Sin sedación. Sin signos de dolor.	Irritable o con ataques de llanto. Se lo puede tranquilizar.	Llanto continuo, silencioso o agudo. No se tranquiliza (inconsolable).
Comportamiento	No se despierta con estímulos. No se mueve.	Se despierta un poco con estímulos. Se mueve muy poco.	Sin sedación. Sin signos de dolor.	Inquieto. Se retuerce. Se despierta seguido.	Se arquea y patea. Está despierto todo el tiempo o se despierta un poco. No se mueve (no está sedado).
Expresión facial	Tiene la boca relajada. Sin expresión.	Poca expresión con estímulos.	Sin sedación. Sin signos de dolor.	Demuestra dolor esporádicamente.	Demuestra dolor continuamente.
Tono muscular de brazos y piernas	Sin reflejo de agarre o reflejo palmar. Flacidez.	Reflejo de agarre o palmar débil. Menor tono muscular.	Sin sedación. Sin signos de dolor.	Ocasionalmente, los dedos de los pies o los puños apretados, o abre y separa los dedos de la mano. No tiene el cuerpo tenso.	Los dedos de los pies y los puños apretados o abre y separa los dedos de la mano. Tiene el cuerpo tenso.
Signos vitales: ritmos cardíaco y respiratorio, presión arterial, saturación de oxígeno (SatO2)	No hay cambio con estímulos. Hipoventilación o apnea.	Variación <10% de los valores iniciales, con estímulos.	Sin sedación. Sin signos de dolor.	↑10-20% por encima de los valores iniciales. SaO2 a 76-85% con estímulos. Aumento brusco.	↑ >20% de los valores iniciales. SaO2 ≤ 75% con estímulos, aumento lento. Resistencia al respirador.

Evaluación del dolor en el prematuro: +3 si <28SG, +2 si 28-31 SG, +1 si 32-35 SG.
El valor total del dolor se mide del 0 → +10.
Se indica tratamiento si >3. El objetivo es un valor ≤3.

Annex 2: Apgar scoring system

Table 5. The Apgar score. Adapted from (30)

	0 Points	1 Points	2 Points
Activity (muscle tone)	Absent	Flexed arms and legs	Active movement
Pulse rate	Absent	< 100bpm	> 100bpm
Grimace (reflex irritability)	Floppy	Minimal response to stimulation	Prompt response to stimulation (sneeze, cough pull away)
Appearance	Blue: pale	Pink body, Blue extremities	Completely pink
Respiration	Absent	Slow and irregular	Vigorous cry

Severely depressed	0-3
Moderately depressed	4-6
Excellent condition	7-10

Annex 3: Data form

DATA FORM

ETIQUETA IDENTIFICATIVA

EN RELACIÓN CON EL PARTICIPANTE

Semanas de gestación	
Pretérmino	
Edad actual	
Peso al nacer	
Bajo peso al nacer	
Peso actual	
Género	
Apgar score a los 5'	

EN RELACIÓN CON LA INTERVENCIÓN

Código de la técnica empleada	
Persona que realiza la cateterización	
Éxito al primer intento	
Número de intentos	
Duración del procedimiento	
Complicaciones a corto-plazo. ¿Cuáles?	

EN RELACIÓN CON LA ESTANCIA EN LA NICU

Dolor (medido con la escala N-PASS)	
Complicaciones tardías. ¿Cuáles?	
Duración del catéter colocado	
Mortalidad	
Días ingresado en NICU	

Annex 4: Informed consent to access into NICU

Hospital Universitari de Girona
Doctor Josep Trueta

Dades del/la pacient
Cognoms:
Nom:
NHC:

Consentiment informat

Nom del procediment:
Procediments derivats de l'Ingrés al Servei de Cures Intensives Neonatals i Pediàtriques.

Descripció del procediment:
El seu fill/a ingressa en la Unitat de Cures intensives Neonatals i Pediàtriques perquè pateix una malaltia greu, que posa en perill la seva vida, i necessita un tractament i/o vigilància especial.

Riscos generals:
Poden ser necessàries mesures o tècniques que denominem de "suport vital", que no estan lliures de riscos que vostè ha de conèixer. En el cas concret del seu fill/a li explicarem quines d'aquestes actuacions seran utilitzades i per quin motiu, sempre que la urgència ho permeti.

Riscos específics:
Aquest riscos són variables en freqüència i gravetat depenent de la tècnica i del propi pacient, però els més freqüents són:
-Els derivats de la col·locació de catèters en venes i artèries que poden donar lloc a complicacions com hemorràgies, coàguls o infecció.
-Intubació i ús de respiradors, utilitzats per ajudar a substituir la pròpia respiració, també poden tenir efectes no desitjats com infeccions pulmonars, fugida d'aire per trencament del pulmó, obturacions o lesions de la tràquea.
-Reaccions adverses, fonamentalment a medicaments, per reacció al·lèrgica o efectes secundaris.
-Toracocentesis: punció de l'espai pleural per fins diagnòstics i extracció d'aire o líquid amb fins terapèutics. Pot tenir efectes no desitjats com fugida d'aire per punció del pulmó, fugida d'aire sota la pell, hemorràgia pulmonar, lesió de vasos intercostals o lesió de les vísceres abdominals.
-Pericardiocentesis: tractament del tamponament cardíac i anàlisi del líquid extret per fins diagnòstics. Pot tenir efectes no desitjats com lesió del miocardi, punció d'una artèria coronària, arítmies, lesió del pulmó o lesió de vísceres abdominals.
Les persones que cuiden al seu fill/a coneixen aquestes possibilitats i estan atents a la seva possible aparició per combatre-les, cosa que generalment transcorre amb èxit. Tot i que els efectes secundaris poden agreujar la situació del pacient, els possibles beneficis d'aquestes mesures o tècniques superen àmpliament els riscos que comporten, és per aquest motiu que només es solen utilitzar en pacients greus.

Riscos personals:
-
-
-
-

.....pare/mare/tutor de.....
expressa que ha estat informat pel Dr/a..... del motiu pel que el meu fill/a ingressa a la Unitat de Cures intensives Neonatals i Pediàtriques, de les tècniques que poden ser necessàries aplicar-li i dels riscos que poden derivar-se de les mateixes. Comprenc el contingut d'aquest document, he rebut la informació suplementària sol·licitada i accepto les mesures necessàries. En qualsevol moment de l'evolució de la malaltia del meu fill/a podré reconsiderar aquesta decisió.

A Girona, a ..... de .....de 20.....

Signatura i DNI de/la pacient o responsable legal. Signatura del metge que informa i número de col·legiat

Annex 5: Informed sheet to legal representatives

HOJA DE INFORMACIÓN AL FAMILIAR RESPONSABLE O REPRESENTANTE LEGAL

TÍTULO DEL ESTUDIO: COMPARACIÓN ENTRE DOS TÉCNICAS DE CATETERIZACIÓN VENOSA CENTRAL EN NEONATOS

INVESTIGADORA PRINCIPAL: Gual Fresneda, Paula

CENTRO: Servicio de Neonatología. Hospital universitario Dr. Josep Trueta. Girona, España.

INTRODUCCIÓN

Nos dirigimos a usted para informarle sobre un estudio de investigación en el que se le invita a participar.
El estudio ha sido aprobado por el Comité Ético de Investigación Clínica del Hospital Universitari de Girona Dr. Josep Trueta, de acuerdo con la legislación vidente, Ley 14/207 de 3 de julio, de investigación biomédica con procedimientos invasivos.
Nuestra intención es tan solo que usted reciba la información correcta y suficiente para que pueda evaluar y juzgar si quiere o no participar en este estudio. Para ello, lea esta hoja informativa con atención y nosotros le aclararemos las dudas que le puedan surgir después de la explicación. Además, puede consultar con las personas que considere oportuno.

PARTICIPACIÓN VOLUNTARIA

Debe saber que su participación en este estudio es voluntaria y que puede decidir no participar o cambiar su decisión y retirar el consentimiento en cualquier momento, sin que ello altere la relación con su médico ni se produzca perjuicio alguno en su tratamiento.

DESCRIPCIÓN DEL ESTUDIO

La cateterización venosa central es un procedimiento ampliamente utilizado en la UCI Neonatal con el objetivo de monitorizar constantes y administrar fluidos, medicación y nutrición a nuestros pacientes por via intravenosa. Últimamente se ha demostrado que el abordaje de otras venas, aparte de la más típica, es eficaz para la cateterización. Sin embargo, los médicos de nuestro centro solo están especializados en el abordaje clásico. Por este motivo, el objetivo de nuestro objetivo es establecer un plan de entrenamiento y aprendizaje para nuestros médicos de los tres distintos procedimientos que se emplean para este fin, con el fin de seleccionar la mejor técnica e implementarla en la práctica clínica. Para ello, se ha diseñado este ensayo clínico donde se realizará de forma aleatoria la cateterización venosa central usando una de las tres venas principales. Al ser un proceso aleatorizado, todos los pacientes tienen las mismas posibilidades de ser cateterizado por una técnica u otra.

PROCEDIMIENTOS DEL ENSAYO

La cateterización venosa central se llevará a cabo solo en aquellos casos en los que el paciente lo necesite y será realizado por un médico previamente especializado en las distintas técnicas.

BENEFICIOS Y RIESGOS DERIVADOS DE SU PARTICIPACIÓN EN EL ESTUDIO

Este estudio pretende ser una referencia, para establecer un entrenamiento y aprendizaje sobre la cateterización en especialistas poco especializados en este procedimiento.
Se realizarán análisis evaluadores internos durante el transcurso del estudio, para asegurar que no hay diferencias clínicamente relevantes entre los tres grupos de estudio.
La cateterización venosa central presenta una serie de complicaciones asociadas como cualquier procedimiento invasivo explicados en la hoja de acceso a la UCI Neonatal que usted a tenido que firmar.

COMPENSACIÓN ECONÓMICA

Su participación en el estudio no le supondrá ningún gasto. Usted no tendrá que pagar por la cateterización ni recibirá una compensación económica.

CONFIDENCIALIDAD

El tratamiento, la comunicación y la cesión de los datos de carácter personal de todos los sujetos participantes se ajustará a lo dispuesto en la Ley Orgánica 15/1999, de 13 de diciembre de protección de datos de carácter personal. De acuerdo con lo que establece la legislación mencionada, usted o su hijo podrán ejercer los derechos de acceso, modificación, oposición y cancelación de datos, para lo cual deberán dirigirse a su médico del estudio. Los datos recogidos para el estudio estarán identificados mediante un código y solo su médico de estudio/colaboradores podrá relacionar dichos datos con su hijo y con su historia clínica.
Sólo se transmitirán a terceros y a otros países los datos recogidos para el estudio que en ningún caso contendrán información que le pueda identificar directamente, como nombre y apellidos, dirección, número seguridad social, etc. En el caso de que se produzca esta cesión, será para los mismos fines del estudio descrito y garantizando la confidencialidad como mínimo con el nivel de protección de la legislación vigente en nuestro país. El acceso a su información personal quedará restringido al médico del estudio/colaboradores, autoridades sanitarias (Agencia Española del Medicamento y Productos Sanitarios), al Comité Ético de Investigación Clínica y personal autorizado por el promotor, cuando lo precisen para comprobar los datos y procedimientos del estudio, pero siempre manteniendo la confidencialidad de los mismos de acuerdo con la legislación vigente.
Si usted decide retirar el consentimiento para participar en este estudio, ningún dato nuevo será añadido a la base de datos y puede exigir la destrucción de todas las muestras identificables previamente retenidas para evitar la realización de nuevos análisis.

Annex 6: Informed consent to be added in the study

Hospital Universitari de Girona Doctor Josep Trueta

CONSENTIMIENTO INFORMADO DEL FAMILIAR RESPONSABLE O REPRESENTANTE LEGAL

Yo..... (nombre y apellidos) en calidad de ..... (relación con el participante) de ..... (nombre y apellidos del participante).

He leído la hoja de información que se me ha entregado.
He podido hacer preguntas sobre el estudio.
He recibido suficiente información sobre el estudio.
He hablado con:
……
(nombre del investigador)
Comprendo que la participación del paciente es voluntaria.
Comprendo que puede retirarse del estudio.

1º Cuando quiera.
2º Sin tener que dar explicaciones.
3º Sin que esto repercuta en sus cuidados médicos.

Presto mi conformidad para que …… (nombre del participante) participe en este estudio y doy mi consentimiento para el acceso y utilización de los datos en las condiciones detalladas en la hoja de información.

FIRMA FAMILIAR O TESTIGO:	**FIRMA DEL INVESTIGADOR:**
Nombre:	Nombre:
Fecha:	Fecha: