Central venous catheterisation - clinical studies on mechanical complications in the ultrasound-guided era

Adrian, Maria

2022

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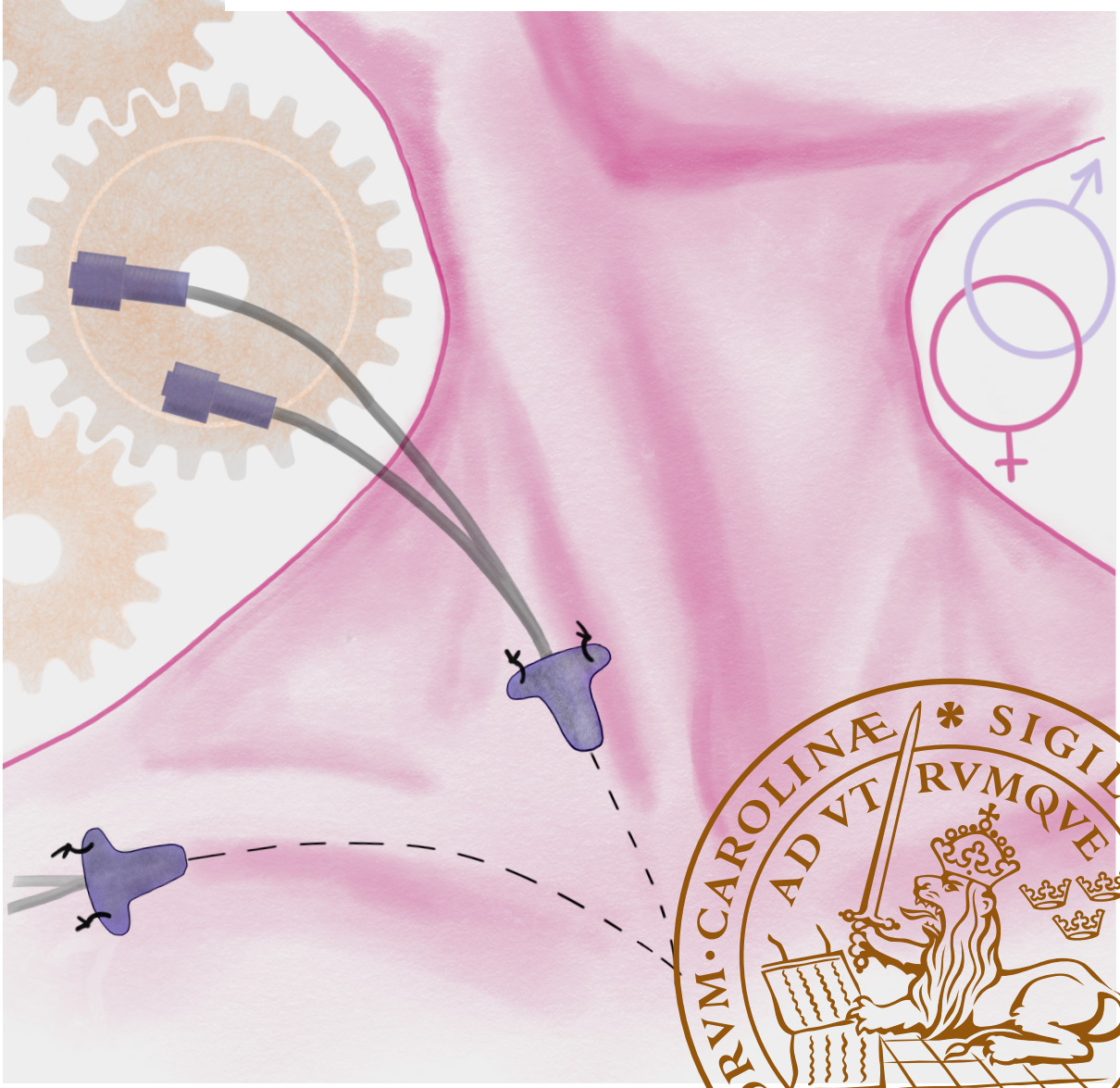
ANAESTHESIOLOGY AND INTENSIVE CARE | FACULTY OF MEDICINE | LUND UNIVERSITY



Printed by Media-Tryck, Lund 2022 NORDIC SWAN ECOLABEL 3041 0903

MARIA ADRIAN is a specialist in anaesthesiology and intensive care at Skåne University Hospital Lund, Sweden. Her thesis focuses on various aspects of ultrasound-guided central venous catheterisation and associated mechanical complications.

LUND UNIVERSITY

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Department of Clinical Sciences
Anaesthesiology and Intensive Care

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2022:46
ISBN 978-91-8021-207-6
ISSN 1652-8220

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LUND
UNIVERSITY

DOCTORAL DISSERTATION

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To be defended on the 8th of April 2022 at 09:00 in Belfragesalen, BMC D15, Klinikgatan 32, Lund, Sweden

Faculty opponent
Docent Sophie Lindgren
Göteborg University, Sahlgrenska University Hospital, Göteborg, Sweden

Organization	Document name
LUND UNIVERSITY	Doctoral Dissertation
	Date of issue 2022-04-08
Author: Maria Adrian	

Title and subtitle
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Abstract
Central venous catheterisation is one of the most common invasive procedures performed on patients in secondary care. Unfortunately the catheterisation procedure is associated with mechanical complications that both can be life-threatening and may force postponement of life-saving treatments such as surgery and chemotherapy. The use of real-time ultrasound guidance increases success rates and reduces the numbers of mechanical complications – but major mechanical complications still occur. The general aim of this thesis was to explore various aspects of ultrasound-guided central venous catheterisation and associated mechanical complications in order to enable future quality improvements of the procedure.

Papers I and II investigate the incidence of mechanical complications within 24 hours after central venous catheterisation and analyse possible associated risk factors. In total, 12 667 central venous catheter insertions in 8 586 patients were included. We found that in hospitals where real-time ultrasound guidance is standard of care for central venous access, the incidence of major mechanical complications was only 0.4%. We also identified patient BMI <20 kg/m^2, male operator gender, limited operator experience and more than one skin puncture as independent risk factors for major mechanical complications. In addition, subclavian vein catheterisation was an independent risk factor for pneumothorax compared to internal jugular vein catheterisation.

Paper III evaluates the use of a micro-convex probe and the right supraclavicular fossa ultrasound view for aiding guidewire positioning to avoid catheter misplacements in right infraclavicular subclavian vein catheterisation. We prospectively included 103 patients and showed that with the ultrasound method described, 14 of the 15 initially misplaced guidewires were detected and 12 of them were successfully adjusted to a correct position, which in turn helped avoid 12 catheter misplacements at the time of insertion.

Paper IV estimates the minimal guidewire length required to avoid guidewire retraction, thereby maintaining a guidewire tip position in the lower segment of the superior vena cava throughout an ultrasound-guided infraclavicular catheter placement in the right subclavian vein. Based on vessel measurements in 100 patients, we concluded that the majority of the assessed 15–16 cm central venous catheter kits contain guidewires that are too short for right subclavian vein catheterisation, i.e., guidewire retraction is needed prior to catheter insertion.

Paper V examines the effect of an implementation package on the documentation of central venous catheter insertions. We found that introduction of an updated central venous catheter insertion form, delegated information responsibility of the new local directions for central venous catheter placement, and follow-up of all registered insertion forms during a limited period of time reduced the porportion of missing data with 55%.

The general conclusion of this thesis is that there are possibilities for further quality improvements of central venous catheterisation also in the ultrasound-guided era and that the combination of appropriate recording of central venous catheter insertions, possibilities to track patient outcomes, and clinical research contribute to advanced understanding and delivering of patient-safe healthcare.

Key words Central venous catheterisation, ultrasound, mechanical complication, subclavian vein, guidewire

Classification system and/or index terms (if any)

Supplementary bibliographical information		**Language** English
ISSN 1652-8220		**ISBN** 978-91-8021-207-6
Recipient's notes	**Number of pages** 67	Price
	Security classification	

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Cover illustration by Gabriel Adrian

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ISSN 1652-8220
Lund University, Faculty of Medicine Doctoral Dissertation Series 2022:46

Printed in Sweden by Media-Tryck, Lund University, Lund 2022

To mum and dad

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Sammanfattning på svenska

Centrala venkatetrar (CVKer) är en viktig komponent i modern sjukvård. De används vid en rad olika situationer, till exempel vid administration av kärlretande läkemedel, övervakning av blodcirkulationen, intravenös näringstillförsel, och bloddialys. I Sverige läggs ungefär 45 000 CVKer in på patienter varje år, vilket gör CVK-inläggning till ett av de absolut vanligaste riskfyllda momenten vi utsätter patienter för inom slutenvården.

De komplikationer som kan uppstå i samband med CVK-inläggning kallas gemensamt för mekaniska komplikationer och kan vara allt ifrån obetydliga till direkt livshotande om de inte behandlas omedelbart. De kan också fördröja livräddande behandlingar som kirurgi och cellgifter. Exempel på allvarliga mekaniska komplikationer är hål på lungsäcken, stor blödning, oavsiktlig inläggning av CVKn i en artär, akut behandlingskrävande hjärtrytmrubbning och ihållande nervskada. Tidigare studier har övertygande visat att ultraljudsvägledning i realtid minskar komplikationsfrekvensen vid CVK-inläggning, men trots ultraljudsanvändning inträffar fortfarande allvarliga mekaniska komplikationer. För att ytterligare kunna minska komplikationsfrekvensen behövs ökad kunskap om förekomsten av mekaniska komplikationer efter modern ultraljudsvägledd CVK-inläggning och identifiering av viktiga riskfaktorer. I tillägg bör de nya ultraljudstekniker som används vid CVK-inläggning utvärderas.

I denna avhandling har olika aspekter av ultraljusvägledd CVK-inläggning och associerade mekaniska komplikationer undersökts.

De två första arbetena utgör internationellt sett den största granskningen av CVK-inläggning och mekaniska komplikationer som hittills genomförts. Vi studerade 12 667 CVK-inläggningar på 8 586 patienter och fann att förekomsten av allvarliga mekaniska komplikationer är låg på sjukhus där ultraljudsvägledning i realtid är klinisk praxis vid CVK-inläggning. Tack vare studiens storlek kunde vi även identifiera flera viktiga riskfaktorer för allvarliga mekaniska komplikationer: patient med body mass index (BMI) <20 kg/m^2, manlig inläggare, oerfaren inläggare och mer än ett stickförsök. CVK-inläggning i nyckelbensvenen var en riskfaktor för hål på lungsäcken jämfört med CVK-inläggning i inre halsvenen.

CVK-inläggning i nyckelbensvenen är förknippad med en ökad risk för felaktiga CVK-spetslägen. En felplacerad CVK minskar dess användningsområde, kan försena livräddande behandlingar och ökar risken att CVKn slutar fungera i förtid

på grund av blodproppsbildning. Ett felaktigt CVK-spetsläge kan också leda till sällsynta men allvarliga komplikationer som kärlskador, blödning i bröstkorgen, ansamling av blod i hjärtsäcken och hjärtrytmrubbningar. En korrekt placerad CVK-spets är därför en viktig säkerhets- och kvalitetsaspekt vid CVK-inläggning.

Det tredje arbetet utvärderar en ultraljudsmetod som kan användas för att minska risken för felaktiga CVK-spetslägen vid CVK-inläggning i den högra nyckelbensvenen. Metoden innebär att korrekt ledarläge verifieras med ultraljud och felaktiga ledarlägen korrigeras innan själva CVKn förs in. Vi inkluderade 103 patienter i studien och visade att tolv av femton felaktiga CVK-spetslägen kunde undvikas med hjälp av den beskrivna ultraljudsmetoden. I det fjärde arbetet undersökte vi hur lång en ledare bör vara vid CVK-inläggning i den högra nyckelbensvenen då vi noterat att de ledare vi använder ofta behöver backas. Att behöva backa ledaren för att kunna föra in CVKn efter att man konstaterat korrekt ledarläge ökar risken att CVK-spetsen hamnar fel. Genom att utföra kärlmätningar på röntgenbilder av 100 patienter och mätningar av utrustning som tillhandahålls i vanliga kommersiella 15–16 cm CVK-set visade vi att majoriteten av de CVK-set vi använder innehåller för korta ledare för CVK-inläggning i den högra nyckelbensvenen.

I det femte arbetet undersökte vi om dokumentationen av CVK-inläggningar i Region Skåne förändrats efter genomförandet av ett förbättringsprojekt som inkluderade uppdatering av den befintliga CVK-inläggningsmallen i det gemensamma journalsystemet, delegerat informationsansvar gällande de nya gemensamma riktlinjerna för CVK-inläggning, samt uppföljning av alla dokumenterade CVK-inläggningar under en begränsad tid. Vi fann att andelen saknade data i CVK-inläggningsmallar minskade med 55% efter genomförandet av förbättringsprojektet.

Den övergripande slutsatsen är att det finns möjligheter att ytterligare förbättra ultraljudsledd CVK-inläggning och att kombinationen av kvalitetsförbättrings-projekt och klinisk forskning bidrar till ökad förståelse och tillhandahållande av patientsäker sjukvård.

Abbreviations

AVA	advanced vessel analysis
BMI	body mass index
CI	confidence interval
CT	computed tomography
CVC	central venous catheter
EHR	electronic health record
GW	guidewire
ICU	intensive care unit
ISP	IntelliSpacePortal
LBCV	left brachiocephalic vein
LSCV	left subclavian vein
OR	odds ratio
PICC	peripherally inserted central venous catheter
PL	pleural line
RIJV	right internal jugular vein
RPA	right pulmonary artery
RSCV	right subclavian vein
SVC	superior vena cava
TTE	transthoracic echocardiography
US	ultrasound

Introduction

A central venous catheter (CVC) is, by definition, a catheter whose tip resides in the central circulation.[1,2] It provides reliable access to the bloodstream, enables monitoring of haemodynamic variables that cannot be measured accurately by non-invasive means, allows safe delivery of vasoactive drugs, chemotherapy, and nutritional support, and can be used for haemodialysis.[3,4] In modern health care, CVCs are necessary for treatment of many medical disorders. They are commonly used in intensive care units (ICUs) and operating theatres, but also increasingly used in both emergency settings and general wards.[5] Central venous catheterisation has thus become one of the most common invasive procedures performed on patients in secondary care.[6]

Unfortunately, the catheterisation procedure is associated with mechanical complications that can range from being clinically insignificant to life-threatening if untreated.[7,8] In addition, major mechanical complications like pneumothorax, arterial damage and serious bleedings may force postponement of life-saving treatments such as surgery and chemotherapy. The use of real-time ultrasound guidance increases success rates and reduces the number of mechanical complications,[9–11] but despite the use of ultrasound, major mechanical complications still occur.[12] To enable further quality improvements of central venous catheterisation and increase patient safety, knowledge of complications rates, identification of important risk factors for mechanical complications, and evaluation of new ultrasound techniques used in clinical practice is essential. This thesis will explore all these aspects.

Historical perspective

In the early 1900s, the first attempts to access the central venous circuit in humans occurred. Reports describe catheters advanced into the central circulation using the cubital and femoral veins.[13] In 1929, a young German physician named Werner Forsmann advanced a 4 French ureteral catheter into his own heart through a wide bore needle in the antecubital vein of his left arm.[14] He then proceeded up several flights of stairs to the Radiology Department to confirm the catheter tip position in his right atrium using X-ray (Figure 1). Twelve years later, André Cournad and Dickison Richards pioneered right heart catheterisation. In 1956, Forsmann, Cournand and Richards received the Nobel Prize in Medicine for their work in advancing central venous access techniques and right heart catheterisation.[15]

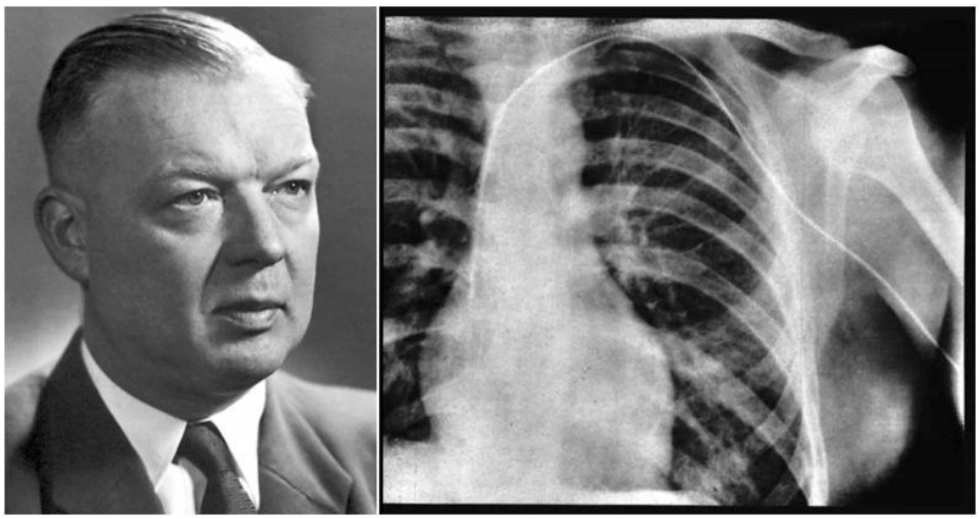

Figure 1
Werner Forsmann (to the left) and a chest X-ray (to the right) showing the catheter inserted via his left arm with the catheter tip poitioned in his right atrium. Image used with permission.

In 1952, Aubaniac first described his 10-year experience with a new vein puncture technique using the subclavian vein for rapid infusion of resuscitation fluids in military causalities.[16] Wilson later refined this technique to introduce a CVC through the subclavian vein and reported the advantages of measurement of central venous pressure in the maintenance of optimal blood volume.[17] In 1953, Sven-Ingvar Seldinger proposed using a flexible metallic guidewire for the introduction of a catheter during peripheral vascular access, rather than using the stiff needle for insertion.[18] With this technique, catheters that were 50–100% wider than the stiff needle could be inserted into the vessel. The catheter-over-wire technique, also called the Seldinger technique, was a key revolution for centrally inserted catheters.

In 1970, Jeremy Swan and William Ganz developed the pulmonary artery catheter, later known as the Swan Ganz catheter, which enables continuous measurement of pulmonary artery pressures, cardiac output, central venous pressure, stroke volume, pulmonary capillary wedge pressure, and systemic vascular resistance.[19] Today the pulmonary artery catheter is gold standard for advanced haemodynamic monitoring.

In 1978, doppler localisation was used to mark the skin overlying the internal jugular vein. In 1982, the first use of ultrasound to guide central venous access was described by Peters et al.[20] Real-time ultrasound guidance for internal jugular vein catheterisation was reported in 1986,[21] but despite the introduction of this new and accurate insertion technique, the use of anatomical landmarks remained standard practice until the 21st century. In 1996, the first meta-analysis on ultrasound guidance for CVC placement was published, suggesting higher success and lower complication rates after ultrasound-guided internal jugular and subclavian vein catheterisation compared to the anatomic landmark technique.[22] In 2001, the Agency for Healthcare Research and Quality Evidence Report listed real-time ultrasound guidance for central venous access as 1 of 11 practices with "strength of evidence for supporting more widespread implementation."[23] At present, clinical guidelines worldwide recommend the use of ultrasound as a key safety measure for CVC insertions.[24–28]

Central venous catheters (CVCs)

Modern health care is highly dependent on secure and reliable venous access in adult hospitalized patients.[1] CVCs are a key component of this practice. They are used for a wide range of indications and for some patients they are the only option for vascular access.[4] The contraindications are usually relative, and most of them depend on clinical indication and situation. Contaminated, traumatised, and burned insertion sites should of course be avoided, as well as insertion of catheters in obstructed veins (due to venous thrombosis or stenosis).[1]

CVCs are mainly used within perioperative and intensive care medicine, but are also used in the management of medical, surgical, paediatric, and oncological patients.[5] According to the Swedish Society of Anaesthesia and Intensive Care (SFAI), approximately 45 000 CVCs are inserted annually at the different hospitals in Sweden. Most of the insertions are performed by anaesthesiologists, but also surgeons and interventional radiologists/cardiologists are involved. In the United States, about 3 million CVCs are inserted each year[29] and for the United Kingdom the estimated figure is about 250 000.[30] Central venous catheterisation is thus performed more often than many common surgical procedures and although CVC insertions are not considered surgery, the associated severe complications of central

venous catheterisation are highly comparable to the serious complications that can occur in connection with major surgery.

Indications

A CVC is indicated:

- when peripheral venous access is limited
- for administration of potent vasoactive drugs such as norepinephrine, epinephrine, vasopressin, or dobutamine
- when intravenous fluids requiring dilution within the central circulation to avoid vascular damage are infused (i.e., chemotherapy, total parental nutrition, potassium chloride)
- when acute or subacute haemodialysis or haemofiltration is needed
- for invasive haemodynamic monitoring and measurement of central oxygen saturation levels
- for facilitation of extremely rapid infusion of resuscitation fluid (large bore catheter)
- when transvenous cardiac pacing is needed
- for intravenous medical treatment over a long period of time (>4 weeks)

Types of catheters

There are various types of CVCs with different areas of use.[1] Single-lumen or double-lumen CVCs are often inserted for intermittent or continuous infusion of medication or fluid. They are applicable for the administration of chemotherapy, antibiotics and nutritional therapies and are mainly used in general wards. Multi-lumen CVCs allow for multiple therapies to be performed through a single venous access site and are commonly used in the critical care environment where vasoactive drugs, fluid therapy, and nutritional support often are infused simultaniously.[3] Dialysis catheters are large bore CVCs used for exchanging blood to and from a haemodialysis machine. They typically have two lumen, one venous and one arterial. The arterial lumen withdraws blood from the patient and carries it to the dialysis machine, while the venous lumen returns the blood to the patient. Introducers are used to direct and place intravascular catheters within a designated blood vessel, for example pulmonary artery (Swan Ganz) catheters or catheters for transvenous cardiac pacing. Peripherally inserted CVCs (PICCs) are long, small gauge catheters inserted via a vein in the upper extremity. They are predominately used for chemotherapy but have in later years also gained popularity for hospitalized patients in the need of prolonged fluid therapy, intravenous antibiotics, and total parenteral nutrition.[31]

When the subcutaneous part (distance between the skin puncture site and vessel puncture site) of the catheter is prolonged, it is called a tunnelled CVC. This technique has been shown to be effective in reducing the number of CVC-related infections when the catheter is inserted via the internal jugular or femoral veins.[32,33] When a tunnelled CVC is attached to a surgically implanted subcutaneous infusion chamber, it is called a totally implanted port (port-a-cath). Tunnelled CVCs and port-a-caths are used when longer duration of chemotherapy or total parental nutrition (>3 months) is indicated, and both types are commonly used in the home setting.

Insertion sites

The three main vascular insertion sites for CVCs are the internal jugular, subclavian and femoral veins.[1,2] Each insertion site has its advantages and disadvantages, and no randomized controlled trials clearly suggest that any of these vessels should be the first choice in all clinical situations.[3] The choice of insertion site thus depends on clinical indication, site availability and operator preference. In adults, an upper body insertion site is generally chosen to minimize the risk of CVC-related infections.[26]

Internal jugular vein

The right internal jugular vein (Figure 2) is the most frequently chosen insertion site for CVCs. It is located relatively superficial on the neck and is therefore easy to visualize with ultrasound and readily accessible.[3] Due to its rather short, straight, and direct pathway to the lower superior vena cava (SVC) and the heart, it is associated with a lower risk of catheter misplacements compared to the left internal jugular and subclavian veins.[34–36] Arterial punctures and hematoma formation are more frequently reported after catheterisation of the internal jugular veins compared to the subclavian veins.[37] Fortunately, the area on the neck is easily compressible in case of accidental puncture of the carotid artery or major bleeding.

Subclavian vein

The subclavian vein (Figure 2) begins at the lateral border of the first rib and arches through the space between the first rib and the clavicle. It joins the internal jugular vein to form the brachiocephalic vein, which then flows into the SVC to the heart. CVC insertion in the subclavian vein is associated with lower rates of central-line associated blood stream infection and thrombosis,[38,39] as well as higher patient comfort compared to the internal jugular and femoral veins. However, subclavian

vein catheterisation is technically more challenging, comes with a higher risk of pneumothorax,[36,38] and in case of a major bleeding or puncture of the subclavian artery, the bleeding site is difficult to compress if the vascular puncture site is located under the clavicle.

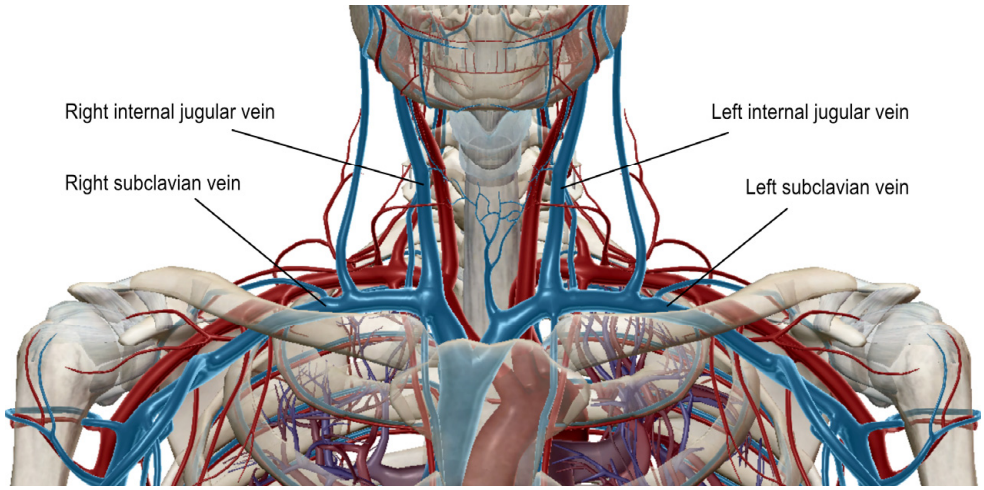

Figure 2
Vessel anatomy. Image courtesy of Visible Body®

Femoral vein

The femoral vein is the major deep vein of the lower extremity. The vessel traverses the thigh, takes a superficial course at the femoral triangle before passing beneath the inguinal ligament into the pelvis as the external iliac vein, which then flows into the inferior vena cava to the heart. The femoral vein is often used when central venous access is not available at the upper body insertion sites and remains a reliable access site under urgent or emergency circumstances. It is also commonly used for the introduction of venous devices (e.g., inferior vena cava filter, iliac venous stent, and various catheters for cardiac electrophysiology studies and interventions). Femoral CVCs are appropriate only for bedridden patients and also associated with higher risk of infectious and thrombotic complications compared to CVCs inserted in the internal jugular and subclavian veins.[38,39] Moreover, accidental puncture of the adjacent femoral artery is not uncommon, especially in the absence of ultrasound guidance (which still appears to be standard practice in most cardiac electrophysiology laboratories).[11,40]

Insertion techniques

CVCs are either inserted with real-time ultrasound guidance,[41] or with a "blind" technique based on anatomical landmarks. Regardless of insertion technique, the skin puncture site should be carefully prepared with a disinfection solution prior to CVC insertion and maximal sterile-barrier precautions, including a mask, a cap, a sterile gown, sterile gloves, and a large sterile drape should be used by the inserting physician.[27,28] After vein puncture with either one of the two insertion techniques, a guidewire is usually inserted through the hollow cannulation needle into the vein. While leaving the guidewire in place, the cannulation needle is removed and the CVC is then inserted over the guidewire into the vein (i.e., the Seldinger technique).[18]

Anatomical landmarks

When using the anatomic landmark technique, CVC placement is based on the knowledge of anatomic structures and palpation of arteries next to the central vein.[3] The technique cannot account for anatomical variations at the insertion site, neither can the presence of venous thrombosis or central vein stenosis be identified prior to catheter insertion. In developing countries where ultrasound is not available in most hospitals, physicians must rely on the landmark-based insertion techniques.[42,43] Moreover, in situations when time is limited, the technique is still considered useful by some physicians although it is associated with a higher risk of mechanical complications compared to real-time ultrasound-guidance.[9–11]

Real-time ultrasound guidance

> *I have lived in my house for 11 years. I know where virtually everything is. I still put the lights on when I need to find something.*
>
> - Dr. Segun Olusanaya, intensivist & ultrasound educator, Twitter, 22 Jan 2021

Ultrasound can be used to visualize anatomic structures, confirm patency of the central vein, help guide the needle towards its target vessel, and verify guidewire/catheters within a vessel.[44] It can also be used for information on guidewire/catheter tip positions and for recognition of complications.[45,46] Since the 1990s, several randomized controlled trials and meta-analyses have demonstrated that the use of real-time ultrasound guidance for CVC insertion increases success rates and decreases the number of mechanical complications compared to the anatomic landmark technique.[9–11,47–49] These clinical benefits in combination with a reduction in access time also contributes to lower health economic costs.[49–52]

Ultrasound guidance for central venous access is thus considered one of the most cost-effective practices for saving time and enhancing the safety of hospitalized patients.[6] However, despite the convincing evidence that exits regarding the clinical use of ultrasound, it has not yet been universally adopted for central venous access and there are still clinicians unwilling/unable to use its full potential for vascular access.[11,53]

Short axis view with out-of-plane needling

The short axis view with out-of-plane needling is the most common approach for internal jugular vein catheterisation.[41] The target vessel is visualized in a transverse plane and its relationship to the adjacent vessels/structures is clearly seen.[54] The needle is placed perpendicular to the ultrasound transducer and only a portion of the needle will be seen as it passes under the transducer.[55] The short axis/out-of-plane approach is usually easier to learn for physicians not familiar with ultrasound,[56] but continuous and accurate visualization of the needle tip is difficult and may therefore result in accidental puncture of the posterior wall of the central vein.[54,57,58]

Long axis view with in-plane needling

In the long-axis view, the target vessel is visualized in a longitudinal plane.[41] The needle is placed in line with and parallel to the ultrasound transducer (ultrasound beam). The entire needle, including the tip, can be continuously visualized during the cannulation procedure, but the relationship of the target vessel to adjacent vessels/structures may be lost.[55] In addition, although needle visualization is improved, the acquisition of the technique is technically more difficult compared to the short axis view with out-of-plane needling.[59]

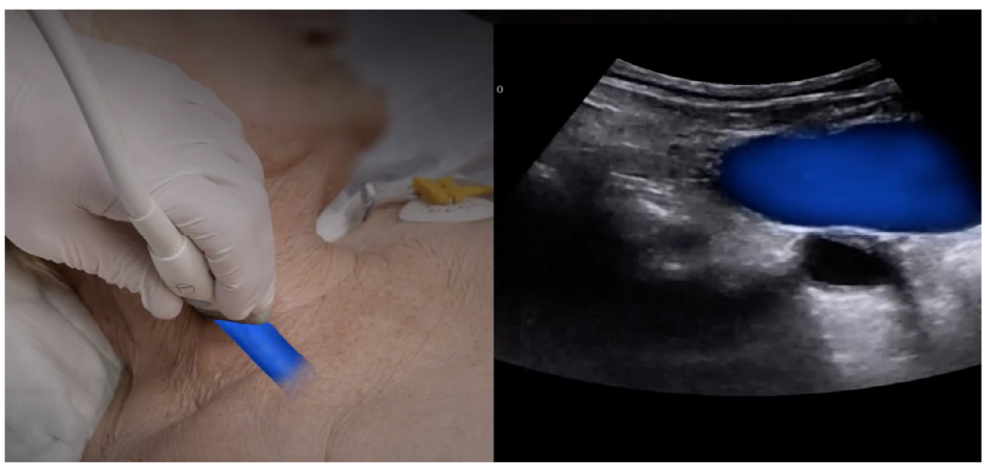

Figure 3
Oblique ultrasound view of the right intenal jugular vein (marked in blue) and the right carotid artery (the black round structure just below). Image courtesy of interanest.org.

Oblique view with in-plane needling

The oblique view (Figure 3) with in-plane needling is an alternative approach for internal jugular vein catheterisation. This technique tries to take advantage of the strengths of both previously described approaches.[54] Oblique visualization provides a longer view of the internal jugular vein along with the carotid artery and with this approach, real-time visualization of the entire needle, including the tip, is possible.[60] Unfortunately, the needle often needs to be directed towards the carotid artery during cannulation.

Ultrasound-guided tip navigation & tip location

Ultrasound can also be used to help the operator in directing the guidewire and/or catheter towards its desired location (i.e., lower SVC or cavoatrial junction). The use of the right supraclavicular fossa ultrasound view for ultrasound-guided tip navigation has been demonstrated for CVC insertions in the right internal jugular vein[61] and in the right subclavian vein with a supraclavicular approach,[62] but not for right infraclavicular subclavian vein catheterisation, which probably is the preferred approach in adult patients.

Transthoracic echocardiography (TTE) is an alternative for ultrasound-based tip location. The subcostal TTE window allows for visualization of the lower SVC, inferior vena cava, cavoatrial junction and the right atrium, and can thus be used to verify the guidewire and/or catheter tip in any of these locations.[63] Disadvantages of TTE are that the upper SVC cannot be visualized, two different ultrasound transducers are needed and consequently usually a second operator, and it may be of no use when trying to reposition a guidewire (it is not possible to see if the guidewire is in the right internal jugular vein or in the left brachiocephalic vein).

Mechanical complications

Like all invasive procedures, central venous catheterisation is associated with procedural complications, commonly called mechanical complications.[37] They include bleedings, cardiac arrhythmias, arterial puncture, arterial catheterisation, pneumothorax/haemothorax, nerve injury, failed catheterisation, and catheter tip malposition.[5,7] Severity and frequencies vary but considering the high numbers of CVCs that are inserted each year, even rare but serious mechanical complications contribute to significant patient suffering and health economic costs.[24,50] Efforts to minimize and prevent their occurrence should therefore be a routine element of quality improvement programs.

There is considerable variation in reported rates of mechanical complications after CVC insertion with incidences ranging from 1.1 to 34%.[35,39,42,43,64–67] Plausible reasons for this variation are differences in definition, cohort, case mix, insertion

techniques and bias in the collection of data in retrospective studies. The majority of the studies were conducted prior to the global implementation of ultrasound guidance and no systematic multicentre data on incidence and risks factors for mechanical complications after ultrasound-guided central venous catheterisation have yet been published.

Identified risk factors for mechanical complications also vary between studies. Both patient-related and physician-related variables have been reported as independent risk factors. Suggested patient-related risk factors are age, sex, body mass index (BMI), coagulopathy, and positive pressure ventilation.[7,12,35,64,66] Examples of physician-related risk factors are level of training, choice of insertion technique, insertion during the night, and number of insertion attempts.[12,35,39,68] Results from previous studies are partly diverging though – male patient sex has for example been shown to be associated with both higher and lower risk of mechanical complications.[35,65] Moreover, the various insertion sites are associated with different mechanical complications[37,38] and the catheter-related variable bore size has been reported as an independent risk factor for bleeding.[69] Given the wide variety of mechanical complications and suggested predictors, risk stratification and further quality improvements of central venous catheterisation are challenging. At present, the strongest known independent risk factor for major mechanical complications is increasing number of unsuccessful insertion attempts.[12,35,42,43,64,66] However, this variable has primarily been analysed in studies where the anatomic landmark technique was used for most of the catheter insertions. To enable better prediction of the occurrence of serious adverse events in the ultrasound-guided era, new studies designed to identify possible risk factors for mechanical complications after ultrasound-guided central venous catheterisation are needed.

According to national and international guidelines, it is recommended that every hospital department responsible for central venous catheterisation continuously records and monitors relevant clinical data associated with CVC insertions, including complications rates.[26–28,70] Unfortunately, such recording and monitoring has been lacking at the hospitals within Region Skåne, Sweden.[64] Further, a cross-sectional study from 2012, in which most of the anaesthesia and intensive care clinics in Sweden participated, found that just under half (45%) of the clinics could state the annual frequency of CVC-associated pneumothoraces, less than half (38%) were able to indicate the annual incidence of serious vascular complications, and slightly more than half (51%) knew the number of CVC-related infections diagnosed per year.[71] The expert consensus guideline on safe vascular access by the Association of Anaesthetists of Great Britain and Ireland (published 2016) also identified a lack of precise data regarding the incidence of procedural complications that occur in conjunction with CVC insertions.[24] As knowledge about complication rates and risk factors for mechanical complications is a prerequisite for improving the overall quality of the procedure, efforts to enhance documentation and follow-up of CVC insertions should be made.

CVC-associated infectious complications are usually monitored by quality improvement programs and their impact on patient outcomes has been well reported in the literature.[72,73] Unfortunately, far less is known about the potential impact of mechanical complications. Although most of the major mechanical complications may require urgent medical treatment, sometimes invasive interventions, and usually prolonged observation of the patient, there is no firm data on increased patient mortality or prolonged hospital stay.[5] Only significantly longer ICU-stay has been reported.[7] Nevertheless, even though CVC-associated mechanical complications seldom are lethal, they are not without clinical significance and deserves more attention.

Catheter tip malposition

The preferred CVC tip position is the in the lower third of the SVC or at the cavoatrial junction.[24] This position is believed to minimise the risk of complications during clinical use such as vascular perforation, local venous thrombosis, and catheter dysfunction.[74–76] Correct CVC tip positioning is therefore particularly important when the catheter is intended for infusion of local irritant drugs like chemotherapy, high flow infusions, measurement of central venous pressure or long-term use.

Catheter tip malposition is the only mechanical complication that has not been shown to decrease significantly when ultrasound is used to guide the cannulation of the central vein.[48] It occurs more frequently after CVC insertions in the subclavian veins compared to the internal jugular veins,[77] and the highest reported incidence is for the right subclavian vein.[34,35] Intracavitary ECG is the preferred method for intraprocedural assessment of the proper CVC tip location according to current guidelines,[78] but this method requires appropriate modifications of the basic technique in patients with atrial fibrillation and is not applicable in patients with a pacemaker or with other arrhythmias.[79] Furthermore, it cannot be used to aid repositioning manoeuvres of misplaced guidewires. The use of ultrasound to aid guidewire and catheter tip positioning is likely more appealing in many departments due to the greater availability of ultrasound. However, ultrasound-guided tip navigation and tip location during central venous catheterisation is not yet as well-studied as intracavitary ECG.

Aims

The general aim of this thesis was to explore various aspects of ultrasound-guided central venous catheterisation and associated mechanical complications in order to enable future quality improvements of the procedure.

Papers I & II

To determine the incidence of mechanical complications within 24 hours after central venous catheterisation and to identify associated risk factors in hospitals where real-time ultrasound guidance is clinical practice for central venous access.

Paper III

To evaluate the usefulness of a micro-convex probe and the right supraclavicular fossa ultrasound view to aid guidewire positioning in right infraclavicular subclavian vein catheterisation.

Paper IV

To determine the minimal guidewire length required to avoid guidewire retraction, thereby maintaining a guidewire tip position in the lower segment of the superior vena cava throughout an ultrasound-guided infraclavicular CVC placement in the right subclavian vein.

Paper V

To estimate the effect of an implementation package on the documentation of central venous catheter insertions by assessing the proportion of clinically relevant missing data before and after the introduction of the implementation package.

Methods

Papers I & II

We performed a prospective, controlled, multicentre, observational cohort study. Prior to performing the study, we published a peer-reviewed protocol where all outcomes, independent variables, and statistical analyses were pre-specified.[80]

All recorded CVC insertions in patients ≥16 years at four emergency care hospitals in Region Skåne, Sweden from 2nd of March 2019 to 31st of December 2020 were considered eligible for inclusion. CVC insertions with missing insertion date, patients with fictitious social security number and arterial catheters accidentally recorded as CVC insertions were excluded. The participating hospitals followed the same clinical guidelines for CVC placement, based on national recommendations,[27] and they all used the same electronic health record (EHR) system (Melior™, Cerner Corporation, North Kansas City, Missouri, USA) where each CVC insertion was recorded according to a specific CVC insertion form. A dedicated collaborator at each study site reviewed all registered CVC insertion forms during the study period, thereby enabling operators to correct missing or incorrect values. The collaborator also examined medical records and chest X-rays for each patient with respect to mechanical complications that occurred within 24 hours after the CVC insertion. All complications hence identified and not previously documented in the CVC insertion form were recorded in separate files.

An independent IT-technician extracted the predefined data points included in the CVC insertion forms and patient characteristics (age, height, weight, results on routine coagulation tests) from the EHR and exported all data to Microsoft Excel V.2013 (Microsoft, Redmond, Washington, USA). Information on operator characteristics, collected by the responsible researcher at each study site, as well as the mechanical complications recorded in separate files by the dedicated collaborators, were manually added to the main Excel file, which then was used for all statistical analyses. The primary outcome measures were mechanical complications defined as bleeding, cardiac arrhythmia, arterial puncture, arterial catheterisation, nerve injury, pneumothorax, failed catheterisation, and catheter tip malposition. All primary outcome measures and their classifications are presented in Table 1. The independent variables are presented in Table 2.

Table 1. Primary outcome measures

Minor mechanical complication	Major mechanical complication
Bleeding grade 2[a]	Bleeding grades 3–4[b]
Cardiac arrhythmia grades 1–2[c]	Cardiac arrhythmia grades 3–4[d]
Arterial puncture	Arterial catheterisation
Non-persistent nerve injury[e]	Persistent nerve injury[f]
Failed catheterisation	Pneumothorax
Catheter tip malposition[g]	

[a]Bleeding requiring external compression, [b]bleeding/haemothorax requiring invasive intervention and/or blood transfusion and bleeding with life-threatening consequences, [c]asymptomatic, self-limiting, or symptomatic arrhythmia requiring non-urgent medical intervention, [d]symptomatic or life-threatening arrhythmia requiring urgent medical intervention, [e]nerve injury with clinical signs persisting <72 h, [f]nerve injury with clinical signs persisting >72 h, [g]catheter tip not in the lower superior vena cava, at the cavoatrial junction, in the proximal superior vena cava (when aligned with the vessel) or in the upper part of the right atrium.

Table 2. Independent variables

Patient age
Patient sex
Patient BMI
Coagulopathy[a]
Positive pressure ventilation
Insertion by night[b]
Insertion site[c]
Operator handedness
Operator gender
Operator experience[d]
Use of ultrasound
Number of punctures[f]
Catheter bore-size

[a]Prothrombin time/INR >1.8, activated partial thromboplastin time >1.3 × normal value (>43 s) or platelet count $<50\times10^9$/L, [b]between 21:00 and 07:00, [c]internal jugular vein dx/sin, external jugular vein dx/sin, subclavian vein dx/sin and and femoral vein dx/sin, [d]<100 or ≥100 individual CVC insertions, [f]skin and vessel punctures respecively.

Statistics

A statistician performed the sample size calculation, which according to previous data was based on an estimation of the incidence of major mechanical complications to be 1%.[12,35,38,39,64] To achieve a narrow 95% confidence interval (CI) of 0.6 to 1.4% of the incidence of major mechanical complications, the necessary sample size was calculated to 10 029 insertions using the exact Clopper-Pearson binomial CI method. A detailed statistical analysis plan was defined prior to assessing the data. Multivariable logistic regression was used as main analysis to determine associations between independent variables and mechanical complications. Separate multivariable logistic regressions were performed for minor mechanical complication, major mechanical complication, and pneumothorax. The number of events per outcome measure determined the number of the independent variables to be included in each multivariable logistic regression model. When less than eight events per variable were identified, independent variables were excluded, starting with the least important one as determined by univariable logistic regression analyses.

All statistical analyses were performed with RStudio, version 1.2.5019 (© 2009-2019 RStudio, Inc). Primary outcome measures are presented as number and percentage per vascular insertion site. Results from the multivariable logistic regression analyses are reported as odds ratio (OR) with 95% CI. A p-value <0.05 was considered statistically significant.

Sensitivity analyses

To exclude patient characteristics posing a bias, subsample sensitivity analyses that included only one selected CVC insertion per patient (based on worst case-selection or randomly selected if no complications occurred) were performed, as well as sensitivity analyses excluding patients with more than one CVC inserted in the same vein at the same time (i.e., cardiac surgery patients). Finally, comparison of differences in complication rates between the participating hospitals was performed using chi-square test.

Paper III

We performed a prospective single-centre observational study. The study was conducted at Skåne University Hospital in Lund/Malmö, Sweden and we collected data from January to October 2019. Patients ≥18 years with an indication for CVC placement and under the care of one of three intensivists responsible for the study were consecutively included. A preprocedural ultrasound scan of the right subclavian vein was performed on all patients eligible for inclusion. Patients were excluded if they already had a central line/pacemaker/similar device in place (due to risk for misinterpretation of the ultrasound image in those patients), if the right subclavian vein could not be visualized (e.g., in those with subcutaneous emphysema of the chest wall), or if the right subclavian vein was deemed inappropriate for cannulation (thrombosis within the vessel, tumour compressing the vessel or narrow vessel due to hypovolaemia in combination with severe respiratory insufficiency).

The catheterisations were performed with real-time ultrasound guidance using a micro-convex probe. A long-axis, infraclavicular approach with an in-plane needling technique was used for all vein punctures. Following insertion of approximately 20 cm of the guidewire into the vein, the probe was placed on the neck and the right internal jugular vein was scanned to exclude cranial malposition of the guidewire. The probe was then shifted to the right supraclavicular fossa and tilted in a caudal direction to obtain a view of the guidewire within the SVC and exclude malposition of the guidewire in the left brachiocephalic vein (Figure 4). Repositioning-attempts of malpositioned guidewires were performed under real-time ultrasound guidance via the right supraclavicular fossa view. After confirmation of correct guidewire J-tip position in the lower SVC, the CVC

insertion was performed using the Seldinger technique. As a safety measure, the presence of lung sliding was verified with post-procedural lung ultrasound in difficult cases. An instructional video produced by three of the authors, including the full catheterisation procedure and confirmation of a correct guidewire J-tip position in the lower SVC via the right supraclavicular fossa ultrasound view, can be viewed at https://youtu.be/DyeLjNF-PtA.

A post-procedural chest X-ray was obtained in all patients and interpreted by a radiologist unaware of the study. A CVC tip position anywhere within the lower SVC or at the cavoatrial junction was considered optimal, whereas a tip location within the upper part of the right atrium or in the proximal SVC (when aligned with the vessel) was considered acceptable. All other CVC tip positions were considered to be misplaced. The primary outcome measure was the incidence of CVC misplacements, and our hypothesis was that when using the ultrasound method described, the incidence of CVC misplacements could be reduced to 1%.

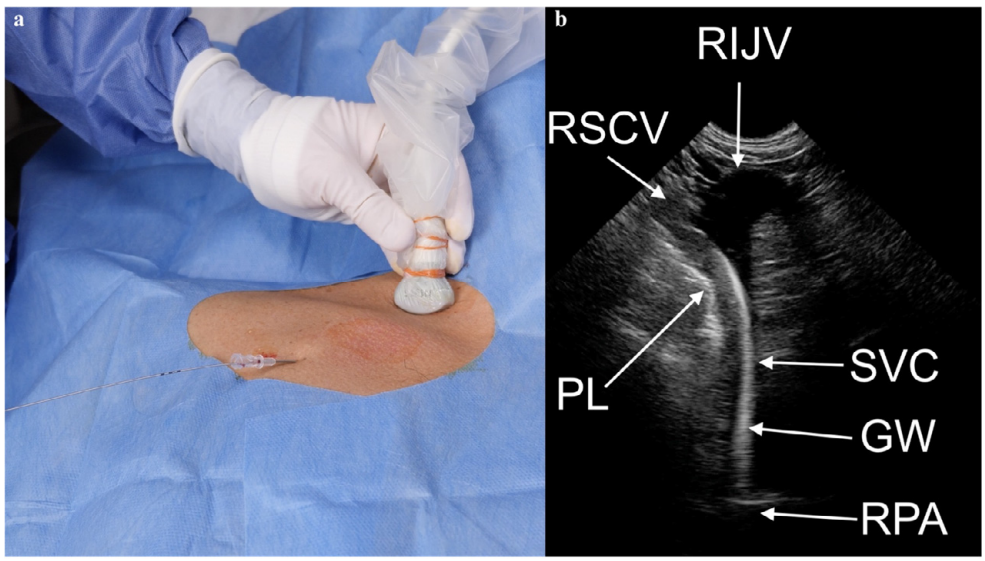

Figure 4. The right supraclavicular fossa ultrasound view
(a) Infraclavicular cannulation of the right subclavian vein, an inserted guidewire and a micro-convex probe placed just above the medial part of the clavicle in the right supraclavicular fossa; (b) The guidewire clearly visualised within the superior vena cava. RIJV, right internal jugular vein; RSCV, right subclavian vein; PL, pleural line; SVC, superior vena cava; GW, guidewire; RPA, right pulmonary artery.

Statistics

We performed a sample size calculation using the sample size calculator at https://clincalc.com/Stats/SampleSize.aspx. After summarizing the results of seven previous studies,[34,35,48,63,77,81,82] the mean incidence of CVC misplacements after catheterisation of the subclavian vein was estimated to be 7.1%. Based on the assumption of an incidence of CVC misplacements of 1% in the study cohort and a

historical control population incidence of 7.1%, the sample size calculation showed that 93 patients were required to detect this difference with an α of 0.05 and power of 80%.

Paper IV

We performed a retrospective consecutive case series. The study population was selected among patients admitted to the ICU at Skåne University Hospital in Lund, Sweden. All patients ≥18 years who had a computed tomography (CT) scan with intravenous contrast of diagnostic quality with a protocol covering the chest performed during the ICU-stay or up to 6 months prior to the ICU admittance were included from January 2019 and backwards. Patients who did not have their arms positioned above the head during the CT scan and patients with body height above the 95th percentile for the Swedish population (>177 cm for women and >190 cm for men) were excluded. CT scans in which the right subclavian/axillary vein, the junction of the right and left brachiocephalic veins or the SVC could not be visualized accurately, and CT scans with technical issues were excluded. When the a priori decided number of 50 women and 50 men was reached, the backward inclusion ended in June 2017.

A radiologist performed the image reconstructions and vessel measurements. Using thin-sliced images (<1 mm), multiplanar reconstructions were made with the Advanced Vessel Analysis (AVA) application in the Philips IntelliSpacePortal (ISP). A point in the right subclavian/axillary vein cranial to the superior medial border of the 2nd rib was defined as the most plausible distal puncture site. The distance from this point to the junction of the brachiocephalic veins was calculated by the AVA application of the Philips ISP and defined as distance 1 (Figure 5a). The optimal guidewire tip position was defined in the lower segment of the SVC and the upper level of the right pulmonary artery (RPA) was used as the corresponding CT landmark for this position. The distance from the junction of the brachiocephalic veins to the optimal guidewire tip position was measured in the coronal view of the CT scan and defined as distance 2 (Figure 5b). The total distance from the most plausible distal puncture site of the right subclavian/axillary vein to the optimal guidewire tip position in the SVC (distance 1 + distance 2) was then calculated and defined as “vessel length” (Figure 5). In addition, measurements of equipment provided in eleven commonly used 15–16 cm CVC kits were performed.

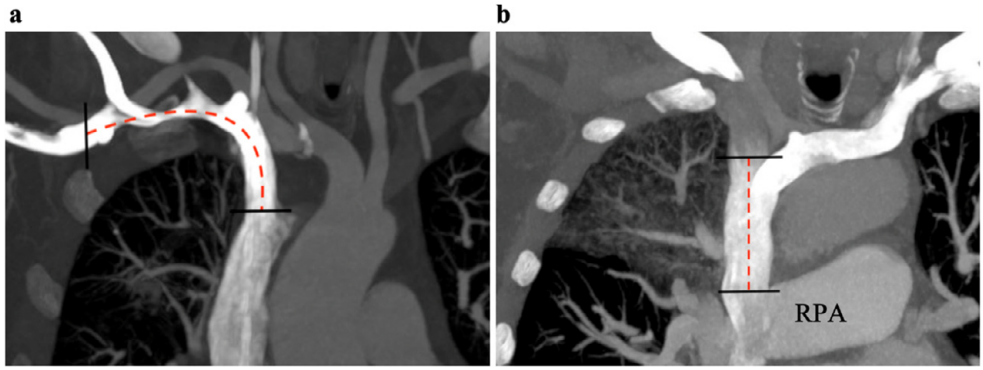

Figure 5
Coronal view of the CT scans showing measurements of the vessel length: (a) distance 1 = the distance from the most plausible distal puncture site of the right subclavian/axillary vein to the junction of the brachiocephalic veins and (b) distance 2 = the distance from the junction of the brachiocephalic veins to the level in the superior vena cava where the upper border of the right pulmonary artery (RPA) crosses. Vessel length = distance 1 + distance 2.

To estimate the minimal guidewire length required to avoid guidewire retraction during right subclavian vein catheterisation for each CVC kit, the sum of the following distances was calculated: (A) The 95th percentile of the vessel length, (B) the length of the steel cannula that can be inserted into the patient (corresponding to the maximum distance from the skin puncture site to the vessel puncture site), (C) the entire length of the distal lumen of the CVC, (D) 10 mm (corresponding to the part of the guidewire that must extend from the CVC before CVC insertion).

Statistics

To determine if the measurements were normally distributed and symmetrical, the value of the mean and median of the vessel length were compared and skewness-test was performed. Further subgroup analyses were performed for men and women, respectively. Independent t-test was used to determine if there was a significant difference in mean vessel length between men and women. Linear regression analysis was performed to determine correlation between patient's body height and the measured vessel length. All statistical analyses were performed with RStudio, version 1.2.5019 (© 2009-2019 RStudio, Inc). A p-value <0.05 was considered significant.

Paper V

We introduced an implementation package in March 2019 with the purpose to decrease the proportion of missing data in registered CVC insertion forms in the common EHR system used by the hospitals within Region Skåne, Sweden. The implementation package included an updated CVC insertion form in the common

EHR system that all CVC-responsible physicians at the participating hospitals had agreed on, adoption of new local directions for CVC placements in combination with delegated responsibility for each CVC-responsible physician to inform all personnel affected by the changes at their own department, and a continuous review of all registered CVC insertion forms including a reminder to the inserting physician to supplement missing data. A year after the introduction of the implementation package, we performed a retrospective observational study. Data from all documented CVC insertions on patients ≥16 years between 3rd of March 2019 and 2nd of March 2020 at eight hospitals in Region Skåne, Sweden were extracted using an automated script and exported to Microsoft Excel. The primary outcome was the number of terms with missing data for 13 predefined variables in the CVC insertion form. The secondary outcome was to compare the proportion of missing data for three specific terms in the CVC insertion form (vascular insertion site, catheter bore size/number of lumens and number of skin punctures) with the results from a previous similar study in the same health care system performed prior to the introduction of the implementation package.[64] In that study, the three specific terms were responsible for all the missing data.

Statistics

If all 13 predefined terms were without missing data, the CVC insertion form was considered complete. The ratio of missing terms per CVC insertion form for each individual CVC inserting physician was calculated and cases with a ratio greater than one were noted. Chi-square test was used to determine differences between the observed frequencies of missing data. P-values were not adjusted for multiple comparisons since the number of tests were limited. Microsoft Excel 2013 and MedCal (Online version, Medcal Software Ltd, Ostend, Belgium) were used for the statistical analyses.

Ethical considerations

The studies included in this thesis are patient-centred clinical research and they were all approved by the Swedish Ethical Review Authority in Lund, Sweden prior to study start. The main focuses were to not expose the study participants to unnecessary risks, to handle their personal data in a correct and safe manner, and to ensure that information about the studies, as well as contact information to the responsible researchers, was readily available. Moreover, the researchers involved in the different studies were well aware that the processing of sensitive personal data entailed an invasion of privacy of the study participants.

All data in study II was prospectively collected according to clinical practice, retrospectively extracted, and deidentified prior to analysis. The CVC insertions were performed on strict clinical indications and documented in the EHR according

to normal routine. As the study was an observation of current clinical practice and did not entail increased risk for the included patients, the Ethical Review Authority waived the requirement for written informed consent. The consent principle was met via "opt-out" where the participants could request withdrawal via e-mail or telephone contact. Advertisements with contact information to the responsible researchers were available at all study sites. The main ethical risk was considered the processing of personal sensitive data, which therefore was coded prior to analysis and treated in strict confidence. Study III was no actual intervention but rather an observation of an ultrasound method that has been used in clinical practice in the recent years. All the included CVC insertions were performed on strict clinical indications and written informed consent was obtained from all study participants. Study IV and V were retrospective observational studies, entailed no risk for the included patients, and there was no requirement for written informed consent. All personal data were deidentified prior to analysis and the results were reported at group level.

Results

Papers I & II

A total of 14 071 CVC insertions were assessed for eligibility in the study. After the exclusion criteria had been applied, we included and analysed 12 667 CVC insertions in 8 586 patients performed by 281 individual operators. Mechanical complications occurred in 978 (7.7% [95% CI 7.2 – 8.2]) of all CVC insertions – some insertions had more than one complication. 48 (0.4% [0.3 – 0.5]) of the CVC insertions were associated with major mechanical complications. Bleeding grade 2, catheter tip malposition and arterial puncture were the most common minor mechanical complications. Pneumothorax and arterial catheterisation were the most common major mechanical complications. All primary outcome measures are reported in detail per vascular access site in Table 3.

The results from the multivariable logistic regression analyses are presented in Tables 4–6. We chose to exclude the complication "catheter tip malposition" in the model for minor mechanical complication as it is probably not related to the cannulation procedure but rather to vessel anatomy, patient habitus or the length of the catheter. CVC insertions with "catheter tip malposition" as sole complication were therefore considered without mechanical complication in the statistical analyses. We also chose to exclude the variable "operator handedness" since it had 10% missing data, introduced a bad goodness of fit and contributed to less power in the model for minor mechanical complication. The five independent variables included in the model for major mechanical complication were those with significant association in univariable logistic regression analyses. The two independent variables included in the model for pneumothorax were the most important ones as determined by univariable logistic regression analyses.

In summary, we found that limited operator experience, increasing number of skin/vessel punctures, and CVC bore size ≥9 French were associated with higher risk of minor mechanical complication, whereas patient BMI <20 kg/m^2, positive pressure ventilation, CVC insertion in the right subclavian vein and the use of ultrasound guidance were associated with lower risk of minor mechanical complication (Table 4). Regarding major mechanical complication, the following variables were associated with higher risk: patient BMI <20 kg/m^2, male operator gender, limited operator experience and increasing number of skin punctures (Table 5). We also found that subclavian vein catheterisation was associated with a higher

risk of pneumothorax compared to internal jugular vein catheterisation, despite real-time ultrasound guidance being standard of care (Table 6).

Sensitivity analyses

The sensitivity analyses showed most similar results in the multivariable logistic regression analyses for major mechanical complication. Concerning minor complication, the model including only one selected CVC insertion per patient showed similar results except that all insertion sites besides the subclavian veins were associated with higher risk of minor mechanical complication compared to the right internal jugular vein, and that ultrasound guidance was not associated with lower risk of minor mechanical complication. The model excluding patients with more than one CVC inserted in the same vein at the same time also showed similar results except that coagulopathy was associated with higher risk of minor mechanical complication, and that ultrasound guidance was not associated with lower risk of minor mechanical complication. Finally, chi-square test showed no difference in complication rates between Lund hospital (where 58% of all insertions were performed) and the other participating hospitals (p=0.1866).

Table 3. Mechanical complications per vascuar insertion site

	Right internal jugular vein n=9 118	Left internal jugular vein n=1 346	Right subclavian vein n=1 256	Left subclavian vein n=346	Right femoral vein n=161	Left femoral vein n=76	Right external jugular vein n=68	Left external jugular vein n=17	Missing data n=279	Total
Minor complications, n (%)	**579 (6.4)**	**228 (17)**	**149 (12)**	**49 (14)**	**19 (12)**	**11 (14)**	**12 (18)**	**5 (29)**	-	**1052**[h]
Failed catheterisation	38 (0.4)	27 (2.0)	20 (1.6)	3 (0.9)	1 (0.6)	3 (3.9)	1 (1.5)	1 (5.9)	-	94
Bleeding grade 2[a]	277 (3.0)	73 (5.4)	26 (2.1)	12 (3.5)	15 (9.3)	8 (11)	6 (8.8)	2 (12)	-	419
Arrhythmia grades 1–2[b]	50 (0.5)	6 (0.4)	4 (0.3)	4 (1.2)	-	-	-	-	-	64
Arterial puncture	67 (0.7)	24 (1.8)	15 (1.2)	7 (2.0)	3 (1.9)	-	2 (2.9)	-	-	118
Non-persistent nerve injury[c]	-	-	-	-	-	-	-	-	-	-
Catheter tip malposition[d]	147 (1.6)	98 (7.3)	84 (6.7)	23 (6.6)	-	-	3 (4.4)	2 (12)	-	357
Major complications, n (%)	**33 (0.3)**	**2 (0.1)**	**8 (0.6)**	**4 (1.2)**	**4 (1.9)**	-	-	-	-	**51**[i]
Bleeding grades 3–4[e]	7 (0.1)	-	-	1 (0.3)	1(0.6)	-	-	-	-	9
Arrhythmia grades 3–4[f]	7 (0.1)	1 (0.1)	1 (0.1)	-	-	-	-	-	-	9
Arterial catheterisation	12 (0.1)	-	-	-	3 (1.9)	-	-	-	-	15
Pneumothorax	6 (0.1)	1 (0.1)	7 (0.6)	3 (0.9)	-	-	-	-	-	17
Persistent nerve injury[g]	1 (0.01)	-	-	-	-	-	-	-	-	1

[a]Bleeding requiring external compression, [b]asymptomatic, self-limiting, or symptomatic arrhythmia requiring non-urgent medical intervention, [c]nerve injury with clinical signs persisting <72 h, [d]catheter tip not in the lower superior vena cava, at the cavoatrial junction, in the proximal superior vena cava (when aligned with the vessel) or in the upper part of the right atrium, [e]bleeding requiring invasive intervention, blood transfusion or with life-threatening consequences, [f]symptomatic or life-threatening arrhythmia requiring urgent medical intervention, [g]nerve injury with clinical signs persisting >72 h, [h]some insertions were associated with more than one minor mechanical complication, [i]some insertions were associated with more than one major mechanical complication.

Table 4. Multivariable regression analysis for minor mechanical complication

	Minor mechanical complication		
Independent variables	*Odds Ratios*	*95% CI*	*p*
Male patient sex	0.92	0.76 – 1.13	0.425
Patient age	1.00	0.99 – 1.01	0.939
Patient BMI <20[1]	**0.55**	0.35 – 0.84	**0.008**
Patient BMI >30[1]	0.90	0.72 – 1.12	0.359
Coagulopathy[2]	1.22	0.94 – 1.57	0.125
Positive pressure ventilation	**0.67**	0.55 – 0.83	**<0.001**
Insertion by night[3]	1.15	0.86 – 1.53	0.333
Left internal jugular vein catheterisation[4]	1.28	0.97 – 1.66	0.077
Right subclavian vein catheterisation[4]	**0.51**	0.34 – 0.75	**0.001**
Left subclavian vein catheterisation[4]	0.80	0.45 – 1.33	0.416
Right femoral vein catheterisation[4]	1.18	0.58 – 2.20	0.628
Left femoral vein catheterisation[4]	1.19	0.45 – 2.76	0.703
Male operator gender	0.94	0.77 – 1.15	0.520
Limited operator experience [<100][5]	**1.80**	1.43 – 2.26	**<0.001**
Ultrasound guidance	**0.51**	0.31 – 0.91	**0.015**
Number of skin punctures	**1.90**	1.66 – 2.16	**<0.001**
Number of vessel punctures	**1.53**	1.30 – 1.80	**<0.001**
CVC bore size [≥9 Fr]	**2.04**	1.62 – 2.56	**<0.001**
Observations	10 817		
Hosmer-Lemeshow Goodness of fit	p>0.05		

[1]Compared to patients with BMI 20–30 kg/m^2, [2]prothrombin time/INR >1.8, activated partial thromboplastin time >1.3 × normal value (>43 s) or platelet count <50 × 10^9/L, [3]between 21:00 and 07:00, [4]compared to right internal jugular vein catheterisation (standard insertion site at the participating hospitals), [5]compared to operators with ≥100 individual CVC insertions at the beginning of the study period.

Table 5. Multivariable regression analysis for major mechanical complication

	Major mechanical complication		
Independent variables	*Odds Ratios*	*95% CI*	*p*
Patient BMI <20[1]	**2.63**	1.20 – 5.32	**0.010**
Patient BMI >30[1]	0.77	0.34 – 1.57	0.488
Positive pressure ventilation	0.75	0.41 – 1.35	0.330
Male operator gender	**2.65**	1.36 – 5.57	**0.007**
Limited operator experience [<100][2]	**3.12**	1.71 – 5.60	**<0.001**
Number of skin punctures	**2.11**	1.58 – 2.72	**<0.001**
Observations	10 634		
Hosmer-Lemeshow Goodness of fit	Not performed (small number of events)		

[1]Compared to patients with BMI 20–30 kg/m^2, [2]compared to operators with ≥100 individual CVC insertions at the beginning of the study period.

Table 6. Multivariable regression analysis for pneumothorax

	Pneumothorax		
Independent variables	*Odds Ratios*	*95% CI*	*p*
Subclavian vein catheterisation[1]	**6.09**	2.15 – 18.15	**0.001**
Limited operator experience [<100][2]	**3.43**	1.21 – 10.23	**0.022**
Observations	10 875		
Hosmer-Lemeshow Goodness of fit	Not performed (small number of events)		

[1]Compered to internal jugular vein catheterisation, [2]Compared to operators with ≥100 individual CVC insertions at the beginning of the study period.

Paper III

A total of 137 patients were considered eligible for inclusion. We excluded 18 due to a central line/pacemaker/similar device already in place. A further 16 were excluded as we deemed the right subclavian vein to be inappropriate to cannulate. The remaining 103 patients were included in the study.

Successful puncture of the right axillary/subclavian vein was achieved in all patients. We were able to visualize the SVC from the right supraclavicular fossa ultrasound view in all but three patients: one patient had a BMI 60 kg/m^2 in combination with a very short neck, which made it impossible to angle the ultrasound probe to obtain a proper view of the SVC; two patients were agitated and could not cooperate properly to allow for adequate visualization of the SVC. Although the described ultrasound method for guidewire positioning was not possible to use in these three patients, we included them in the primary intention to treat analysis.

The guidewire J-tip was initially misplaced in 15 patients into either the ipsilateral jugular vein (n=8) or the left brachiocephalic vein (n=7). In 12 patients it was possible to adjust the guidewire J-tip to a correct position in the lower SVC using real-time ultrasound guidance via the right supraclavicular fossa view, whereas it was impossible in two patients. In one patient, a misplaced guidewire in the left brachiocephalic vein was not detected at the time of insertion as the SVC was impossible to visualize from the right supraclavicular fossa ultrasound view. All initial guidewire tip positions, numbers of successful repositioning manoeuvres, and final CVC tip positions are summarized in Figure 6.

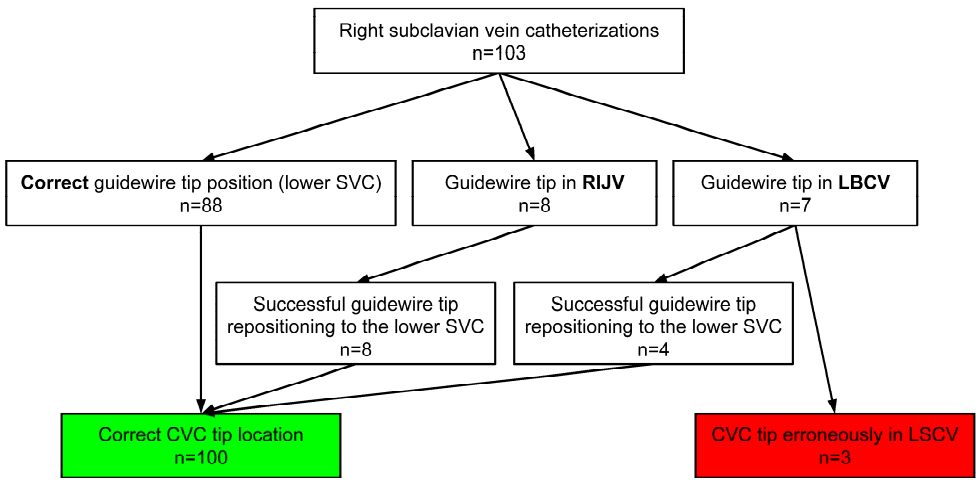

Figure 6
Initial guidewire positions, successful repositioning manoeuvres, and final CVC tip positions. SVC, superior vena cava; RIJV, right internal jugular vein; LBCV, left brachiocephalic vein; LSCV, left subclavian vein.

Post-procedural chest X-ray confirmed correct CVC tip position in 100 patients and CVC misplacement with the CVC tip in the left subclavian vein in three patients, corresponding to a CVC misplacement incidence (95% CI) of 2.9 (0.6 – 8.3) %. All the final ultrasound-determined guidewire tip positions were consistent with the chest X-ray-determined definitive CVC tip positions. There were no mechanical complications (defined as bleeding requiring intervention; arterial puncture; arterial catheterisation; pneumothorax; and persisting cardiac arrhythmia).

Paper IV

We screened a total of 144 ICU-patients who had performed a CT scan covering the chest with intravenous contrast. After excluding patients with erroneous arm-position (one or both arms placed along the body during the CT scan) and patients with CT scans that had either poor image quality in the areas of interest or technical issues when using the AVA application, 100 patients (50 men and 50 women) remained and were included in the study. Mean (SD) body height was 177 (5.9) cm for men and 163 (5.9) cm for women. Independent t-test showed significant difference in mean body height between men and women ($p<0.001$).

The data from the vessel measurements were normally distributed. The mean (SD) vessel length, defined as the distance between the most plausible distal puncture site of the right subclavian/axillary vein to the optimal guidewire tip position in the lower SVC (Figure 5, Methods section), was 130 (16.3) mm for men, 126 (15.1) mm for women and 128 (15.7) mm for all patients (n=100). Independent t-test showed no difference in mean vessel length between men and women ($p=0.23$). The 95th percentile of the vessel length was 153 mm for all patients (n=100). Linear regression analyses showed no correlation between patient body height and the measured vessel length for men ($R^2=0.03$, $p=0.13$), whereas there was a weak correlation for women ($R^2=0.09$, $p=0.02$).

By adding the distances A–D defined in the Methods section and reported in Table 7, we calculated the required minimal guidewire length for each of the included 15–16 cm CVC kits. We also noted the discrepancy between the length of the guidewire provided in the CVC kit and the calculated minimal guidewire length. In summary, we found that eight of the eleven investigated commercial 15–16 cm CVC kits contained guidewires that were up to 108 mm too short for an US-guided infraclavicular CVC placement in the right subclavian vein. The results from the CVC kit measurements and the calculated minimal guidewire lengths are summarized in Table 7.

Tablel 7. CVC kits measurements and the calculated minimal guidewire length

Manufacturer	Model	Nr. of lumens	CVC length[1] (mm)	Steel cannula length[2] (mm)	Actual guidewire length[3] (mm)	Minimal guidewire length[4] (mm)	Discrepancy (mm)[5]
Arrow	Blue FlexTip 16 cm, 7 Fr	2	298	63	590	524	66
Arrow	Blue FlexTip 16 cm, 9.5 Fr	5	312	63	590	538	52
Bactiguard	BIP CVC 16 cm, 7 Fr	2	298	70	440	531	-91
Bactiguard	BIP CVC 16 cm, 7 Fr	3	298	70	440	531	-91
Bactiguard	BIP CVC 16 cm, 8.5 Fr	4	307	70	440	540	-100
B Braun	Certofix V715 15 cm, 7 Fr	3	302	73	495	538	-43
B Braun	Certofix HF 15 cm, 12 Fr	3	310	73	495	546	-51
Cook Medical	Spectrum 15 cm, 10 Fr	5	280	70	595	513	82
Merit Medical	Careflow 15 cm, 7 Fr	2	305	70	445	538	-93
Merit Medical	Careflow 15 cm, 7 Fr	3	320	70	445	553	-108
Merit Medical	Careflow 15 cm, 9.5 Fr	5	315	70	445	548	-103

[1]The entire length of the distal lumen of the CVC, [2]the length of the steel cannula that can be inserted into the patient, [3]the length of the guidewire from the proximal end to the bottom/curve of the J-tip, [4]minimal guidewire length = 153 mm (95th percentile of the vessel length) + steel cannula length (the length that can be inserted into the patient) + CVC length (the entire length of the distal lumen) + 10 mm (the part of the guidewire that must extend from the CVC before CVC-insertion can be performed), [5]the discrepancy in mm between the length of the guidewire provided in the CVC kit and the calculated minimal guidewire length.

Paper V

We included a total of 7 126 CVC insertion forms. Of these, 78% were complete and 22% contained one or more missing fields. Between the first and second quarter of the study period, there was a significant increase in the proportion of complete CVC insertion forms (72% vs 83%, $p<0.001$). From the second to the last quarter, the proportion of complete CVC insertion forms stabilized around 80%. Further, 17% of the CVC inserting physicians had ≥1 field of missing data per CVC insertion form. The proportion of complete data for three specific terms in the CVC insertion form (vascular insertion site, catheter bore size/number of lumens and number of skin punctures) increased from 38% in the historical control to 93% in the present study. This represented an absolute reduction (95% CI) of the proportion of missing data of 55 (53 – 56) %, $p<0.001$ (Table 8).

Table 8. Comparison of proportions of missing data

CVC insertion form field	This study (n=7126)	Historical control (n=10 949)	p-value*
Vascular insertion site	235 (3.3)	3 288 (30)	<0.001
Catheter bore size/number of lumens	376 (5.3)	5 694 (52)	<0.001
Number of skin punctures	418 (5.9)	4 897 (45)	<0.001
All three fields complete	6 602 (93)	4 203 (38)	<0.001

Data are presented as numbers (%). *Chi-square test, p-values are not adjusted for multiple comparisons.

Discussion

Papers I & II

After a comprehensive systematic literature review, we noticed a paucity of multicentre data on the incidence of mechanical complications after ultrasound-guided central venous catheterisation and that large prospective observational studies regarding risk factors for mechanical complications are missing. Previous studies demonstrate considerable variation in reported rates of mechanical complications and the identified independent risk factors also vary between studies. Due to the scattered results, we concluded that risk stratification and further quality improvements of ultrasound-guided central venous catheterisation are challenging and that new well-designed studies are needed.

Our study is the largest prospective multicentre observational cohort study to date regarding incidence and risk factors for mechanical complications after central venous catheterisation. Given that 281 individual operators at four different hospitals performed the catheterisations and that the documentation of every CVC insertion was monitored for accuracy, the study provides a broad representation of the incidence of mechanical complications in the ultrasound-guided era.

We found that in hospitals where real-time ultrasound guidance is standard of care for central venous access, the incidence of major mechanical complications was only 0.4%. Due to the large sample size, we were also able to identify several important risk factors for major mechanical complications and the importance of all these risk factors remained in the sensitivity analyses. Our results suggest that it is possible to amend the risk of a major mechanical complication after ultrasound-guided central venous catheterisation. For example, the risk is likely lower when an experienced operator performs the subclavian CVC insertion in an underweight patient but increases when two or more insertion attempts are performed, regardless of operator experience. Further, the finding of male operator gender as an independent risk factor for major mechanical complication indicate that there are differences in complication rates between male and female physicians. We must however emphasize that gender among anaesthesiologists never has been evaluated as a risk factor before. To understand why male operators may encounter more serious mechanical complications, gender differences in risk behaviours during invasive procedures and in the ability to assess risks/call for supervision should be explored. This is probably not done without controversy though. On the other hand,

patient sex is assessed in most clinical and epidemiological studies without controversy. We also need to ask why it is important to study potential differences in patient outcomes between male and female physicians and what the results will lead to. If male physicians are prone to take greater risks, is it reasonable to consider that this must change completely? Some degree of risk behaviour is likely necessary for development and progress. However, patients should never be exposed to major risks due to lack of judgement or absence of appropriate supervision. Furthermore, in line with the results in the present study, two recently performed large epidemiological studies showed worse patient outcomes for male internists/surgeons compared to female internists/surgeons.[83,84] Female physicians should thus at least be equal to their male colleagues with the same academic degree and number of working hours when it comes to career development and wages. It is a main concern that gender equality still is not achieved in most medical specialities.[85,86]

Limitations

The study is observational and like all observational studies it comes with a risk of confounding and various biases. The identified independent risk factors for mechanical complications should therefore be further evaluated in future studies. Secondly, coagulopathy, which not was found to be associated with mechanical complications in this study, is usually known prior to the CVC insertion and may have contributed to a bias regarding operator experience or to the choice of giving pre-procedural procoagulants. Thirdly, as the study used data from clinical practice, missing values could not completely be avoided and may have introduced another bias. However, the continuous review of all recorded CVC insertions contributed to a small proportion of missing data. Fourthly, even though there is a strong tradition at the participating hospitals to document every CVC insertion in the common EHR system, there may be a small number of CVC insertions with associated mechanical complications that were not entered at all. Finally, hypovolemia, vascular anatomy, and the patient's ability to cooperate, which all may act as possible confounders, were not assessed in the study.

Paper III

Although the incidence of CVC misplacements was not reduced to 1% as indicated in the hypothesis, we demonstrated that the right supraclavicular fossa ultrasound view using a micro-convex probe is applicable to facilitate guidewire positioning and intra-procedural guidewire adjustment, thereby avoiding CVC misplacements in right infraclavicular subclavian vein catheterisation. With the ultrasound method described, 14 of the 15 initially misplaced guidewires were detected and 12 of them were successfully adjusted to a correct position, which in turn helped avoid 12 CVC

misplacements at the time of insertion. Further, all ultrasound-determined final guidewire tip positions were consistent with the post-procedural chest X-ray determined CVC tip positions. As no mechanical complications occurred, the results also suggest that the infraclavicular, long-axis approach with an in-plane needling technique using a micro-convex probe is a safe method for subclavian vein catheterisation when performed by trained operators.

At present, the most commonly used reference standard to detect CVC misplacement is post-procedural chest X-ray.[87] Unfortunately, chest X-ray include patient exposure to ionised radiation, increased workload for both ICU and radiology staff, and costs.[36] Using ultrasound to aid both cannulation and guidewire/catheter positioning is thus appealing for several reasons. It likely saves both time and costs, enables intraprocedural adjustment of misplaced guidewires which lowers the risk of repeated cannulations, reduces the need for post-procedural chest X-ray to determine the CVC tip position and consequently the patients' exposure to ionised radiation, and minimizes the delay until catheter use. Moreover, the ultrasound-method described in our study is non-invasive, applicable to most patients, and can be performed by a single operator. Ease of learning the method has not been studied, but our experience is that most anaesthetists with prior experience of real-time ultrasound guidance master the method after approximately 10–20 catheterisations.

Limitations

Our choice to base the sample size calculation on a population mean calculated from the reported number of CVC misplacements from seven randomly selected studies, instead of performing a systematic review, entailed some limitation. Our rational was that the seven studies together included as many as 2 107 subclavian vein catheterisations. Of these, 149 resulted in CVC misplacements, corresponding to an incidence (95% CI) of 7.1 (6.0 – 8.3) %. Another limitation was that the investigators responsible for all catheterisations in the study had considerable training performing CVC insertions with micro-convex probes, which could have imposed a potential operator bias. Most importantly though, the study was an observational cohort study without concurrent control, and the ultrasound method described should be further evaluated in a randomized controlled trial.

Paper IV

In clinical practice we have noticed that despite an initially confirmed correct guidewire tip position in the lower SVC via the right supraclavicular fossa ultrasound view, the guidewire tip may dislocate during the CVC insertion procedure as the guidewires provided in many commercial 15–16 cm CVC kits must be retracted several centimetres before CVC insertion can be performed. If the

guidewire tip is retracted to a level above the junction of the brachiocephalic veins, the catheter tip may dislocate towards the right internal jugular or left subclavian vein during catheter insertion.

In this study, we estimated the minimal guidewire length for right subclavian vein catheterisation based on vessel measurements in CT-images of 100 ICU-patients (50 men and 50 women) and measurements of equipment provided in commonly used commercial 15–16 cm CVC kits. We found that the majority of the included CVC kits contain guidewires that are too short for ultrasound-guided infraclavicular CVC placement in the right subclavian vein, i.e., guidewire retraction is needed prior to catheter insertion. We also found that there was no difference in mean vessel length between men and women and that patient height correlated poorly with the measured vessel length. Many operators assume that tall patients have greater distances to the cavoatrial junction compared to short patients, but our results suggest that clinical data such as patient sex and height are unreliable criteria to use when estimating the optimal length of a CVC, or the length of the guidewire that safely can be introduced into the vein.

It is presumably generally accepted among CVC manufactures that a long guidewire increases the risk of cardiac arrhythmias due to the greater possibility of inserting an excessive length of the guidewire into the vein.[88] This may explain their choice of providing rather short guidewires in 15–16 cm CVC kits. However, most physicians are well aware of this risk and usually only insert about 15–20 cm of the guidewire into the vein, regardless of its full length. Our hope is that the results from this study will call on CVC manufacturers to provide guidewires that are sufficiently long to avoid having to retract them during CVC insertions and according to our results, placement of a 15–16 cm CVC in the right subclavian vein requires an approximately 550 mm long guidewire.

Limitations

The study is a retrospective consecutive case series, and the level of evidence is inferior compared to prospective studies. In addition, no sample size calculation was performed. The included number of patients was instead based on the fact that the normal distribution is a good estimate of the distribution of the mean value if $n \geq 50$. Nevertheless, inclusion of a larger number of individuals would have contributed to a more exact calculation of the mean and SD of the measured vessel length. A further limitation was that all the included patients had both arms positioned above the head during the CT-scans and during a CVC insertion the patient´s arms are usually positioned along the body. However, since the 2nd rib and the right pulmonary artery (which were used as anatomical landmarks in the CT-images) do not move significantly during elevation of the arms, the arm position likely did not affect the vessel measurements. The exclusion of patients with body height above the 95th percentile for the Swedish population is yet another limitation. Although the statistical

analyses showed no or weak correlation between patient height and the measured vessel length, inclusion of very tall patients might have shown different results.

Paper V

We found that an implementation package including introduction of an updated credible CVC insertion form, new local directions for CVC placement in combination with delegated information responsibility to every separate department, and follow-up of all CVC insertions during a limited period of time, was highly effective in reducing the proportion of missing data of central venous catheterisation. The effect was not immediate, but a significant increase in the proportion of completely filled in CVC insertion forms was observed between the first and second quarter. This indicates that implementation measures may not have effect directly, but rather with some delay. It should also be noted that a relatively small proportion of the inserting physicians (17%) accounted for all the incomplete filled in CVC insertion forms.

There are strong national and international recommendations regarding appropriate documentation of CVC insertions and monitoring of associated complication rates.[26–28,70] Further, according to the Swedish National Board of Health and Welfare, it's mandatory for physicians in Sweden to record invasive procedures like central venous catheterisation in the patient's medical health record. We believe that the CVC insertion form implemented prior to this study enables high-quality prospective recording of relevant clinical data associated with central venous catheterisation. We also believe the improvement of CVC insertion documentation achieved by the implementation package evaluated in this study will contribute to increased knowledge of complication rates and facilitate quality improvements of central venous catheterisation.

Limitations

As the study is a post hoc analysis in a single healthcare system, there is a risk of bias and limited external validity. Further, there may be a small number of CVC insertions that were not registered in the EHR and the number of incomplete entries may therefore be underestimated. Moreover, many operators knew that the CVC insertion forms were being continuously reviewed. This cognizance may have contributed to the higher proportion of completely filled in forms and the observation time was too short to rule out a Hawthorne effect.

Conclusions

Papers I & II

In hospitals where real-time ultrasound guidance is standard of care for central venous access, the incidence of major mechanical complications was low. Several independent risk factors for major mechanical complications were identified: Patient BMI <20 kg/m^2, male operator gender, limited operator experience and more than one skin puncture. In addition, subclavian vein catheterisation was an independent risk factor for pneumothorax compared to internal jugular vein catheterisation.

The findings of modifiable risk factors for major mechanical complications can be used for risk stratification prior to the catheterisation procedure and may affect clinical practice. Moreover, the results indicate that there are differences in complications rates between male and female CVC-inserting physicians, which should be further studied.

Paper III

Real-time ultrasound guidance via the right supraclavicular fossa ultrasound view was useful to aid guidewire positioning, thereby avoiding CVC misplacements, in right infraclavicular subclavian vein catheterisation. The method is inexpensive, non-invasive, and applicable to all patients in which the superior vena cava can be visualized from the right supraclavicular fossa ultrasound view. When the described ultrasound method is used, the need for post-procedural chest X-ray to confirm the catheter tip position is redundant.

Paper IV

Sufficiently long guidewires are required to maintain a guidewire tip position in the lower superior vena cava throughout the CVC insertion procedure. Unfortunately, the majority of the investigated commonly used 15–16 cm CVC kits contain

guidewires that are too short for infraclavicular CVC placement in the right subclavian vein, i.e., guidewire retraction is needed prior to CVC insertion. Further, clinical data such as patient sex and height may be unreliable criteria to use when estimating the optimal length of a CVC.

Paper V

An implementation package including introduction of an updated CVC insertion form, new local directions for CVC placement in combination with delegated information responsibility to every separate department, and follow-up of all documented CVC insertions for a limited period of time was highly effective in reducing the proportion of missing data in the documentation of central venous catheterisation.

General conclusion

The overarching conclusion of this thesis is that there are possibilities for further quality improvements of central venous catheterisation also in the ultrasound-guided era and that the combination of appropriate recording of CVC insertions, possibilities to track patient outcomes, and clinical research contribute to advanced understanding and delivering of patient-safe healthcare.

Future perspectives

It is well known that CVC-related infections are associated with increased mortality, morbidity, and prolonged hospitalization.[72,73] Regarding mechanical complications the same associations have not been confirmed, likely at least partially due to the lack of accurate recording of mechanical complications in combination with insufficient sample sizes in previous studies. The secondary outcome measures stated in paper I of this thesis (mortality, length of hospital stay, and costs)[80] have not yet been examined, but the collection of additional data is almost completed, and further analyses are planned during 2022. We also plan to perform a post-hoc analysis to further investigate the differences in rates of major mechanical complications between male and female operators. In addition, catheter tip malposition, which was not included in the statistical analyses in paper II, will be further analysed regarding associated risk factors. Development of a prediction model for major mechanical complications after ultrasound-guided central venous catheterisation is yet another subject for future studies.

It seems reasonable to believe that the occurrence of certain mechanical complications may increase the risk of CVC-related thrombosis and infections, and such associations should be further examined. Catheter tip malposition has already been shown to increase the risk of CVC-related thrombosis,[89,90] but it is unclear if all the different incorrect CVC tip positions carry the same risk for thrombus formation and premature failure of the catheter function. Furthermore, bleedings and haematoma, which commonly occur in conjunction with CVC insertions, could be a substrate for bacteria and may therefore increase the risk of CVC-related infections. The same applies for CVC-associated pneumothorax as chest tube insertion, which often is needed to treat this complication, also may be a route for bacteria.

Another subject for future studies is exploration of potential differences in risk behaviours and self-evaluated need for supervision between male and female physicians. Previous data suggest that men and women may practice medicine and adhere differently to clinical guidelines.[91] In addition, lower mortality and readmission rates have been reported for hospitalized patients treated by female internists compared to male internists,[83] as well as a decrease in 30-day mortality and similar surgical outcomes (length-of-stay, complications, and readmission rate) for patients treated by female surgeons compared to male surgeons.[84] Moreover, a recent study evaluating surgeon-patient sex concordance with postoperative

outcomes showed that sex discordance between surgeons and patients negatively affected outcomes following common elective or emergent surgical procedures.[92] Subgroup analyses demonstrated that this was driven by worse outcomes among female patients treated by male surgeons. The reasons for the differences in patient outcomes between male and female physicians are unknown and future studies designed to investigate potential explanatory mechanisms are thus warranted.

Additional interesting aspects to evaluate regarding the risk of mechanical complications are operator training and supervision. There is limited agreement on how to define procedural competence for central venous catheterisation and the learning curve may be highly variable for different operators. At present, no definition of minimum experience needed to independently perform central venous catheterisation exists.[25] Unfortunately, the phrase “see one, do one, teach one,” is still used by many senior colleagues when teaching practical skills to junior residents, despite the fact that appropriate training and supervision probably are the most important components to reduce the risk of major mechanical complications for inexperienced operators.

Acknowledgements

Thomas Kander, main supervisor. I will forever be grateful that you asked me to become a part of your research group and for believing in me from the very beginning, although my prior research experience was absolute zero. All through medical school and residency I thought that research was not for me. I also had the feeling that the academic world mainly was a bunch of self-centred old men with large egos. Thank you for proving me wrong. You are one of the most intelligent, thoughtful, and humble people I have ever met, and you have introduced me to the world of research in the best possible way.

Ola Borgquist, co-supervisor. You are an amazing clinician, work more efficiently than anyone I know, are phenomenal at writing manuscripts and have inspired me to dare to try new things. Thank you for showing me that research can be fun, but more importantly, for becoming my craziest but at the same time sensible and most warm-hearted friend. You are always there, ready to listen to whatever I need to talk about, and also possess the great ability to make me feel better. Unfortunately, you no longer fear my dark eyes.

Peter Bentzer, co-supervisor. Thank you for your excellent guidance throughout this process. Your support, deep knowledge and brilliance has contributed to many important perspectives of this thesis.

Rikard Linnér and Snejana Hyllén, my current bosses. Thank you for being great role models and for encouraging me to become a cardiothoracic anaesthetist. You made it possible to combine clinical work with research and without your support, this thesis would not have been completed at this moment.

Tina Kröger, co-author. Without you, the data from study II still would not be organized. Thank you for your accurate and hard work. I highly cherish your contribution.

Erik Linné, co-author. Thank you for being my personal Excel-support and for all the valuable work you did in papers II & V.

Robin Lundén, co-author. Thank you for your perfect illustrations and outstanding filming skills, for being overexcited about pretty much everything, and for making me laugh. My need for your technical support will likely be forever.

Martin Spångfors, Jonas Åkeson and Anders Holmström, co-authors. Thank you for excellent collaboration and contributions in papers I & II.

Sophie Håkansson, Yvonne Roshagen, Susann Schrey, and Rainer Gatz – I am very grateful for your work regarding data monitoring in paper II.

Pär Bengtsson and Gracijela Bosovic, co-authors. Thank you for your expertise, methodological input, and important contributions in paper IV.

Josef Dankiewicz, cardiologist. Thank you for taking the time to discuss statistical matters, even though you were quite busy publishing TTM2. I really wish I had your statistical knowledge, R-skills, and perfect British accent.

Fredrik Hansson, statistician. Thank you for excellent statistical guidance in papers I & II. I could not have done this without you.

Mikael Bodelsson, Head of the Department of Clinical Sciences in Lund. Thank you for creating a stimulating research environment.

Anja Lindén, my dearest friend and colleague. Being around you is a true life-inspiration. Thank you for supporting me, believing in me, and making me sing. I have almost forgiven you for leaving our room but will never stop hoping for your return.

Emilie Mörtsell and Alain Dardashti, my true companions and great friends. I really want to become a clinician as brilliant as the two of you, and if I keep running after you, hopefully one day I will. Thank you for being such amazing friends and for making work a great place to be.

Martin Stenlo, we have followed each other from the very first tentative steps as young doctors at Ängelholm Hospital to the present a bit more confident steps in the corridors of Lund University Hospital. It has been a great pleasure all the way. Thank you for sharing invaluable tips for the writing of this thesis.

Lina Dalesjö, my friend, colleague, and excellent scheduler. Not once was my time for research withdrawn. Thank you for being the best coffee-break company, always somehow knowing when I am in the need of something sweet.

Martin Bjurström, my friend and colleague. You are the most enthusiastic, dedicated, and optimistic researcher I know. Thank you for always spreading the best of vibes and for the awesome publication tips. I still owe you a bottle of champagne.

Maria Lengquist, my friend and colleague. It is always a delight to discuss research with you and I very much hope for future collaborations.

All my colleagues at the department of Cardiothoracic Surgery, Anaesthesia, and Intensive Care. Being surrounded by so many talented, devoted, and hard-working people is truly inspiring.

Suzanne and Per, my parents. Thank you for teaching me what matters most in life, for encouraging me to think and for always being my greatest fans. Mum – you are my feminist role model. Dad – I will always be your girl.

Lisa and Peter, my siblings. You are my closest friends and the most wonderful and fun people I know. Life would be absolutely miserable without you.

Gabriel, my husband and best friend. You are undoubtedly the finest and smartest man I know. I love, admire, and respect you on so many levels. Thank you for putting up with all my sides and for helping me master various life and research-related challenges, even when I am not in the best of moods. You bring the perfect mix of reason, energy, and optimism to my life.

Dag och Edith, mina älskade barn. Ni är det finaste jag åstadkommit. Att få vara er mamma är livets största skatt. Tack för att ni varje dag påminner mig om det som betyder mest.

Financial support

The Gyllenstierna Krapperup's Foundation and the Skåne University Hospital Foundation.

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