


BMJ Open Research protocol for mechanical complications after central venous catheterisation: a prospective controlled multicentre observational study to determine incidence and risk factors of mechanical complications within 24 hours after cannulation

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ABSTRACT

Introduction Central venous catheterisation is a common procedure in intensive care therapy and the use of central venous catheters is essential for treatment of many medical disorders. Although rare, central venous catheterisation is associated with mechanical complications that can be life-threatening if untreated. Real-time ultrasound guidance reduces the incidence of mechanical complications when compared with the anatomic landmark method. The purpose of this study is to determine the incidence of and potential risk factors associated with early mechanical complications of central venous catheterisation in an era where real-time ultrasound guidance has become clinical practice.

Methods and analysis This is a prospective, controlled, multicentre, observational study. All participating hospitals follow the same clinical guidelines for central venous catheterisation. Each central venous catheter insertion will be recorded in the common electronic chart system according to a recently revised template. An automated script-based search will identify all recorded central venous catheter insertion templates during the study period and relevant variables will be extracted. Outcome measures and independent variables are pre-defined in this study protocol. Multivariable and univariable logistic regression analysis will be used to determine associations and risk factors of mechanical complications.

Ethics and dissemination The Regional Ethical Review Board in Lund, Sweden has approved this study. The results will be submitted for publication in peer-reviewed medical journals and presented at national and international scientific meetings.

Trial registration number NCT03782324.

INTRODUCTION

The use of central venous catheters has become an essential component of modern

Strengths and limitations of this study

- This study is a large, prospective, controlled, multicentre, observational study in a region where more than 6000 central venous catheters are inserted annually.
- There has been no prospective audit of the incidence and risk factors of mechanical complications after central venous catheterisation since ultrasound guidance became standard of care.
- During the study period, the recording of each central venous catheter insertion and catheterisation-related complication will be continuously reviewed to ensure correctly recorded data.
- All study sites follow the same clinical guidelines for central venous catheter insertions, implying that one routine rather than a mixture of routines will be evaluated.
- Although a multicentre study, the study will be performed in a small region in southern Sweden and does not include departments outside the region or outside the country.

healthcare and a necessity for treatment of many medical disorders. Central venous catheters provide reliable access to the bloodstream, which allows delivery of medications and nutritional support that cannot be administered safely by peripheral venous routes. Moreover, they enable measurement of haemodynamic variables that cannot be measured accurately by non-invasive means. The exact number of annual central venous catheterisations in Sweden is not known, but based on reported use at different Swedish

hospitals, it is estimated to be at least 50 000. Data from our previous study¹ indicate that a total number of 6–7 000 central venous catheters are inserted annually at the hospitals within Region Skåne in southern Sweden.

Unfortunately, central venous catheterisation is associated with mechanical, infectious and thrombotic complications.² Mechanical complications range from being clinically insignificant to life-threatening if untreated,^{3 4} but there is no firm data on association with increased patient mortality or hospital stay. Regarding infectious complications, it is well known that central venous catheter-related bloodstream infection is associated with increased morbidity, mortality and prolonged hospitalisation.^{5 6} It is also known that extra-luminal microbial colonisation of the central venous catheter is associated with thrombosis.⁷

Mechanical complications of central venous catheterisation include bleeding (such as haematoma and haemothorax), cardiac arrhythmia, arterial puncture, arterial catheterisation, nerve injury, pneumothorax, failed catheterisation and catheter tip malposition.^{2 8–10} The most common mechanical complications are haematoma formation, arterial puncture and pneumothorax. The risk of pneumothorax is higher in subclavian than in internal jugular vein catheterisation.^{1 9 11 12} Arterial puncture and haematoma formation are more common in femoral and internal jugular vein catheterisations compared with subclavian ones.^{13 14} The risk of infectious and thrombotic complications is lower in subclavian than in femoral or internal jugular catheterisation.^{11 15}

The incidence of mechanical complications associated with central venous catheterisation varies between 1.1% and 34%.^{1 9 14–19} Plausible reasons for this variation are differences in definition, cohort, case mix, insertion techniques and bias in the collection of data in retrospective studies. Although real-time ultrasound guidance reduces the incidence of mechanical complications,^{17 20–26} it is still not being routinely used for central venous access.

Both patient-related and physician-related risk factors have been reported to be associated with mechanical complications of central venous catheterisation, but those factors vary between studies. Patient-associated factors may be age, body mass index, gender and existing coagulopathy.^{1 4 9 19 27} Suggested physician-associated factors are level of training and experience, use of the anatomic landmark method or real-time ultrasound guidance, catheter insertion during the night, and increasing number of attempts.^{9 15 16 18}

After the widespread introduction of ultrasound guidance, there is, to the best of our knowledge, no large prospective observational study on the incidence of, and risk factors associated with mechanical complications of central venous catheterisation. We recently performed a multicentre, retrospective registry study based on 10 949 central venous catheter insertions.¹ That study was an audit of clinical practice and missing data was a reality. To avoid this problem and to collect valid data on all the central venous catheterisations at the participating

hospitals, we plan to perform a prospective controlled multicentre observational study.

METHODS AND ANALYSES

Aims

The primary aim of this study is to determine the incidence of mechanical complications within 24 hours after central venous catheterisation. The secondary aim is to identify risk factors associated with mechanical complications within 24 hours after catheterisation. The third aim is to investigate the effects of mechanical complications on mortality, length of hospital stay and costs.

Study population

Four hospitals in Region Skåne in southern Sweden will participate in the study: one university hospital with approximately 1300 beds and three county hospitals with about 200–300 beds each. The overall hospital catchment area is approximately 1.25 million people. All central venous catheter insertions at the participating hospitals during the study period will be considered for inclusion. Patients who die within the first 24 hours after central venous catheterisation will be excluded unless the cause of death is related to a mechanical complication.

Based on previous data^{1 9 14–19} the incidence of major mechanical complications after central venous catheterisation was estimated to be 1%. To achieve a narrow 95% CI of 0.6 % to 1.4 % of the incidence of mechanical complications, the necessary sample size was calculated to 10 029 insertions using the exact Clopper-Pearson binomial CI method (PASS V.16; Method: Exact). To allow for 20% missing data, the study will aim to include 10 029/0.8=12 537 insertions. Data collection has started in March 2019 and will end when the calculated number of insertions (12537) has been included.

Study design

All participating hospitals follow the same clinical guidelines for insertion of central venous catheters, based on published national recommendations.²⁸ Furthermore, they all use the same electronic chart system where each central venous catheter insertion is recorded according to a recently revised template (see online supplementary file 1). The revision has been made by clinicians responsible for this study to ensure adequate prospective recording of relevant clinical data associated with central venous catheterisation. Before the study starts, information about the new insertion template and the current clinical insertion guidelines will be given to all participating hospitals. The clinician or researcher connected to the study at each study site is responsible for the clinical implementation of the new insertion template as well as for information regarding the current guidelines. A dedicated collaborator (research nurse or researcher) at each study site will review all insertion template recordings during the study period, thereby enabling operators to correct missing or inadequate values and ensuring that

Table 1 Primary outcome measures

Minor mechanical complications	Major mechanical complications
Bleeding grade 2*	Bleeding grades 3 and 4†
Arrhythmia grades 1 and 2‡	Arrhythmia grades 3 and 4§
Arterial puncture	Arterial catheterisation
Non-persistent nerve injury¶	Persistent nerve injury**
Failed catheterisation	Pneumothorax
Catheter tip malposition††	

*Bleeding/haematoma formation requiring external compression.

†Bleeding/haemothorax requiring invasive intervention or blood transfusion and bleeding with life-threatening consequences.

‡Asymptomatic arrhythmia not requiring intervention and asymptomatic/symptomatic arrhythmia requiring non-urgent medical intervention.

§Symptomatic arrhythmia requiring urgent medical intervention and arrhythmia with life-threatening consequences.

¶Nerve injury with clinical signs persisting up to 72 hours.

**Nerve injury with clinical signs persisting more than 72 hours.

††Catheter tip malposition requiring correction before use.

all catheterisation-associated mechanical complications are recorded. In addition to the data in the electronic chart, a screening log at each study site will be kept for additional information on central venous catheterisations that are not included in the electronic chart but necessary for the study. An English copy of the central venous catheter insertion template is available as a supplementary file (see online supplementary file 1).

Primary outcome measures

Mechanical complications (table 1) are defined as bleeding (including haematoma and haemothorax), cardiac arrhythmia, arterial puncture, arterial catheterisation, nerve injury, pneumothorax, failed catheterisation and catheter tip malposition requiring correction before use.

Bleeding and cardiac arrhythmia will be classified according to the Common Terminology Criteria for Adverse Events (version 5.0).²⁹ Grade 1 bleedings (small bleedings not requiring intervention) often occur after central venous catheterisation but are rarely documented and will not be included in this study since they lack clinical significance. Grade 2 bleeding/haematoma formation (bleeding requiring external compression) will be considered a minor mechanical complication. Grade 3 bleeding/hemothorax (bleeding requiring invasive intervention or blood transfusion) and grade 4 bleeding/hemothorax (bleeding with life-threatening consequences) will be classified as major mechanical complications. Grade 1 arrhythmia (asymptomatic arrhythmia not requiring intervention) and grade 2 arrhythmia (asymptomatic or symptomatic arrhythmia requiring non-urgent medical intervention) will be considered minor mechanical complications. Grade 3 arrhythmia (symptomatic arrhythmia requiring urgent medical intervention) and grade 4 arrhythmia (symptomatic arrhythmia with

life-threatening consequences) will be classified as major mechanical complications.

Arterial puncture will be considered a minor mechanical complication. Arterial catheterisation will be classified as a major mechanical complication. Nerve injury will be categorised as a minor mechanical complication if clinical signs persist for up to 72 hours and as a major mechanical complication if clinical signs persist for more than 72 hours. Pneumothorax will be classified as a major mechanical complication. Failed catheterisation and catheter tip malposition requiring correction before use will be considered minor mechanical complications. All primary outcome measures and their classifications are summarised in table 1.

Secondary outcome measures

Mortality, length of hospital stay and costs for mechanical complications will be compared between patients who suffered from mechanical complications and those who did not. Prior to the analyses of mortality and length of hospital stay, corrections will be made for all baseline characteristics available in the electronic chart including but not limited to age, gender, diagnosis, intensive care unit care during the stay and body mass index. Evaluation of costs will be made by individual examination of the chart of patients with mechanical complications.

Independent variables

Based on previous studies, the following independent variables with possible correlation to clinical outcome will be used: patient age, gender, body mass index and coagulopathy (none, corrected, uncorrected or ongoing anticoagulant therapy), use of invasive positive pressure ventilation, vascular insertion site, insertion during the night, left-handed operator, right-handed operator, operator gender and operator experience, use of ultrasound (real-time ultrasound guidance constitutes standard of care and all primary outcome measures will be compared with ultrasound-guidance before insertion only, real-time in-plane ultrasound guidance, real-time out-of-plane ultrasound guidance and the anatomic landmark method), catheter bore size and number of punctures (through skin and through vessel wall, respectively). All independent variables are summarised in box 1.

Data analysis plan

The central venous catheter insertion template (see online supplementary file 1) in the common electronic chart system will serve not only as a clinical documentation tool but also as an electronic case report form. An automated script-based search in the electronic chart system will identify all recorded central venous catheter insertion templates during the study period and all relevant variables will be extracted. Special cases, for example, one insertion and two operators, will be tagged in the automated data extraction and manually processed if needed.

**Box 1 Independent variables**

Patient age
 Patient gender
 Patient body mass index
 Patient coagulopathy*
 Invasive positive pressure ventilation
 Vascular insertion site†
 Insertion during the night‡
 Left-handed operator
 Right-handed operator
 Operator gender
 Operator experience§
 Use of ultrasound¶
 Number of punctures**
 Catheter bore size

*None, corrected coagulopathy, uncorrected coagulopathy or ongoing anticoagulant therapy

†Internal jugular vein dx/sin, external jugular vein dx/sin, subclavian vein dx/sin or femoral vein dx/sin

‡Insertion of a central venous catheter between 21:00 and 07:00

§Junior resident, senior resident, junior consultant and senior consultant

¶Ultrasound before insertion only, real-time in-plane ultrasound guidance, real-time out-of-plane ultrasound guidance or the anatomic landmark method

**Number of punctures through skin and number of punctures through vessel wall

Multivariable logistic regression analysis will be used to determine risk factors of mechanical complications defined as primary outcome measures. The number of events for each outcome measure will determine how many of the independent variables that are possible to include in each regression analysis. Given that there are at least eight outcome events per independent variable in the model, the independent variables described above will be included in each multivariable logistic regression. If fewer events are identified, independent variables will be excluded starting with the least important one as determined by univariable regression analyses. Depending on the amount and pattern of missing data, single or multiple imputation models may be applied. Different multivariable logistic regression analyses will be reported with ORs, including 95% CIs for each independent variable. In addition, univariable analyses will be made for some outcome events and independent variables as sensitivity analyses.

Patient involvement

Patients were not involved in the design of this study, but the study is developed and performed in the interest of the patients. The research questions and outcome measures were developed from former scientific studies on the same topic and our hope is that the results from the study will contribute to increased patient safety. Patients will not be involved in the recruitment and conduct of the study. Since the study is an observation of current clinical practice, the patients included will not be subjects for any intervention.

ETHICS AND DISSEMINATION

This study is an observation of current clinical practice and does not entail increased risk for the patients included. All participants and parents to participants below 18 years of age will be offered an opt out by advertisements at the study sites and by individually provided information sheets. The Ethical Review Board waived the requirement for written informed consent. Results from the study will be submitted for publication in peer-reviewed medical journals and reported at national and international scientific meetings.

According to national and international guidelines,^{28 30} it is recommended that every hospital department responsible of central venous catheterisation continuously records and monitors outcome measures including complications. Like in many other hospital departments, such recording and monitoring is currently lacking at the participating hospitals.¹ Since central venous catheterisation is a very common, invasive and potentially dangerous procedure,^{3 8 16} we believe that common guidelines and similar recording and monitoring of insertions and complications would improve patient safety and thereby the overall quality of the procedure.

This study aims to determine the incidence and identify risk factors of early mechanical complications after central venous catheterisation in an era where ultrasound guidance in real time has become clinical practice. Beyond this, the present study will promote standardised insertion routines of all central venous catheters at the participating hospitals. Our ambition is to contribute to increased patient safety for those requiring a central venous catheter. The creation of a platform for adequate clinical recording and monitoring of central venous catheterisation will also enable future prospective multicentre interventions and large observational and epidemiological studies.

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Contributors TK was the originator of the study. MA, OB and TK designed the study. MA wrote the first version of the manuscript. MA, OB, TK, PB, JA, MS, JW, AH and RL contributed to the study design and revised the manuscript critically. All authors gave final approval of the version to be published.

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Competing interests None declared.

Patient consent for publication Not required.

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