INTRODUCTION

Central venous catheters (CVCs) are routinely placed in hematologic patients, providing an access point for drug administration, laboratory testing, and parenteral nutrition. These patients are frequently pancytopenic and have been reported to be at higher risk for catheter-related complications such as bleeding and catheter-related infections (CRIs). In the last decade, routine improvements of CVC insertion and management, such as ultrasound-guided catheter placement and the introduction of hygiene bundles, have been
implemented worldwide. These measurements have been shown to decrease the incidence of CVC-associated complications and overall hospital costs. A few studies have been published outlining mechanical and infectious CVC-related complications in hematologic patients. However, those studies were either small, or the CVC insertion in the studies was mainly performed without ultrasound guidance and included only tunneled silicone CVCs. Therefore, we designed this retrospective observational study with the primary aim of investigating the prevalence and incidence of CVC-related mechanical and infectious complications after insertion of nontunneled, noncoated CVCs in a cohort of hematologic patients. The secondary aim was to explore factors potentially associated with CVC complications. We hypothesized that hematologic patients have a high risk of both mechanical and infectious complications after CVC insertions and that several risk factors for complications can be identified.

2 | METHODS

This study was approved by the Swedish Ethical Review Authority (dnr 2014/916 and 2018/866). The requirement for written informed consent was waived. The study was carried out at the Department of Intensive and Perioperative Care at Skåne University Hospital, Lund, Sweden. The manuscript was prepared according to the STROBE guidelines for observational studies. Details on the study methods are presented in Figure 1. The subclavian vein was the preferred site of CVC insertion, since the patients were considered at high risk of infection and because the CVC was expected to remain in situ for more than a week.

2.1 | Outcomes

The primary outcomes were moderate and severe mechanical complications and infectious complications.

Mechanical complications included bleeding complications, arterial puncture, pneumothorax, arrhythmia, and nerve injury/rhizopathy within 48 h of insertion. Severity of mechanical complication was graded according to the Common Terminology Criteria for Adverse Events (CTCAE, Version 5.0) and further classified into mild, moderate, and severe as demonstrated in Table 1.

Infectious complications were defined in accordance with recent publications based on the definitions used by the Centers for Disease Control and Prevention.

2.1.1 | Suspected catheter-related infection (sCRI)

Either a positive catheter tip culture or a positive peripheral blood culture together with at least two of three systemic inflammatory response syndrome (SIRS) criteria at the removal of the CVC (fever >38°C or <36°C, heart rate > 90 beats per min, respiratory rate > 20 breaths per min). Leukocytosis or leukopenia was not considered an SIRS criterion because hematologic patients already have disturbed leukocyte counts due to reasons other than infections.

and

no likely infectious cause other than the catheter.

and

no likely noninfectious cause, for example, drug- or transfusion-related adverse reaction, venous thromboembolism, or mucositis.

or

local inflammation and signs of infection.

Catheter-related bloodstream infection (CRBSI): Growth of the same microorganism on both the catheter tip and in peripheral blood (within 48 h prior to the removal of the CVC) together, with at least two of four SIRS criteria (three in the current study) with no likely explanation for a cause other than the catheter.

2.2 | Statistical analyses

The sample size was based on the number of available patients during the study period. Results were expressed as a median (interquartile range) for continuous variables and a number (percentage) for categorical variables. When comparing binary variables, the chi-square

FIGURE 1 Flow charts describing the study methods. All inserted catheters together with the daily inspections and their management were documented in the patient’s electronic file. Detailed data on catheter insertion and management, together with all microbiological data, were manually extracted and analyzed. Every patient had the right to opt out from the study. Blood samples were obtained within 24 h prior to cannulation, and prophylactic coagulation enhancement was considered in patients with preprocedural coagulopathy, defined as platelet count <50 × 10^9/L, prothrombin time (PT-INR) > 1.8, or APTT > 43 s (equal to more than 1.3× upper normal value). CDC, central dialysis catheter; CVC, central venous catheter. Management of catheters is described in reference [13] (Thorarinssottir et al.).

All catheter insertions and any preprocedural complication were documented in the electronic medical chart using a standardized CVC insertion template described in reference [12] (Björkander et al.). Nonantimicrobial transparent catheter dressings (Tegaderm™; 3M) were changed every fifth day or more frequently if needed. Once the old dressing was removed, the insertion site was cleaned with 0.9% saline solution and washed with 0.5% chlorhexidine/70% alcohol (SCHA) solution. The CVCs were removed after site treatment with 0.5% chlorhexidine/70% alcohol (SCHA) solution and the distal 5 cm of the catheter was cut and submerged in a culture tube, which was sonicated in 10 ml of broth. 0.1 ml of the broth was quantitatively cultured on blood agar plates. Growth of >10^5 CFU/catheter was considered significant colonization. The BACT/ALERT system (BioMérieux) was used for blood cultures. All bottles were incubated until microbial growth was detected or for a maximum of 5 days. Electronic medical records of all patients eligible for inclusion were manually reviewed, and relevant data were extracted and entered in the research database (Microsoft Access, version 2016)
test was applied. To evaluate the associations between independent variables and grades 2–4 bleeding and CRI, univariable and multivariable logistic regression analyses were applied. The selection of independent variables in the regression analyses was based on results from previous studies and the significant results in the univariate analysis were further analyzed in a multivariable analysis. The Hosmer-Lemeshow test was used to test the goodness of fit for multivariable testing. $p < .05$ was considered significant and all tests were two-tailed. All analyses were performed using SPSS 25 (SPSS Inc/IBM).

3 | RESULTS

Baseline characteristics of patients and CVCs are presented in Table 2. In summary, a total of 589 catheter insertions were
performed in 387 patients, during the study period of 71 months. The majority of catheters inserted were single lumen 469/589 (80%) and most catheters were inserted in the subclavian vein 433/589 (74%). Of all patients \((n = 387)\), 256 (66%) were men and the most common diagnosis was acute myeloid leukemia 153/387 (40%).

| Severity of mechanical complication | Complications                                      |
|-------------------------------------|---------------------------------------------------|
| Mild                                | Bleeding grade 1\(^{a}\)                           |
|                                     | Arrhythmia grades 1–2\(^{b}\)                     |
|                                     | Transient rhizopathy                              |
| Moderate                            | Bleeding grade 2\(^{c}\)                           |
| Severe                              | Bleeding grades 3–4\(^{d}\)                       |
|                                     | Pneumothorax                                      |
|                                     | Arrhythmia grades 3–4\(^{e}\)                     |
|                                     | Persistent rhizopathy                             |

\(^{a}\)Slight oozing from the insertion site not requiring intervention.

\(^{b}\)Transient arrhythmia not requiring intervention.

\(^{c}\)Bleeding requiring prolonged external compression.

\(^{d}\)Grade 3 bleeding requiring transfusions or subacute invasive measures. Grade 4 bleeding is defined as a life-threatening condition in need of urgent intervention.

\(^{e}\)Grade 3: Significant arrhythmia in need of medical intervention. Grade 4: significant arrhythmia causing hemodynamic compromise.

### TABLE 1: Mechanical complications classified according to their severity, based on the terms defined by the Common Terminology Criteria for Adverse Events\(^{8}\)

| Reason for removal                  | Count (Percentage) |
|-------------------------------------|--------------------|
| Ceased usage                        | 373 (63)           |
| Suspected or confirmed infection    | 89 (15)            |
| Patient death                       | 49 (8.0)           |
| Catheter malfunction                | 10 (2.0)           |
| Accidental removal                  | 10 (2.0)           |
| Misposition                         | 11 (2.0)           |
| Confirmed venous thrombosis         | 3 (0.5)            |
| Mechanical complication (bleeding)  | 2 (0.5)            |
| Missing                             | 42 (7.0)           |
| Preprocedural coagulopathy\(^{b}\) | 219 (37)           |
| Missing data                        | 20 (3.4)           |

#### TABLE 2: Characteristics of central venous catheters and patients\(^{a}\)

| Catheter characteristics            | Count (Percentage) |
|-------------------------------------|--------------------|
| Central venous catheters inserted, total | 589 (100)          |
| Days with catheter                  | 25 [9.0–43]        |
| Type of catheter                    |                    |
| CVC                                 | 564 (96)           |
| Central dialysis catheter           | 25 (4.2)           |
| Site of insertion                   |                    |
| Subclavian vein                      | 433 (74)           |
| Internal jugular vein               | 150 (25)           |
| Femoral vein                        | 5 (0.8)            |
| Missing                              | 1 (0.2)            |
| Number of lumens                     |                    |
| 1                                   | 469 (80)           |
| 2                                   | 33 (6.0)           |
| 3                                   | 12 (2.0)           |
| 4                                   | 6 (1.0)            |
| 5                                   | 14 (2.0)           |
| Central dialysis catheter           | 25 (4.0)           |
| Missing                              | 30 (5.0)           |
| Number of needle passes              |                    |
| 1                                   | 385 (66)           |
| 2                                   | 85 (14)            |
| 3                                   | 38 (6.0)           |
| >4                                  | 26 (4.0)           |
| Missing                              | 55 (10)            |
| Ultrasound guidance                 | 415 (70)           |

#### TABLE 2 (Continued)

| Diagnosis                            | Count (Percentage) |
|--------------------------------------|--------------------|
| Acute myeloid leukemia (AML)         | 153 (40)           |
| Acute lymphoblastic leukemia (ALL)   | 50 (13)            |
| Lymphoproliferative neoplasms/lymphoma | 48 (12)          |
| Myeloma                              | 34 (9.0)           |
| Acute promyelocytic leukemia (APL)\(^{d}\) | 22 (5.0)         |
| Myelodysplastic syndrome (MDS)       | 15 (4.0)           |
| Myeloproliferative neoplasms (MPN)   | 12 (3.0)           |
| Other\(^{e}\)                        | 53 (14)            |

\(^{a}\)Data are presented as median IQR [Q1–Q3] or number (percentage).

\(^{b}\)Number of cases with coagulopathy defined as ≥1 abnormal preprocedural blood coagulation tests, that is, platelet count <50 × 10^9/L, PT-INR >1.8, or APTT (activated partial thromboplastin time) >43 s which equals more than 1.3× the normal value.

\(^{c}\)Spleen and liver status on day of catheter insertion based on estimations using either abdominal CT scan or ultrasound (performed in 102/124 cases) or documented clinical examination at admission. There were no splenectomized patients.

\(^{d}\)APL is a subgroup of AML with tendency toward more aggressive coagulopathy.

\(^{e}\)Other diagnoses included amyloidosis, demyelinating polyneuropathies, Ewing sarcoma, idiopathic thrombocytopenic purpura, monoclonal gammopathy, multiple sclerosis, necrobiotic xanthogranuloma, plasmocytoma, scleroderma, and thombotic thrombocytopenic purpura.
3.1 | Outcomes

Detailed data on outcomes per insertion site are presented in Table 3.

3.2 | Mechanical complications

In 64/589 (11%) of all insertions, a moderate 50/589 (8.5%) or severe 14/589 (2.4%) mechanical complication occurred. Ultrasoundography was used in the majority of insertions that resulted in grades 2–4 bleeding 46/61 (75%) but did not show statistical significance in the univariable logistic regression analysis and was therefore not included in the multivariate analysis.

Arterial punctures occurred in 18/589 (3.1%) insertions, where 4/18 (22%) resulted in grades 3–4 bleeding and 4/18 (22%) in grade 2 bleeding. Out of all grades 2–4 bleedings, 8/61 (13%) occurred after an arterial puncture. Detailed data on preprocedural coagulopathy and correction of hemostasis is described in Figure 2 and File S1.

In the multivariable logistic regression analyses for both grades 2–4 bleeding and sCRI, the goodness of fit showed a valid chi-square value (p > .05) for all outcomes. Detailed results of the univariable logistic regression analyses on grades 2–4 bleeding are shown in Tables 4 and 5. The results of the univariable regression analyses were used to identify variables for the multivariable analyses. Corrected or uncorrected preprocedural coagulopathy (p < .001), number of needle passes (p = .008), and arterial puncture (p = .004) were all independently associated with grades 2–4 bleeding in the multivariable analysis.

Three cases (0.5%) presented with a pneumothorax on the same side as the catheter insertion, all verified with a plain chest X-ray. In 2/3 cases (67%), ultrasound-guided insertion was applied.

3.3 | Infectious complications

A detailed description of each case with sCRI can be seen in File S2. In summary, 69 patients were diagnosed with sCRI (12%), yielding an incidence of 3.7 sCRI/1000 catheter days. Given that mechanical complications are common in hematologic patients, optimization of conditions at insertion is of utmost importance. One example of such optimization may be a routine preprocedural ultrasound scan to anticipate any insertion problem, such as an anatomically challenging positioning of the vein. Based on that information, the clinician can decide on any prophylactic coagulopathic treatment. Although logistically challenging, this approach is appealing.

Ultrasound-guided technique was used in the majority of all catheter insertions (70%), however, in this study, its use was not associated with reduced risk for mechanical complications. Previous studies have convincingly demonstrated that real-time ultrasound reduces the risk for mechanical complications. The lack of shown usefulness of ultrasound in the present study may be explained by

4 | DISCUSSION

This retrospective observational study on non-tunneled and non-coated CVC insertions in hematologic patients demonstrated an overall high prevalence of moderate to severe mechanical complications and a high sCRI prevalence (12%) with an sCRI incidence of 3.7 sCRI/1000 catheter days. These results are compared with previously published studies on hematologic patients and higher than earlier reports on general cohorts and should therefore be carefully considered before cannulation of hematologic patients.

4.1 | Mechanical complications

In a previous study on CVC insertions in an unselected cohort of 10,949 patients >16 years of age, from the same hospital as the present study, we reported a prevalence of mechanical complications of 1.1%. In other studies in unselected adult cohorts frequencies of mechanical complications are reported with a wide interval of 1.1% and 7.6%, mostly dependent on different definitions of mechanical complications. In hematologic patients, Dix et al. prospectively studied 174 nontunneled CVC insertions and reported immediate mechanical complications in 7.5% of cases, whereas Morano et al. demonstrated mechanical complications in 7.2% of hematologic patients in a retrospective study on tunneled CVCs inserted. These results should be compared with the prevalence of moderate and severe mechanical complications, occurring in 11% of cases, in the present study. However, it should also be noted that in the referred studies, bleeding complications were not graded nor defined according to their time of occurrence, which complicates the comparison with the present study.

Given that mechanical complications are common in hematologic patients, optimization of conditions at insertion is of utmost importance. One example of such optimization may be a routine preprocedural ultrasound scan to anticipate any insertion problem, such as an anatomically challenging positioning of the vein. Based on that information, the clinician can decide on any prophylactic coagulopathic treatment. Although logistically challenging, this approach is appealing.
inconsistent use at the discretion of the inserting operator and not always in real time as in previous studies.

The number of needle passes and arterial punctures was associated with grades 2–4 bleeding. Both variables have previously been described as risk factors for mechanical complications in general cohorts.\(^2,12,14–16\) Moreover, preprocedural coagulopathy was associated with grades 2–4 bleeding. In the majority of these bleedings, the patients were preprocedurally given platelets (Tables 4 and 5; Figure 2; File S1), yet coagulopathy was still correlated with moderate to severe bleeding. This observation is described by van der Weerdt et al., who noted no beneficial effect from prophylactic platelet administration.\(^14\) One possible explanation for these findings is that the clinician may be more likely to give platelet transfusions to more compromised patients. Further, in the present study, posttransfusion platelet count was generally not controlled, which implies that patients with low numbers of preprocedural platelets may not have reached the recommended platelet count of 50 \(\times\) 10\(^9\)/L. Moreover, both the present study and the study by van der et al. rely on retrospective observations with a risk of bias.

| Outcome                        | Subclavian \(n = 433\) | Internal jugular \(n = 150\) | Femoral \(n = 5\) | Total \(n = 589\) |
|--------------------------------|-------------------------|-----------------------------|------------------|------------------|
| **Mechanical complications**   |                         |                             |                  |                  |
| Bleeding grade\(^b\)           |                         |                             |                  |                  |
| 1                              | 77 (18)                 | 12 (8.0)                    | 0 (0)            | 89 (15)          |
| 2                              | 33 (7.6)                | 16 (11)                     | 1 (20)           | 50 (8.5)         |
| 3                              | 8 (1.8)                 | 0 (0)                       | 0 (0)            | 8 (1.4)          |
| 4                              | 2 (0.5)                 | 1 (0.7)                     | 0 (0)            | 3 (0.5)          |
| Aggregated grades 2–4          | 43 (10)                 | 17 (11)                     | 1 (20)           | 61 (10)          |
| Pneumothorax                   | 3 (0.7)                 | 0 (0)                       | 0 (0)            | 3 (0.5)          |
| Arrhythmias                    |                         |                             |                  |                  |
| Mild                           | 3 (0.7)                 | 0 (0)                       | 0 (0)            | 3 (0.5)          |
| Moderate-severe                | 0 (0)                   | 0 (0)                       | 0 (0)            | 0 (0)            |
| Nerve injury                   |                         |                             |                  |                  |
| Mild                           | 4 (0.9)                 | 1 (0.7)                     | 0 (0)            | 5 (0.8)          |
| Moderate-severe                | 0 (0)                   | 0 (0)                       | 0 (0)            | 0 (0)            |
| Prevalence of mechanical       |                         |                             |                  |                  |
| complications\(^c\)            |                         |                             |                  |                  |
| Mild mechanical complications  | 84 (19)                 | 13 (8.7)                    | 0 (0)            | 97 (16)          |
| Moderate mechanical            | 33 (7.6)                | 16 (11)                     | 1 (20)           | 50 (8.5)         |
| complications\(^d\)            |                         |                             |                  |                  |
| Severe mechanical              | 13 (3.0)                | 1 (0.7)                     | 0 (0)            | 14 (2.4)         |
| complications\(^e\)            |                         |                             |                  |                  |
| **Infectious complications**   |                         |                             |                  |                  |
| Days with catheter, total      | 16077                   | 2692                        | 40               | 18814           |
| Catheter days                  | 28 [17–53]              | 13 [5–27]                   | 7 [5–12]         | 25 [9–43]       |
| sCRI prevalence, n (%)         | 53 (12)                 | 15 (10)                     | 0 (0)            | 69 (12)\(^f\)   |
| sCRI incidence/1000 catheter   | 3.3                     | 5.6                         | 0                | 3.7             |
| days                           |                         |                             |                  |                  |
| CRBSI prevalence, n (%)         | 9 (2.0)                 | 3 (2.0)                     | 0 (0)            | 12 (2.0)         |
| CRBSI incidence/1000 catheter  | 0.56                    | 1.11                        | 0                | 0.64            |

\(^a\)Data presented as numbers (%) or median IQR [Q1–Q3].
\(^b\)Bleeding observed within the first 48 h after insertion.
\(^c\)Mild mechanical complications included bleeding grade 1, arrhythmia grades 1–2, and transient rhizopathy.
\(^d\)Moderate mechanical complications included bleeding grade 2.
\(^e\)Severe mechanical complications included grades 3–4 bleeding and pneumothorax.
\(^f\)Presented as infection incidence (%) and infection rate/1000 catheter days.
\(^g\)Data on the location of one infected catheter are missing.
As CVCs inserted in the subclavian vein have been reported to result in less infectious complications, and clinicians experience less infusion disruptions and the patients probably encounter less discomfort, this was the standard site of insertion. However, 13 of totally 14 severe mechanical complications occurred after subclavian insertion. Even though 433 cases with subclavian insertion and only 155 cases with insertions in other veins were studied, this supports previous studies showing a higher risk for mechanical complications after subclavian insertions.

4.2 Infectious complications

Our observation of sCRI incidence (3.7/1000 catheter days) is in the range of infection rates previously reported, where the CRI and CRBSI incidences in similar cohorts as the present study ranged between 1.3 and 7.6/1000 catheter days. However, it should be highlighted that the type of CVCs included and the definition of CRI vary between these studies and the present one, which complicates the comparison. As postulated by Tomlinson et al. in a systematic review on 191 studies reporting CRIs, uniformity of definition is lacking and some studies even fail to cite or report a definition. Moreover, the term CRI and central line-associated bloodstream infection (CLABSI) are frequently interchanged. By definition, CLABSI or CABS (catheter-associated bloodstream infection) occurs when there is the growth of a microorganism in blood cultures with a CVC present at the time of infection or within 48 h prior to the development of infection, with no likely explanation for a cause other than the catheter. Since these terms differ, a more recent definition—suspected CRI—used in this manuscript, has been suggested in recent expert consensus-based clinical practice guidelines. Many use CRBSI as a measure of CRI. However, as pointed out by others, one problem with the strict CRBSI definition in hematologic patients is that the majority of patients are treated with intravenous antibiotics both prior to catheter insertion and throughout its usage. As many organisms in significant CRIs are hidden from antibiotics in a biofilm on the catheter but killed by antibiotics if released into the bloodstream, many blood cultures could yield false-negative results. Therefore, we argue that a broader definition such as sCRI, despite lowering the specificity, increases the sensitivity for CRIs.

In a recent report from our group, Thorarinsdottir et al. studied CRIs in a general patient cohort, after the implementation of hygiene bundles, reported a CRI prevalence of 2.6% with an incidence of 1.9/1000 catheter days. In the present study on hematologic patients the prevalence was 12% and the incidence 3.7/1000 catheter days. These higher numbers underline the importance of daily inspections, evaluation of future needs, and extra precautions to avoid CRI in these susceptible hematologic patients.

Higher BMI and male gender were associated with sCRI in this cohort. Obesity has previously been identified as a risk factor for sCRI in critically ill patients. In a prospective study on nonhematologic patients, Dossett et al. suggested that obese patients have an increased risk of sCRI because of longer severity-adjusted ICU stays, increasing their risk of nosocomial infections. Another theory is that it could be due to increased perspiration, as bandages are more

| Correction of coagulopathy prior to catheter insertion: |
| (x) = cases receiving platelet transfusions, n = 150 |
| (x)* = cases receiving plasma transfusions, n = 10 |
| (x)** = cases receiving prothrombin complex concentrate, n = 5 |

FIGURE 2 The Venn Diagram shows the relationship between preprocedural coagulation defects and the correction of hemostasis. The total number of isolated coagulopathies are presented separately, whereas the number of cases receiving any pro-coagulative treatment before insertion are presented within brackets, as explained in the figure above. Two hundred and two cases presented isolated platelet count <50 x 10⁹/L, two cases presented isolated PT-INR > 1.8, and three cases had an isolated APTT > 43 s. For more details on the preprocedural correction of coagulopathy, see File S1. APTT, activated partial thromboplastin time; PT-INR, prothrombin time-international normalized ratio.
prone to detach leading to a risk of wound infection. Further studies are needed to determine the association between high BMI and sCRI in hematologic patients.

Reports on male gender being a risk factor for sCRI in hematologic patients are scarce but has been described as a risk factor for sCRI in nonselected patients. However, in one randomized

---

TABLE 4 Univariable regression analyses for each outcome variables. Independent variables were chosen based on previous studies. Highlighted variables were further analyzed in a multivariable regression analysis (Table 5)

| Independent variables                           | Early grades 2–4 bleeding, n = 61 | Univariable analyses<sup>a</sup> |
|------------------------------------------------|-----------------------------------|---------------------------------|
|                                                 | No  | Yes          | OR       | 95% CI        | p value |
| Body mass index                                 | 26 [23–29] | 26 [23–29] | 0.998 | 0.945–1.054 | .933   |
| Male gender                                     | 233 | 23 [38]     | 1.305 | 0.756–2.252 | .339   |
| Hepatosplenomegaly                              | 486 [92] | 59 [96]     | 2.549 | 0.602–10.804 | .204   |
| Operator experience >5 year                     | 355 [67] | 43 [70]     | 1.237 | 0.644–2.377 | .523   |
| Male operator                                   | 406 [77] | 49 [80]     | 1.227 | 0.632–2.381 | .545   |
| Number of needle passes<sup>a</sup>             | 1 [1–2] | 1 [1–2]     | 1.317 | 1.070–1.620 | .009   |
| Site of insertion                               | Subclavian vein                    | 390 (74) | 43 (70) | 0.845 | 0.472–1.515 | .572   |
|                                              | Internal jugular vein              | 133 (25) | 17 (28) | 1.147 | 0.634–2.077 | .649   |
|                                              | Femoral vein                       | 4 (8.0)  | 1 (2.0)  | 2.183 | 0.240–19.854 | .488   |
|                                              | Left sided CVC insertion           | 297 (57) | 34 (56)  | 0.971 | 0.569–1.656 | .914   |
|                                              | Number of lumens                   | 1 [1–1]  | 1 [1–1]  | 0.975 | 0.779–1.220 | .823   |
|                                              | Ultrasound guidance                | 369 (70) | 46 (75)  | 1.321 | 0.717–2.436 | .372   |
|                                              | Arterial puncture                  | 10 (2.0) | 8 (13)   | 7.819 | 2.959–20.661 | .000   |
|                                              | Coagulopathy<sup>b</sup>           | 171 (32) | 36 (59)  | 2.931 | 1.704–5.039 | .000   |
| Diagnosis AML<sup>c</sup> at CVC<sup>d</sup> insertion | 260 (49) | 28 (46)    | 0.875 | 0.514–1.488 | .621   |

| Suspected catheter-related infections (sCRI), n = 69 |
|-----------------------------------------------------|
| Independent variables                           | No  | Yes          | Univariable analyses<sup>d</sup> |
|------------------------------------------------|-----|--------------|---------------------------------|
|                                                 | OR       | 95% CI        | p value |
| Body mass index                                 | 26 [23–29] | 27 [25–30] | 1.040 | 0.993–1.089 | .097   |
| Male gender                                     | 281 (54) | 52 (75)     | 2.602 | 1.465–4.619 | .001   |
| Total catheter days                             | 27 [13–47] | 28 [19–48] | 1.002 | 0.995–1.010 | .549   |
| Number of needle passes<sup>a</sup>             | 1 [1–2] | 1 [1–2]     | 1.185 | 0.957–1.467 | .120   |
| Site of insertion                               | Subclavian vein                    | 380 (73) | 53 (77)  | 1.220 | 0.675–2.205 | .509   |
|                                              | Internal jugular vein              | 135 (25) | 15 (22)  | 0.792 | 0.433–1.450 | .450   |
|                                              | Number of lumens                   | 1 [1–1]  | 1 [1–1]  | 0.685 | 0.470–1.000 | .050   |
|                                              | Arterial puncture                  | 16 (23)  | 2 (3.0)  | 0.940 | 0.212–4.180 | .936   |
|                                              | Bleeding<sup>d</sup>               | 185 (36) | 30 (43)  | 1.393 | 0.838–2.317 | .202   |
|                                              | Coagulopathy<sup>b</sup>           | 187 (36) | 20 (29)  | 0.707 | 0.408–1.226 | .217   |
| Diagnosis AML<sup>c</sup> at CVC<sup>d</sup> insertion | 246 (48) | 42 (60)    | 1.733 | 1.037–2.895 | .036   |

Abbreviation: CVC, central venous catheter.

<sup>a</sup>Increased risk for grades 2–4 bleeding in insertions requiring more needle passes.

<sup>b</sup>Coagulopathy was defined as ≥1 abnormal preprocedural blood coagulation test, that is, platelet count < 50 x 10<sup>9</sup>/L, PT-INR > 1.8, or APTT (activated partial thromboplastin time) > 43 s, which equals more than 1.3x the normal value.

<sup>c</sup>Acute Myeloid Leukemia including APL (Acute Promyelocytic Leukemia), a subgroup of AML with tendency toward more aggressive coagulopathy.

<sup>d</sup>Early or late with the severity mild to severe.

<sup>e</sup>Data are presented as 95% Confidence Interval (CI) of Odds Ratio (OR).
controlled trial by Luft et al., investigating 219 hematologic patients receiving a CVC, the male gender was identified as an independent risk factor for skin colonization, potentially increasing the risk of catheter colonization. Bead growth and shaving were observed to reduce adherence of wound dressing materials, suggesting an increased risk of bacterial contamination.

4.3 | Limitations

One of the major limitations of this study is its retrospective nature and the risk of missing data. Although there is a well-established routine for documenting catheter-related complications and securing infection-suspected catheter tips with simultaneous peripheral blood cultures in the studied departments, adherence to the routines cannot be guaranteed. Furthermore, the lack of uniformity in defining CRIs is an issue when reporting data. Moreover, this study was performed in a selected cohort with low incidences of some outcomes, making it impossible to include some risk factors in the multivariable regression analyses.

4.4 | Conclusions

Patients with hematologic malignancies have a high risk of both grades 2–4 bleeding and sCRI after CVC insertion.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Data was collected and analysed mainly by MMR with contributions from HRT and TK. VL contributed with hematology specific data. Article was written by MMR, HRT, VL, MR and TK.

ORCID

Mika M. Rockholt https://orcid.org/0000-0002-8899-8551
Thomas Kander https://orcid.org/0000-0002-5404-2981

REFERENCES

1. Baier C, Linke L, Eder M, et al. Incidence, risk factors and health-care costs of central line-associated nosocomial bloodstream
infections in hematologic and oncologic patients. PLoS One. 2020;15(1):e0227772.

2. Dix C, Yeung D, Rule M, Ma D. Essential, but at what risk? A prospective study on central venous access in patients with haematological malignancies. Intern Med J. 2012;42(8):901-906.

3. Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med. 2006;355(26):2725-2732.

4. Böll B, Schalk E, Buchheidt D, et al. Central venous catheter-related infections in hematology and oncology: 2020 updated guidelines on diagnosis, management, and prevention by the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO). Ann Hematol. 2021;100(1):239-259.

5. Randolph AG, Cook DJ, Gonzales CA, Pribble CG. Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. Crit Care Med. 1996;24(12):2053-2058.

6. Morano SG, Coppola L, Latagliata R, et al. Early and late complications related to central venous catheters in hematological malignancies: a retrospective analysis of 1102 patients. Mediterr J Hematol Infect Dis. 2014;6(1):e2014011.

7. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Epidemiology. 2007;18(6):805-835.

8. US Department of Health and Human Services NIH & National Institute (NIH). 2017:1-146.

9. Randolph AG, Cook DJ, Gonzales CA, Pribble CG. Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. Crit Care Med. 1996;24(12):2053-2058.

10. Tomlinson D, Mermel LA, Ethier M-C, Matlow A, Gillmeister B, Sung L. Defining bloodstream infections related to central venous catheters in patients with cancer: a systematic review. Clin Infect Dis. 2011;53(7):697-710.

11. Garnier JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control. 1988;16(3):128-140.

12. Björkander M, Bentzer P, Schött U, Broman ME, Kander T. Mechanical complications of central venous catheter insertions: a retrospective multicenter study of incidence and risks. Acta Anaesthesiol Scand. 2019;63(1):61-68.

13. Thorarsdottir HR, Rockholt M, Klarin B, Broman M, Fraenkel CJ, Kander T. Catheter-related infections: a Scandinavian observational study on the impact of a simple hygiene insertion bundle. Acta Anaesthesiol Scand. 2020;64(2):224-231.

14. van de Weerdt EK, Biemond BJ, Baake B, et al. Central venous catheter placement in coagulopathic patients: risk factors and incidence of bleeding complications. Transfusion. 2017;57(10):2512-2525.

15. Cavanna L, Citterio C, Di Nunzio C, Orlandi E, Toscani I, Ambrogi M. Central venous catheterization in cancer patients with severe thrombocytopenia: ultrasound-guide improves safety avoiding prophylactic platelet transfusion. Mol Clin Oncol. 2020;12:435-439.

16. McGee DC, Gould MK. Preventing complications of central venous catheterization. N Engl J Med. 2003;348(12):1123-1133.

17. Parienti J-J, Mongardon N, Mégarbane B, et al. Intravascular complications of central venous catheterization by insertion site. N Engl J Med. 2015;373(13):1220-1229.

18. Mollee P, Jones M, Stackelroth J, et al. Catheter-associated bloodstream infection and risk factors in adults with cancer: a prospective cohort study. J Hosp Infect. 2011;78(1):26-30.

19. Hammerskjöld F, Berg S, Hanberger H, Taxbro K, Malmval B-E. Sustained low incidence of central venous catheter-related infections over six years in a Swedish hospital with an active central venous catheter team. Am J Infect Control. 2014;42(2):122-128.

20. Ryder MA. Catheter-related infections: it’s all about biofilm. Top Adv Pract Nurs eJ. 2005;5(3):1-6.

21. Kaye KS, Marchaim D, Chen TY, et al. Predictors of nosocomial bloodstream infections in older adults. J Am Geriatr Soc. 2011;59(4):622-627.

22. Dossett LA, Dageforde LA, Swenson BR, et al. Obesity and site-specific nosocomial infection risk in the intensive care unit. Surg Infect (Larchmt). 2009;10(2):137-142.

23. Schalk E, Färber J, Fischer T, Heidel FH. Central venous catheter-related bloodstream infections in obese hematologic patients. Infect Control Hosp Epidemiol. 2015;36(8):995-996.

24. Cohen B, Choi YJ, Hyman S, Furuya EY, Neidell M, Larson E. Gender differences in risk of bloodstream and surgical site infections. J Gen Intern Med. 2013;28(10):1318-1325.

25. Luft D, Schmoor C, Wilson C, et al. Central venous catheter-associated bloodstream infection and colonisation of insertion site and catheter tip. What are the rates and risk factors in haematology patients? Ann Hematol. 2010;89(12):1265-1275.

SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

How to cite this article: Rockholt MM, Thorarsdottir HR, Lazarevic V, Rundgren M, Kander T. Central venous catheter-related complications in hematologic patients: An observational study. Acta Anaesthesiol Scand. 2022;66:473-482. doi:10.1111/aas.14020