Received: 19 July 2022 | Accepted: 19 August 2022

DOI: 10.1111/bjh.18442

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

LETTER TO THE EDITOR

Central venous catheter-related bloodstream infections in patients with haematological malignancies during the SARS-CoV-2 pandemic

Patients with haematological malignancies are at increased risk for infectious complications. This also applies to infections due to central venous catheters (CVC), which account for a significant proportion of morbidity and mortality in these high-risk patients.[1] Therefore, implementation of infection prevention bundles is important. Maximal sterile barrier precautions during CVC insertion or guidewire exchange are strongly recommended including wearing a mask.[2] Furthermore, surveillance of patients with a CVC is encouraged to determine and monitor trends in infection rates and to assist in identifying lapses in infection control practice.[2]

To date, the SARS-CoV-2 pandemic has changed our awareness of infection control measures.[3,4]

We therefore hypothesize, that CVC-related bloodstream infections (CRBSI) in patients with haematological malignancies might be less common during the SARS-CoV-2 pandemic due to more stringently applied hygiene measures are not only followed during CVC insertion but potentially throughout the whole patient stay by hospital staff, patients and visitors. Thus, CRBSI surveillance data before and during the SARS-CoV-2 pandemic were compared.

We used data from the SECRECY registry, an ongoing, clinical CRBSI registry established in March 2013, currently active in six German sites. Surveillance data are documented on CRBSI of non-selected, consecutive patients with short-term, non-tunnelled jugular, subclavian or femoral vein CVCs inserted for routine clinical use. All CVCs were inserted according to local standard operating procedures following current guidelines.[5] CRBSI were classified according to the 2012 Infectious Diseases Working Party (AGIHO) of the German Society of Haematology and Medical Oncology (DGHO) definition.[1] No changes were made regarding CVC insertion procedures and CVC care by the sites over time.

For the present analysis, of all cases documented registry data on jugular and subclavian CVC with CVC *in situ* at least one day were used. Only CRBSI cases classified as *definite* CRBSI (dCRBSI) and the combination of *definite* and *probable* (dpCRBSI)[1] were considered. The primary end-point was dCRBSI incidence. *Definite* CRBSI is subject to the strictest diagnostic criteria,[1] and seemed to yield more consistent epidemiological parameters.[6] For epidemiological studies, it is recommended to use CRBSI incidence (incidence density; calculated per 1000 CVC days).[7]

All of the six currently active sites are documenting patients with CVC cases since the third quarter of 2018 (3q2018). As the WHO has declared the SARS-CoV-2 outbreak a global pandemic at the end of the first quarter of 2020 (1q2020), on 11 March 2020,[3] we have chosen the time from the beginning of the second quarter of 2020 (2q2020) to the end of the fourth quarter of 2021 (4q2021) as 'during' the pandemic. The time from 3q2018 to 1q2020 was defined as 'before' the pandemic, so that both time periods are made up of seven quarters each.

Statistical analysis was performed using OpenEpi, version 3.01 (https://www.openepi.com), and IBM® SPSS® Statistics, version 28 (IBM Corp., Armonk, NY, USA). Two-sided *p* values <0.05 were considered statistically significant. Statistical tests used are detailed in Table 1.

We identified a total of 2553 CVC with 1474 CVC inserted before and 1079 during the pandemic (Table 1). Most patients suffered from haematological malignancies [2357 (92.3%)]. The great majority of patients were neutropenic at the time of CRBSI diagnosis and rates of neutropenia at the time of dCRBSI and dpCRBSI during both time periods were not different ($p = 0.121$ for dCRBSI, and $p = 0.144$ for dpCRBSI).

Looking at the primary end-point, the dCRBSI incidence was significantly lower during as compared to before the pandemic (1.9 vs 3.9 per 1000 CVC days; $p < 0.001$), and the same is true for the incidence of dpCRBSI (3.5 vs 6.1 per 1000 CVC days; $p < 0.001$), the dCRBSI rate (2.9% vs 6.0%; $p < 0.001$) and the dpCRBSI rate (5.4% vs 9.4%; $p < 0.001$) (Table 1). In a time-to-event analysis there were also fewer dCRBSI [hazard ratio (HR) 0.47, 95% confidence interval (95% CI) 0.31–0.70; $p < 0.001$] and dpCRBSI (HR 0.56, 95% CI 0.41–0.76; $p < 0.001$) during the pandemic compared to before (Figure 1).

In summary, we found about 50% fewer CRBSI cases during the pandemic as compared to the equivalent time period before. This is somewhat unexpected, as there were no changes regarding CVC insertion procedures or care by the participating sites during the time periods. Also, there were no differences in terms of underlying diseases or most CVC characteristics.

TABLE 1 Comparison of characteristics of patients, CVC and CRBSI of both periods

	Before pandemic *n* = 1474	During pandemic *n* = 1079	*p* value
Patients			
Median age, years (IQR)	59 (49–66)	60 (51–66)	0.010[d]
Men, *n* (%)	827 (56.1)	656 (60.8)	0.019[e]
Underlying disease, *n* (%)			
Acute myeloid leukaemia	532 (36.1)	383 (35.5)	0.160[e]
Acute lymphoblastic leukaemia	117 (7.9)	78 (7.2)	
Non-Hodgkin lymphoma	285 (19.3)	236 (21.9)	
Multiple myeloma	321 (21.8)	229 (21.2)	
Hodgkin lymphoma	41 (2.8)	26 (2.4)	
MDS/MPN	71 (4.8)	38 (3.5)	
Cytopenia	28 (1.9)	10 (0.9)	
Germ cell tumour	26 (1.8)	20 (1.9)	
Carcinoma	25 (1.7)	23 (2.1)	
Sarcoma	19 (1.3)	23 (2.1)	
Infection	3 (0.2)	6 (0.6)	
Others[a]	6 (0.4)	7 (0.6)	
CVC			
Median CVC time, days (95% CI)	15 (14.4–15.6)	15 (14.3–15.7)	0.576[g]
Internal jugular vein, *n* (%)	1306 (88.6)	1048 (97.1)	<0.001[e]
Antimicrobial-coated, *n* (%)	231 (15.7)	187 (17.3)	0.279[e]
CHG-coated dressings, *n* (%)	463 (31.4)	309 (28.6)	0.138[e]
Neutropenia[b] at insertion, *n* (%)	261 (17.7)	177 (16.4)	0.396[e]
Neutropenia[b] at dCRBSI diagnosis, *n*/*N* (%)	68/89 (76.4)	28/31 (90.3)	0.121[e]
Neutropenia[b] at dpCRBSI diagnosis, *n*/*N* (%)	111/138 (80.4)	52/58 (89.7)	0.144[e]
Neutropenia[b] at removal, *n* (%)	476 (32.3)	319 (29.6)	0.153[e]
High-risk CVC for CRBSI[c], *n* (%)	681 (46.2)	541 (51.1)	0.050[e]
CRBSI			
Incidence, *x*/1000 CVC days (95% CI)			
dCRBSI	3.9 (3.2–4.9)	1.9 (1.3–2.6)	<0.001[h]
dpCRBSI	6.1 (5.1–7.2)	3.5 (2.6–4.5)	<0.001[h]
Cumulative incidence, % (95% CI)			
dCRBSI	41.6 (8.1–75.1)	9.1 (3.4–14.8)	<0.001[g]
dpCRBSI	49.3 (19.1–79.5)	15.0 (8.9–21.1)	<0.001[g]
Rate, *n* (% [95% CI])			
dCRBSI	89 (6.0 [4.9–7.4])	31 (2.9 [2.0–4.0])	<0.001[e]
dpCRBSI	138 (9.4 [8.0–11.0])	58 (5.4 [4.2–6.9])	<0.001[e]
Causative pathogens, *n*/*N* (%)			
dCRBSI			
CoNS	63/89 (70.8)	25/31 (80.6)	0.770[f]
Enterobacteriaceae	6/89 (6.7)	1/31 (3.2)	
Other Gram-negative bacteria	5/89 (5.6)	0	
Other Gram-positive bacteria	9/89 (10.1)	3/31 (9.7)	
Candida spp.	3/89 (3.4)	1/31 (3.2)	
Multimicrobial	3/89 (3.4)	1/31 (3.2)	

TABLE 1 (Continued)

	Before pandemic $n = 1474$	During pandemic $n = 1079$	p value
dpCRBSI			
CoNS	91/138 (65.9)	43/58 (74.1)	0.767[f]
Enterobacteriaceae	8/138 (5.8)	2/58 (3.4)	
Other Gram-negative bacteria	5/138 (3.6)	1/58 (1.7)	
Other Gram-positive bacteria	23/138 (16.7)	8/58 (13.8)	
Candida spp.	6/138 (4.3)	1/58 (1.7)	
Multimicrobial	5/138 (3.6)	3/58 (5.2)	

Abbreviations: CHG, chlorhexidine gluconate; CoNS, coagulase-negative staphylococci; CRBSI, CVC-related bloodstream infection; CVC, central venous catheter; dCRBSI, definite CRBSI; dpCRBSI, combined definite plus probable CRBSI; IQR, interquartile range; MDS/MPN myelodysplastic syndrome/myeloproliferative neoplasm; 95% CI, 95% confidence interval.

[a]Including e.g., bleeding, haemophilia, parenteral nutrition.

[b]Neutrophils <500/μl or white blood count <1000/μl.

[c]One point for male or complicated CVC insertion, two points for diagnosis of acute myeloid leukaemia, multiple myeloma, or non-Hodgkin lymphoma; high-risk 3–4 points.[8]

[d]Welch test.

[e]Fisher's exact test.

[f]Pearson's χ^2 test.

[g]Log-rank test.

[h]Mid-P exact test.

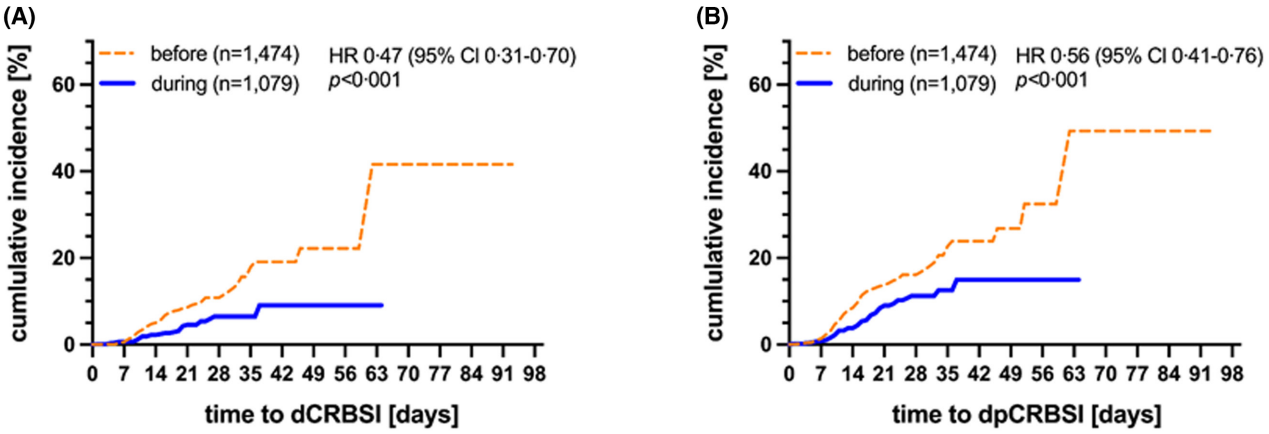

FIGURE 1 Cumulative incidence of (A) dCRBSI and (B) dpCRBSI during and before SARS-CoV-2 pandemic. Abbreviations: CRBSI, central venous catheter-related bloodstream infection; dCRBSI, definite CRBSI; dpCRBSI, combined definite and probable CRBSI; HR, hazard ratio; 95% CI, 95% confidence interval.

As previously shown, male sex, complicated CVC insertion, diagnosis of acute myeloid leukaemia, multiple myeloma or non-Hodgkin lymphoma are independent risk factors for CRBSI at time of CVC insertion (HR 1.59; $p = 0.02$).[8] In the present analysis the number of high-risk CVCs was numerically higher during the pandemic than the before the pandemic (51.1% vs 46.2; $p = 0.050$) so that even more cases of CRBSI should have been expected. Furthermore, although there were numerically more patients neutropenic during the pandemic, this did not translate into more CRBSI. As stated in Table S1, one centre had a markedly reduced CVC insertion/documentation rate during the pandemic, and the six centres had no similar CRBSI incidences/rates. Therefore, a centre effect cannot be ruled out. However, we found an equal (numerical) reduction of dCRBSI incidence/rate at each centre. Due to fewer CVC insertions/documentations during the pandemic, one might assume this may have influenced the result of our study. Therefore, we have compared the data before and during the pandemic without the mentioned centre. Even without this centre we found a significant decrease in dCRBSI incidence (3.7 vs 1.8/1000 CVC days; $p < 0.001$) and dCRBSI rate (5.5% vs 2.7%; $p = 0.001$). Therefore, we think that the change in CVC insertion/documentation rate would not be an explanation for the fewer CRBSIs during the pandemic.

Potential reasons for the lower CRBSI incidence during the pandemic are unclear at the moment. At this point in time we can only speculate that rigorous and stringent hygiene measurements (beyond our standard CVC-related procedures) during the pandemic might have resulted in lower rates of CRBSI.[9] During the pandemic healthcare staff and, to a lesser extent, also patients were consistently

wearing face masks, which may have had an impact on the CRBSI incidence during the pandemic. In addition, contact restrictions during the pandemic reduced the number of visits to the patients by relatives and other non-healthcare professionals. This might have been associated with less CVC manipulations (fewer disconnections of long-running infusions for walks outside the hospital ward, etc.) which in turn may have resulted in a lower CRBSI risk. Intensified hand hygiene/disinfection during the pandemic[3,4,10] may also have had an impact on the CRBSI risk.[1,2]

In conclusion, our data provide some evidence that the incidence of CRBSI in patients with haematological malignancies was reduced during the SARS-CoV-2 pandemic, probably as a result of stricter overall hygiene measures[10] which may also have contributed to a general lower incidence of infectious diseases.[11,12] However, not only hygiene, but also thorough surveillance, including awareness, may have contributed to the significant reduction in CRBSI.

AUTHOR CONTRIBUTIONS

Enrico Schalk designed the study, collected and analysed the data and wrote the manuscript. Timo Schmitt collected the data, interpreted the data and revised the manuscript. Jens Panse interpreted the data and revised the manuscript. Eva Fiegle collected the data, interpreted the data and revised the manuscript. Jan-Hendrik Naendrup collected the data, interpreted the data and revised the manuscript. Martin Schmidt-Hieber interpreted the data and revised the manuscript. Boris Böll interpreted the data and revised the manuscript. Marcus Hentrich interpreted the data and revised the manuscript. Daniel Teschner interpreted the data, and revised the manuscript. Dimitrios Mougiakakos interpreted the data, and revised the manuscript. All authors were involved in patient management and approved the final version of the manuscript.

KEYWORDS

central venous catheter, central venous catheter-related bloodstream infection, epidemiology, haematological malignancies, pandemic, SARS-CoV-2

ACKNOWLEDGEMENT

The authors thank all SECRECY staff for their great support and documentation.

FUNDING INFORMATION

The authors received no financial support for the research, authorship, and/or publication of this article.

CONFLICTS OF INTEREST

All authors have no competing interests to declare that are relevant to the content of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL STATEMENT

The study was approved by the central ethics committee (Magdeburg University Hospital, approval no. 84/14) as well as by respective local ethics committees.

PATIENT CONSENT STATEMENT

Given the nature of routine clinical data and the anonymization of patient data, written informed consent was not required within the study.

CLINICAL TRIAL REGISTRATION

SECRECY (Study to Evaluate Central Venous Catheter-related Infections in Haematology and Oncology) was registered in the German Clinical Trial Register (DRKS; no. DRKS00006551).

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

Enrico Schalk[1]
Timo Schmitt[2]
Jens Panse[3,4]
Eva Fiegle[3,4]
Jan-Hendrik Naendrup[4,5]
Martin Schmidt-Hieber[6]
Boris Böll[4,5]
Marcus Hentrich[7]
Daniel Teschner[2,8]
Dimitrios Mougiakakos[1]

[1]*Department of Haematology and Oncology, Medical Centre, Otto-von-Guericke University Magdeburg, Magdeburg, Germany*
[2]*Department of Haematology, Medical Oncology and Pneumology, University Medical Centre of the Johannes Gutenberg-University, Mainz, Germany*
[3]*Department of Oncology, Haematology, Haemostaseology and Stem Cell Transplantation, University Hospital RWTH Aachen, Aachen, Germany*
[4]*Centre for Integrated Oncology (CIO), Aachen, Bonn, Cologne, Düsseldorf (ABCD), Germany*
[5]*Department of Internal Medicine I, University Hospital of Cologne, Cologne, Germany*
[6]*Clinic of Haematology, Oncology and Pneumology, Carl-Thiem-Hospital Cottbus, Cottbus, Germany*
[7]*Department of Haematology and Oncology, Red Cross Hospital Munich, Munich, Germany*
[8]*Department of Internal Medicine II, University Hospital Würzburg, Würzburg, Germany*

Correspondence
Enrico Schalk, Otto-von-Guericke University Magdeburg, Medical Centre, Department of Haematology and Oncology, Leipziger Str. 44, D-39120 Magdeburg, Germany.
Email: enrico.schalk@med.ovgu.de

ORCID

Enrico Schalk https://orcid.org/0000-0003-1892-5098
Timo Schmitt https://orcid.org/0000-0002-6111-6942
Jens Panse https://orcid.org/0000-0001-6316-3112
Eva Fiegle https://orcid.org/0000-0002-1639-5751
Jan-Hendrik Naendrup https://orcid.org/0000-0002-6420-7938
Martin Schmidt-Hieber https://orcid.org/0000-0002-3071-6945
Boris Böll https://orcid.org/0000-0002-6432-0981
Marcus Hentrich https://orcid.org/0000-0001-5622-348X
Daniel Teschner https://orcid.org/0000-0001-7351-8060
Dimitrios Mougiakakos https://orcid.org/0000-0002-2817-6660

REFERENCES

1. Hentrich M, Schalk E, Schmidt-Hieber M, Chaberny I, Mousset S, Buchheidt D, et al. Central venous catheter-related infections in hematology and oncology: 2012 updated guidelines on diagnosis, management and prevention by the infectious diseases working Party of the German Society of hematology and medical oncology. Ann Oncol. 2014;25(5):936–47. https://doi.org/10.1093/annonc/mdt545
2. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. MMWR Recomm Rep. 2002;51(RR-10):1–29.
3. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020;91(1):157–60. https://doi.org/10.23750/abm.v91i1.9397
4. Lee JK, Bullen C, Ben Amor Y, Bush SR, Colombo F, Gaviria A, et al. Institutional and behaviour-change interventions to support COVID-19 public health measures: a review by the lancet commission task force on public health measures to suppress the pandemic. Int Health. 2021;13(5):399–409. https://doi.org/10.1093/inthealth/ihab022
5. Böll B, Schalk E, Buchheidt D, Hasenkamp J, Kiehl M, Kiderlen TR, 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):239–59. https://doi.org/10.1007/s00277-020-04286-x
6. Schalk E, Vehreschild MJGT, Biehl LM. Influence of different definitions of central venous catheter-related bloodstream infections on epidemiological parameters in cancer patients. Infect Control Hosp Epidemiol. 2021;42(4):501–3. https://doi.org/10.1017/ice.2020.274
7. Bouza E, Burillo A, Muñoz P. Catheter-related infections: diagnosis and intravascular treatment. Clin Microbiol Infect. 2002;8(5):265–74. https://doi.org/10.1046/j.1469-0691.2002.00385.x
8. Schalk E, Toelle D, Schulz S, Einhell S, Prinz J, Pelzer B, et al. Identifying haematological cancer patients with high risk for central venous catheter (CVC)-related bloodstream infections at the time point of CVC insertion. 29th European congress of clinical microbiology and infectious diseases, April 13–16, 2019, Amsterdam, The Netherlands, abstract P2556. [Accessed May 30, 2022]. Available from: https://www.escmid.org/escmid_publications/escmid_elibrary
9. Roshan R, Shahil Feroz A, Rafique Z, Virani N. Rigorous hand hygiene practices among health care workers reduce hospital-associated infections during the COVID-19 pandemic. J Prim Care Community Health. 2020;11:2150132720943331. https://doi.org/10.1177/2150132720943331
10. Giesen N, Sprute S, Rüthrich M, Khodamoradi Y, Mellinghoff SC, Beutel G, et al. Evidence-based management of COVID-19 in cancer patients: guideline by the infectious diseases working party (AGIHO) of the German Society for Haematology and Medical Oncology (DGHO). Eur J Cancer. 2020;140:86–104. https://doi.org/10.1016/j.ejca.2020.09.009
11. Ullrich A, Schranz M, Rexroth U, Hamouda O, Schaade L, Diercke M, et al. Impact of the COVID-19 pandemic and associated non-pharmaceutical interventions on other notifiable infectious diseases in Germany: an analysis of national surveillance data during week 1-2016 - week 32-2020. Lancet Reg Health Eur. 2021;6:100103. https://doi.org/10.1016/j.lanepe.2021.100103
12. Oh DY, Buda S, Biere B, Reiche J, Schlosser F, Duwe S, et al. Trends in respiratory virus circulation following COVID-19-targeted non-pharmaceutical interventions in Germany, January - September 2020: analysis of national surveillance data. Lancet Reg Health Eur. 2021;6:100112. https://doi.org/10.1016/j.lanepe.2021.100112

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.