Impact of the COVID-19 pandemic on therapeutic interventional oncology procedures and diagnostic CT/MRI examinations at a German university hospital

Einfluss der COVID-19-Pandemie auf die Anzahl interventioneller onkologischer Therapien und diagnostischer CTs/MRTs an einem deutschen Universitätsklinikum

Authors

Heiner Nebelung, Christoph Georg Radosa, Felix Schön, Sophia Freya Ulrike Blum, Christian Böhme, Ralf-Thorsten Hoffmann, Verena Plodeck

Affiliations

Institute and Polyclinic for Diagnostic und Interventional Radiology, Faculty of Medicine and University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

Key words

interventional procedures, MR-imaging, CT, COVID-19 pandemic

received 14.01.2023
accepted 16.04.2023
published online 24.05.2023

Bibliography

Fortschr Röntgenstr 2023; 195: 707–712
DOI 10.1055/a-2081-4012
ISSN 1438-9029

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Correspondence

Dr. Heiner Nebelung
Institute und Polyclinic for Diagnostic and Interventional Radiology, University Hospital Carl Gustav Carus, Fetscherstr. 74, 01307 Dresden, Germany
Tel.: +49/351/45 81 16 45
heiner.nebelung@uniklinikum-dresden.de

ABSTRACT

Purpose The COVID-19 pandemic led to the implementation of severe restrictions on public life in Germany and a reduction in the number of non-COVID patients presenting for care. The aim of this study was to measure the impact on the number of therapeutic interventional oncology procedures in relation to diagnostic imaging studies at a high-volume radiology department.

Materials and Methods The numbers of therapeutic interventional oncology procedures and diagnostic CT/MRI examinations for the years 2010 to 2021 were extracted using the hospital information system. Monthly data from January 2010 to December 2019 were used to build forecasting models for the timeframe from January 2020 to December 2021. Real procedure numbers were compared with predicted numbers to calculate residual differences, which were considered statistically significant if the real number was outside the 95 % confidence interval ($p < 0.05$).

Results During the first German lockdown (March/April 2020), the number of outpatient CT/MRI examinations decreased significantly, with a less pronounced decrease of overall CT/MRI numbers. The second German lockdown (January-May 2021) led to lower than predicted outpatient CT numbers, whereas outpatient MRI numbers in part even exceeded predicted numbers and overall CT/MRI numbers stayed within confidence limits. The lockdowns had a more pronounced negative effect on the number of oncological MRI examinations compared to CT examinations. The number of therapeutic interventional oncology procedures showed no significant decrease during both lockdowns.

Conclusion Lockdown measures had minor impact on the number of therapeutic interventional oncology procedures, possibly due to a shift from more resource-intensive therapies like surgery towards interventional oncology. The overall numbers of diagnostic imaging decreased during the first lockdown, while the second lockdown had less negative impact. The number of oncological MRI examinations was affected most severely. To avoid adverse outcomes, specific protocols for patient management during future pandemic outbreaks should be implemented and continuously adapted.

Key Points

- COVID-19 lockdowns had minor effect on therapeutic interventional oncology procedures.
- Numbers of diagnostic outpatient imaging procedures dropped markedly, especially during the first lockdown.
- The number of oncological MRI examinations showed a significant decrease during both lockdowns.

Citation Format

- Nebelung H, Radosa CG, Schön F et al. Impact of the COVID-19 pandemic on therapeutic interventional oncology procedures and diagnostic CT/MRI examinations at a German university hospital. Fortschr Röntgenstr 2023; 195: 707–712

ZUSAMENFASSUNG

Ziel Die COVID-19-Pandemie führte zu schweren Einschränkungen des öffentlichen Lebens in Deutschland und zu einer reduzierten Zahl an Patientenvorstellungen von Non-COVID-Patienten. Das Ziel dieser Studie war es, den Einfluss auf die Zahl interventioneller onkologischer Therapien im Verhältnis zu diagnostischer Bildgebung im radiologischen Institut eines Supramaximalversorgers zu untersuchen.

Material und Methoden Die Anzahl interventioneller onkologischer Therapien und diagnostischer CTs/MRTs der Jahre 2010 bis 2021 wurde über das Krankenhausinformationssystem extrahiert. Monatliche Daten von Januar 2010 bis Dezember 2019 wurden zur Erstellung von Vorhersage-Modellen für Januar 2020 bis Dezember 2021 genutzt. Die realen Zahlen wurden mit den vorhergesagten Zahlen verglichen, um residuale Unterschiede zu berechnen. Diese wurden als statistisch signifikant betrachtet, wenn die reale Zahl außerhalb des 95 %-Konfidenzintervalls lag ($p < 0.05$).

Ergebnisse Während des ersten deutschen Lockdowns (März/April 2020) zeigte sich ein signifikanter Abfall der ambulanten CTs/MRTs, während die Gesamtzahlen weniger deutlich absanken. Der zweite deutsche Lockdown (Januar-Mai 2021) führte zu ambulanten CT-Zahlen unterhalb des Vorhersagewertes, wohingegen die MRT-Zahlen teils sogar oberhalb des Vorhersagewertes lagen. Die Gesamtzahlen blieben innerhalb des Vorhersageintervalls. Die Anzahl onkologischer -MRTs wurde stärker beeinträchtigt als die Anzahl onkologischer CTs. Die Anzahl interventioneller onkologischer Therapien zeigte keinen signifikanten Abfall während der Lockdowns.

Schlussfolgerung Beide Lockdowns nahmen lediglich geringen Einfluss auf die Anzahl interventioneller onkologischer Therapien, möglicherweise durch eine Abnahme und Umverteilung von ressourcen-intensiveren Therapien in Richtung interventioneller Onkologie. Die Gesamt-CT- und -MRT-Zahlen nahmen während des ersten Lockdowns ab, während der zweite Lockdown weniger negativen Einfluss ausübte. Den stärksten Rückgang zeigte die Zahl onkologischer MRTs. Um negative Auswirkungen auf das Patienten-Outcome zu vermeiden, sollten spezifische Protokolle etabliert und kontinuierlich weiterentwickelt werden.

Kernaussagen

- COVID-19-Lockdowns hatten keinen relevanten Einfluss auf die Anzahl interventioneller onkologischer Therapien.
- Ambulante diagnostische Untersuchungszahlen zeigten hingegen deutliche Einbußen, insbesondere während des ersten Lockdowns.
- Die Zahl onkologischer MRTs zeigte während beider Lockdowns signifikante Rückgänge.

ABBREVIATIONS AND ACRONYMS

IR	interventional radiology
IRP	interventional radiology procedure
IOP	interventional oncology procedure
UCC	University Cancer Center

Introduction

The ongoing COVID-19 pandemic has had an unprecedented impact on healthcare systems worldwide. Due to government-imposed restrictions, public life in Germany almost came to a standstill between March and April 2020 [1] and to a lesser degree during the second lockdown between January and May 2021 [2, 3]. This, in combination with fear and uncertainty regarding coronavirus infection among patients, led to a significant decrease in patients presenting for diagnostic imaging and treatment [4–6]. Multiple studies have shown that there were fewer hospital presentations as well as admissions of patients with, e. g., myocardial infarction and stroke, and also of cancer patients [7–10]. A stage shift in cancer patients could be the consequence [11–14].

Interventional radiology (IR) plays an important role in the treatment of oncological patients, especially in patients with hepatic tumors, but increasingly also in pulmonary and renal lesions [15–19]. Interventional oncology as a therapeutic option for oncological patients is of particular interest during times of added strain on resource-intensive areas like surgery. Several studies have investigated the impact of the COVID-19 pandemic on IR services. Studies from the US and UK [20, 21] found a significant decrease in the number of interventional radiology procedures (IRPs), including interventional oncology procedures (IOPs), whereas a Singaporean study found no significant difference in comparison to previous years [22]. A study by Zattra et al. investigated the impact of the COVID-19 pandemic on cancer imaging in the US and concluded that cancer imaging was severely impacted [23].

The aim of our study was to assess the influence of the COVID-19 pandemic and subsequent lockdown measures on the number of therapeutic IOPs and diagnostic imaging studies at a German university hospital with high volumes of IRPs.

Patients and Methods

The number of diagnostic CT and MRI examinations and therapeutic IOPs that were performed at our institution was analyzed retrospectively. Therapeutic IOPs performed at our institution

include transarterial chemoembolization of hepatic tumors as well as radiofrequency and microwave ablation of hepatic, pulmonary, and renal tumors. Non-therapeutic IOPs like biopsies were not included. The number of therapeutic IOPs as well as diagnostic inpatient and outpatient CT and MRI examinations was extracted per month from the radiology information system (ORBIS, Dedalus HealthCare, Germany) for the years 2010 to 2021. In a subgroup analysis, the number of CT and MRI examinations performed on request by our University Cancer Center (UCC) was reviewed. The overall number of oncological imaging examinations is difficult to determine due to multiple requesting departments, incorrect wording on requests, etc. Therefore, we chose referrals by the UCC as a surrogate marker for oncological imaging.

Forecasting models were built using SPSS (IBM Corp. Released 2022. IBM SPSS Statistics for Windows, Version 29.0., USA). We used monthly data from January 2010 to December 2019 to predict expected monthly data from January 2020 to December 2021 with a 95 % confidence interval. The real numbers of procedures from January 2020 to December 2021 were compared with the predicted numbers to calculate residual differences, which were considered statistically significant if the real number was outside of the 95 % confidence interval of the forecasting model's prediction ($p < 0.05$).

Institutional Review Board approval was obtained. Written informed consent was waived by the Institutional Review Board. All performed procedures were part of routine clinical care.

Diagrams and tables were created using Microsoft Office Excel 2019 (Microsoft Corporation, USA).

Results

All results are summarized in ▶ **Fig. 1**.

CT

During the first German lockdown (March/April 2020), outpatient CT examinations showed a significant decrease, which was most pronounced in April 2020. For the remaining year, the number of CT examinations recovered partially but remained below the predicted numbers. During the second lockdown (January to May 2021), the number of examinations did not drop significantly but remained below the predicted numbers.

The number of inpatient CT examinations was also below the predicted numbers in early 2020, with a significant decrease in May immediately after the first lockdown. During the following months, the number of inpatient CT scans stayed close to the predicted numbers, while the number significantly exceeded the predicted number shortly prior to the second lockdown and remained higher than predicted during the lockdown.

The number of CT examinations performed after referrals from the UCC stayed around the predicted number during both lockdowns and did not show a significant decrease.

MRI

During the first German lockdown (March/April 2020), the number of outpatient MRI examinations was below the predicted numbers, with a significant drop in March. In the months after the lockdown, the number of examinations was higher than predicted and during the remaining year stayed close to the predicted level. During the second lockdown (January to May 2021), the number dropped minimally below the predicted level in January, while it exceeded the predicted levels from February to May and even showed a significant increase in March 2021.

The number of inpatient MRI examinations stayed close to the predicted levels during the first lockdown. During the second lockdown, there was a sharp, but not quite significant decrease in January 2021, but the number of examinations recovered by March.

The number of MRI examinations performed after referrals from the UCC decreased significantly at the beginning of the first lockdown in March 2020 and recovered in April up to the predicted number. During the second lockdown, the number of examinations was always below the predicted levels, with significant drops in all months except March 2021.

IOPs

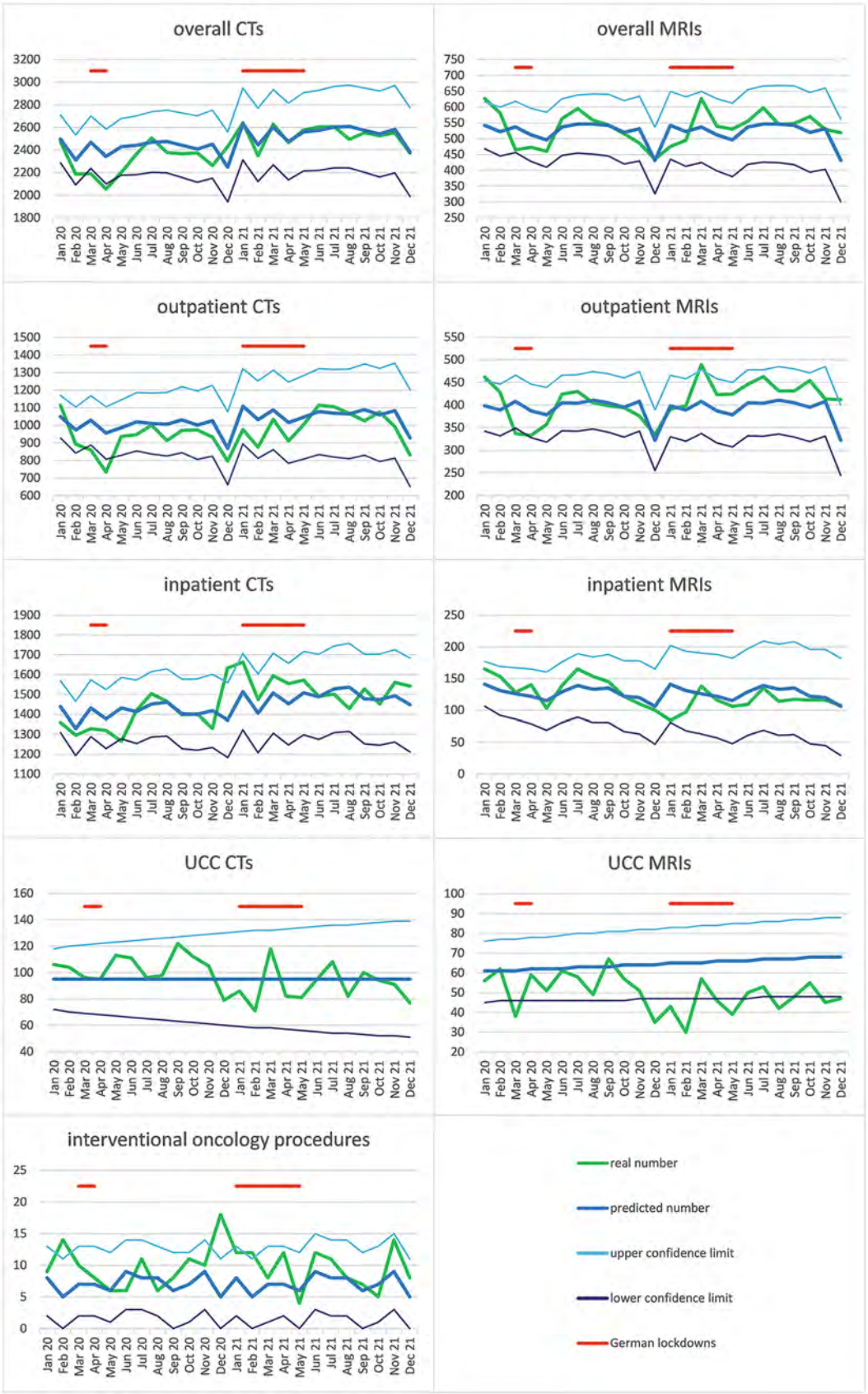
The number of therapeutic IOPs did not show a significant decrease during both lockdowns but moved around predicted levels, with a tendency to higher than predicted numbers in 2021. Immediately prior to both lockdowns (February 2020/December 2020), the number of procedures exceeded the upper confidence limit.

Discussion

The COVID-19 pandemic has had a tremendous influence on health care systems worldwide. Our study shows that the number of outpatient diagnostic CT and MRI examinations decreased significantly during the first lockdown, while the second lockdown had overall less of an effect. Regarding patients referred by the University Cancer Center, the number of CT examinations showed no significant decrease, while the number of MRI examinations dropped significantly during both lockdowns. The number of therapeutic IOPs on the other hand was not affected, showing no decrease during both lockdowns.

We found a more pronounced decrease in the overall number of outpatient CT examinations compared to outpatient MRI examinations, which could be due to a different case composition in MR and CT imaging at our institution and a lower number of patients presenting for, e. g., trauma-related CT scans during the lockdowns. The number of inpatient CT and MRI examinations did not show a significant decrease during the lockdowns, which might be caused by a shift from outpatient to inpatient imaging and a marked increase in thoracic CT examinations in COVID-19-patients. The smaller effect of the second lockdown in 2021 compared to the first lockdown in 2020 could be due to newly established standardized protocols and adapted patient and hospital staff behavior [24–26].

Several studies have assessed the effect of the COVID-19 pandemic on IR services. Two studies found a marked decrease of IRPs in the UK and US in March and April 2020, compared to the same time period in 2019. The study by Cahalane et al. showed a 46 % reduction in the number of IRPs, with a 17 % decrease (35 versus



▶ **Fig. 1** Monthly real and predicted numbers with upper and lower confidence limits in 2020 and 2021 (UCC: University Cancer Center).

29) in IOPs [20]. The IOPs in this study included inter alia ports, catheters, and tumor biopsies, which reduces comparability to our study. Nevertheless, it also demonstrated a less pronounced reduction in the number of IOPs.

A multicenter study including data from six NHS trusts and health boards in the UK by Zhong et al. found a 31 % decrease in the overall IR caseload, with a 91.7 % (24 cases in March/April 2019 compared to 2 in March/April 2020) reduction in the number of image-guided ablation procedures [21]. The number of abdominal embolization procedures dropped by 57.4 % (108 versus 46), but the article does not elaborate on which procedures were included in this number. Different national or local approaches to COVID-19-associated restrictions of hospital resources or differences in patient behavior are possible explanations.

A study from Singapore showed similar results to our study, with only a 5.1 % decrease in the total number of IRPs within the first half of 2020 compared to the same time period in 2019 and a similar distribution of the weekly number of IRPs [22]. IOPs made up 13 % of IRPs in 2019 and 12.1 % in 2020. The overall lower decrease in IRPs in comparison to the abovementioned studies could be due to better preparation in Singapore with regards to pandemic protocols and measures after having gone through the SARS-CoV outbreak in 2003 and the H1N1 pandemic in 2009 [27, 28].

Elective cancer surgery significantly decreased due to the COVID-19 outbreak, particularly during the lockdowns [13]. This development was likely multifactorial, with fewer patient presentations and admissions, staff shortages, and reduced operating room availability playing a role [9–14]. At our hospital, around 30 % of non-emergency surgical procedures were postponed and up to six operating rooms were closed. The reduced offer of surgical services might have caused a shift to therapeutic IOPs, which require fewer resources and allow for shorter hospital stays [29, 30].

Few studies have investigated the effect of the COVID-19 pandemic on diagnostic imaging studies. Zattra et al. analyzed trends in oncological CT imaging between January and November 2020 and concluded that cancer imaging was severely impacted, with the number of outpatient screenings and initial workups in particular not recovering to pre-COVID levels [23]. They also observed an increase in inpatient and emergency department CT examinations from March 2020 on. This is in keeping with our findings of reduced overall outpatient CT and MR imaging during the first German lockdown and a shift towards inpatient CT imaging immediately after the first lockdown and during the second lockdown.

In our study, the number of MRI examinations requested by the UCC decreased significantly during both lockdowns. In contrast, we could not demonstrate a decrease in the number of CT examinations on referral by the UCC, which could be due to a shift of patients from MR towards CT imaging, since resources are generally more limited in MRI and examinations are much more time-consuming. Another possible explanation is our use of referrals by the UCC as a surrogate marker for oncological imaging, which does not include all oncological imaging performed.

The use of the abovementioned surrogate marker for oncological imaging is a limitation of this study, as well as the relatively low monthly number of therapeutic IOPs and the considerable variability of the number of procedures performed each month, which impedes assessment of the influence of external factors.

In conclusion, our single-center study shows less influence of lockdown measures on the number of therapeutic IOPs, compared to the number of overall diagnostic outpatient CT and MRI examinations. Oncological MRI examinations were affected most severely during the lockdowns. To avoid adverse patient outcomes, adequate protocols and pathways for diagnostic imaging during possible future pandemic outbreaks should be implemented.

Clinical Relevance

The COVID-19 pandemic has put an unprecedented strain on healthcare systems worldwide. To guarantee high-quality, timely patient care, data regarding the influence of the pandemic and consecutive government measures is vital. Interventional oncology procedures are resource-sparing and in this study no significant negative influence on the number of procedures during the lockdowns was shown. In contrast, the number of outpatient CT and MRI examinations was in part affected severely. Therefore, adequate triage protocols and pathways for future pandemic outbreaks are essential.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgements

We would like to thank RACOON (NUM) for the ongoing support.

References

[1] Besprechung der Bundeskanzlerin mit den Regierungschefinnen und Regierungschefs der Länder vom 22.03.2020. Webseite Bundesregierung Startseite. Im Internet (Stand: 31.03.2022): https://www.bundesregierung.de/breg-de/themen/coronavirus/besprechung-der-bundeskanzlerin-mit-den-regierungschefinnen-und-regierungschefs-der-laender-vom-22-03-2020-1733248

[2] Videoschaltkonferenz der Bundeskanzlerin mit den Regierungschefinnen und Regierungschefs der Länder am 5. Januar 2021. Bundesregierung Inf Startseite. Im Internet (Stand: 14.01.2023): https://www.bundesregierung.de/breg-de/service/archiv/videoschaltkonferenz-der-bundeskanzlerin-mit-den-regierungschefinnen-und-regierungschefs-der-laender-am-5-januar-2021-1834354

[3] Viertes Gesetz zum Schutz der Bevölkerung bei einer epidemischen Lage von nationaler Tragweite. Bundesgesetzblatt Teil I 2021; 802

[4] Sreedharan S, Mian M, McArdle DJT et al. The impact of the COVID-19 pandemic on diagnostic imaging services in Australia. J Med Imaging Radiat Oncol 2021. doi:10.1111/1754-9485.13291

[5] Alelyani M, Alghamdi A, Shubayr N et al. The Impact of the COVID-19 Pandemic on Medical Imaging Case Volumes in Aseer Region: A Retrospective Study. Medicines 2021; 8: 70. doi:10.3390/medicines8110070

[6] Effect of the COVID-19 Pandemic on Cancer Imaging – The ASCO Post. Im Internet (Stand: 17.03.2022): https://ascopost.com/news/december-2021/effect-of-the-covid-19-pandemic-on-cancer-imaging/

[7] He L, Lu F, Du X et al. Impact of COVID-19 Pandemic on Hospital Admissions of Acute Coronary Syndrome: A Beijing Inpatient Database Study. Lancet

Reg Health – West Pac 2022; 19: 100335. doi:10.1016/j.lanwpc.2021.100335

[8] Ärzteblatt DÄG Redaktion Deutsches. The Effect of the Lockdown on Patients with Myocardial Infarction During the COVID-19 Pandemic (02.07.2021). Dtsch Ärztebl. Im Internet (Stand: 17.03.2022): https://www.aerzteblatt.de/int/archive/article?id=219807

[9] Kapsner LA, Kampf MO, Seuchter SA et al. Reduced Rate of Inpatient Hospital Admissions in 18 German University Hospitals During the COVID-19 Lockdown. Front Public Health 2021; 8: 594117. doi:10.3389/fpubh.2020.594117

[10] Kirchberg J, Rentsch A, Klimova A et al. Influence of the First Wave of the COVID-19 Pandemic on Cancer Care in a German Comprehensive Cancer Center. Front Public Health 2021; 9: 750479. doi:10.3389/fpubh.2021.750479

[11] Maringe C, Spicer J, Morris M et al. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol 2020; 21: 1023–1034. doi:10.1016/S1470-2045(20)30388-0

[12] Stöss C, Steffani M, Pergolini I et al. Impact of the COVID-19 Pandemic on Surgical Oncology in Europe: Results of a European Survey. Dig Surg 2021; 38: 259–265. doi:10.1159/000515186

[13] Eskander A, Li Q, Hallet J et al. Access to Cancer Surgery in a Universal Health Care System During the COVID-19 Pandemic. JAMA Netw Open 2021; 4: e211104. doi:10.1001/jamanetworkopen.2021.1104

[14] Patt D, Gordan L, Diaz M et al. Impact of COVID-19 on Cancer Care: How the Pandemic Is Delaying Cancer Diagnosis and Treatment for American Seniors. JCO Clin Cancer Inform 2020: 1059–1071. doi:10.1200/CCI.20.00134

[15] Reig M, Forner A, Rimola J et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. J Hepatol 2022; 76: 681–693. doi:10.1016/j.jhep.2021.11.018

[16] Gennaro N, Schiaffino S, Mauri G et al. The What, the Why, and the How of Liver Ablations: A Practical Guide for the Medical Oncologist. Oncology 2021; 99: 722–731. doi:10.1159/000518358

[17] Van Cutsem E, Cervantes A, Adam R et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. Ann Oncol Off J Eur Soc Med Oncol 2016; 27: 1386–1422. doi:10.1093/annonc/mdw235

[18] Delpla A, de Baere T, Varin E et al. Role of Thermal Ablation in Colorectal Cancer Lung Metastases. Cancers 2021; 13: 908. doi:10.3390/cancers13040908

[19] Young S, Golzarian J, Anderson JK. Thermal Ablation of T1a Renal Cell Carcinoma: The Clinical Evidence. Semin Interv Radiol 2019; 36: 367–373. doi:10.1055/s-0039-1696650

[20] Cahalane AM, Cui J, Sheridan RM et al. Changes in Interventional Radiology Practice in a Tertiary Academic Center in the United States During the Coronavirus Disease 2019 (COVID-19) Pandemic. J Am Coll Radiol 2020; 17: 873–877. doi:10.1016/j.jacr.2020.05.005

[21] Zhong J, Datta A, Gordon T et al. The Impact of COVID-19 on Interventional Radiology Services in the UK. Cardiovasc Intervent Radiol 2021; 44: 134–140. doi:10.1007/s00270-020-02692-2

[22] How GY, Pua U. Trends of interventional radiology procedures during the COVID-19 pandemic: the first 27 weeks in the eye of the storm. Insights Imaging 2020; 11: 131. doi:10.1186/s13244-020-00938-8

[23] Zattra O, Fraga A, Lu N et al. Trends in cancer imaging by indication, care setting, and hospital type during the COVID-19 pandemic and recovery at four hospitals in Massachusetts. Cancer Med 2021; 10: 6327–6335. doi:10.1002/cam4.4183

[24] Curigliano G, Banerjee S, Cervantes A et al. Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. Ann Oncol 2020; 31: 1320–1335. doi:10.1016/j.annonc.2020.07.010

[25] Minko P, Bücker A, Reimer P et al. Stellungnahme der DeGIR zur Problematik der Verschiebung interventioneller Eingriffe während der COVID-19-Pandemie. Fortschr Röntgenstr 2020; 192: 1021–1022. doi:10.1055/a-1271-1644

[26] Antoch G, Urbach H, Mentzel H-J et al. SARS-CoV-2/COVID-19: Empfehlungen für die Radiologische Versorgung – Eine Stellungnahme der Deutschen Röntgengesellschaft (DRG), der Deutschen Gesellschaft für Neuroradiologie (DGNR), der Gesellschaft für Pädiatrische Radiologie (GPR), der Deutschen Gesellschaft für Interventionelle Radiologie (DeGIR), des Berufsverbands der Neuroradiologen (BDNR) und des Berufsverbands der Radiologen (BDR). Fortschr Röntgenstr 2020; 192: 418–421. doi:10.1055/a-1149-3625

[27] Outbreak of Severe Acute Respiratory Syndrome – Worldwide, 2003. Im Internet (Stand: 06.05.2022): https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5211a5.htm

[28] CDC. 2009 H1N1 Pandemic. Cent Dis Control Prev 2019; Im Internet (Stand: 06.05.2022): https://www.cdc.gov/flu/pandemic-resources/2009-h1n1-pandemic.html

[29] Denys A, Guiu B, Chevallier P et al. Interventional oncology at the time of COVID-19 pandemic: Problems and solutions. Diagn Interv Imaging 2020; 101: 347–353. doi:10.1016/j.diii.2020.04.005

[30] Johnston EW, von Stempel C, Singh S et al. Interventional oncology. Br J Hosp Med 2016; 77: C114–C117. doi:10.12968/hmed.2016.77.8.C114