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Review

Systematic review and meta-analysis determining the effect of implemented COVID-19 guidelines on surgical oncology volumes and clinical outcomes

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ABSTRACT

Background: To provide for Coronavirus Disease 2019 (COVID-19) healthcare capacity, (surgical oncology) guidelines were established, forcing to alter the timing of performing surgical procedures. It is essential to determine whether these guidelines have led to disease progression. This study aims to give an insight into the number of surgical oncology procedures performed during the pandemic and provide information on short-term clinical outcomes.

Materials and methods: A systematic literature search was performed on all COVID-19 articles including operated patients, published before March 21, 2022. Meta-analysis was performed to visualize the number of performed surgical oncology procedures during the pandemic compared to the pre-pandemic period. Random effects models were used for evaluating short-term clinical outcomes.

Results: Twenty-four studies containing 6762 patients who underwent a surgical oncology procedure during the pandemic were included. The number of performed surgical procedures for an oncological pathology decreased (−26.4%) during the pandemic. The number of performed surgical procedures for breast cancer remained stable (+0.3%). Moreover, no difference was identified in the number of ≥T2 (OR 1.00, P = 0.989), ≥T3 (OR 0.95, P = 0.778), ≥N1 (OR 1.01, P = 0.964) and major postoperative complications (OR 1.55, P = 0.134) during the pandemic.

Conclusion: The number of performed surgical oncology procedures during the COVID-19 pandemic decreased. In addition, the number of performed surgical breast cancer procedures remained stable. Oncological staging and major postoperative complications showed no significant difference compared to pre-pandemic practice. During future pandemics, the performed surgical oncology practice during the first wave of the COVID-19 pandemic seems appropriate for short-term results.

1. Introduction

During the pandemic Coronavirus disease-19 (COVID-19), the non-COVID-19 healthcare system was adjusted through newly developed measures, including the identification of surgical prioritization in the oncological field to deliver adequate Intensive Care Unit (ICU) capacity and available healthcare providers [1–4]. Due to the sudden emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and its rapid spread, the above-mentioned measures were developed with limited knowledge of SARS-CoV-2's viral behavior [5]. In addition, in the Netherlands, several guidelines were developed based on expert advice and limited knowledge of COVID-19, including in the field of surgical oncology [6]. The Dutch oncology-oriented guideline consisted of surgical prioritization recommendations. Identifying levels of surgical priority is necessary to determine if procedures can be postponed, balancing the risk between viral exposure and disease progression. The consequences of these implemented measures were noticeable in surgical and non-surgical oncological practice [7,8].

Currently, various vaccines are available to reduce the risk of mortality or severe illness caused by COVID-19 [9–11]. However, as long as COVID-19 continues to spread, there is a risk that new variants will emerge. In addition to the mutating nature of viruses, several factors contribute to an increased risk of developing new variants, including people's reluctance to receive COVID-19 vaccinations and limited or no access to vaccinations [12–14]. The aftermath of the COVID-19 pandemic may be extensive, and future pandemics are plausible,

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resulting in additional pressure on healthcare, and a subsequent scale reduction in surgical care may be insurmountable. Therefore, it is essential to determine whether surgical oncology decisions during the COVID-19 pandemic have led to disease progression and associated additional care. A revision of surgical oncology measures may be possible, if necessary, by evaluating this clinical surgical data. Therefore, this systematic review and meta-analysis aims to provide insight into the number and clinical outcomes of the performed surgical oncology procedures during the COVID-19 pandemic.

2. Materials and methods

2.1. Search strategy

This systematic review and meta-analysis was performed according to the guidelines of the PRISMA Checklist for meta-analysis [15]. A systematic literature search was performed in the PubMed and Embase databases, including all articles published before March 21, 2022. The search strategy contained a combination of keywords (and their synonyms), including “COVID-19”, “SARS-CoV-2”, and “surgical”. The complete search strategy is available in the supplementary data (Supplementary Table 1).

2.2. Study selection

After removing duplicates, four reviewers (EB, OB, EH, and MF) independently screened articles by title and abstract for eligibility. The four reviewers discussed discordant judgments until consensus was reached. All articles meeting the following inclusion criteria were selected for full-article review: surgical procedures involving oncological surgery which provided data on oncological outcomes and/or the number of performed surgical procedures. Studies were excluded from the systematic review for the following reasons: articles including recommendations only based on opinions and guidelines; articles without comparison to pre-COVID-19 cohort, non-human biological sample usage; non-English language articles, case reports, case series, editorials, commentaries, short communications, letters, review articles, conference abstracts; no full text available. The reviewers (EB, MF) reviewed the retrieved full-text articles. Agreement for eligibility was obtained for all articles.

2.3. Data extraction and definitions

The following data were extracted from each eligible study: first author’s surname, publication year, type of malignancy, study period (pre-)pandemic cohort, number of performed surgical procedures, waiting time in days between operation-indication and surgical procedure, if possible.

The influence of the COVID-19 pandemic on performed surgical oncology procedures was evaluated by comparing the total number of performed pre-pandemic surgical procedures to the total number of performed pandemic surgical procedures. To compare as reliably as possible between pre-COVID-19 and COVID-19 groups, most studies cover the same pre-COVID-19 and COVID-19 study period or consist of the same number of days. The author of the included study determined the timeframe of the (pre-)pandemic cohort. To compare the studies as reliable as possible, studies were only included if the COVID-19 cohort underwent a surgical procedure during the first wave of the pandemic.

Of the included studies, data of the most commonly shared clinical outcomes were determined. These clinical outcomes included the pathological T- and N-stages of the TNM classification and the complication rate [16]. Pathological T-stage cut-offs were ≥T2 and ≥T3 to provide inside into short-term disease progression. In addition, for the pathological N-stage, ≥N1 was used as the cut-off for evaluating the difference in clinical outcomes. Moreover, the Clavien-Dindo classification was used to classify the severity of reported major postoperative complications [17]. For this meta-analysis, major postoperative complications Clavien-Dindo classification ≥3 was used as the cut-off for evaluating the clinical outcomes.

2.4. Bias assessment

The risk of bias for each eligible study was evaluated by two reviewers (EB, MF) using the ROBINS-I Tool [18]. The tool consists of seven domains; confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result. Each domain was rated on three levels of bias: low risk, intermediate/unclear risk, or high risk of bias. The two authors discussed discordant judgments until consensus was reached. The summary of the risk of bias is shown in the supplementary data (Supplementary Fig. 1). The full risk of bias assessment is displayed in the supplementary data as well (Supplementary Table 2).

2.5. Statistical analysis

Descriptive statistics were used to describe patient characteristics. Meta-analysis was performed to visualize the number of performed surgical oncology procedures before and during the COVID-19 pandemic using the *ggplot2* package in R. The effect of heterogeneity was quantified using I^2, where a p-value < 0.05 indicated significant heterogeneity across the studies. In addition, a random-effects model was used to assess pooled oncological outcomes. The odds ratio (OR) was estimated with its variance and 95% confidence interval (CI). Statistical significance was defined as a p-value <0.05. Statistical analyses were carried out using the *meta* package in the R statistical software (version 4.0.2).

3. Results

A total of 12,782 articles were identified after duplicate removal. Of these, 12,406 were excluded during the titles and abstract screening, 376 articles were screened in full text (Fig. 1).

Overall, 24 studies were included, 6762 surgical oncology procedures were reviewed. Table 1 summarizes the main characteristics of the included studies. Study publication dates ranged from 2020 to 2022, with most studies being published in 2020 and 2021.

The eligible studies delivered data on variant oncological disciplines including central nervous system (CNS), thyroid, thoracic, breast, colorectal, hepatocellular, endocrine, genitourinary, prostate cancer, skin and soft tissue sarcomas [19–28,30–43]. Of these included studies, eight evaluated surgical procedures for breast cancer [23,25,32,37,39–42]. In addition, six studies described the waiting time between pathological examination or diagnosis of cancer and the date the surgical procedure was performed [20,23–25,39,40]. Of these studies, three described shorter waiting times compared to pre-pandemic practice, of 0.5, 3 and 14 days, respectively [20,24,39]. The remaining three studies showed minimally prolonged waiting times compared to pre-pandemic practice, of 4.0, 2.7 and 0.4 days, respectively [23,25,40]. In addition, all of these studies reported information regarding performed breast cancer procedures [23,25,40].

All studies were classified as overall methodological sufficient quality according to ROBINS-I Tool. The more comprehensive risk assessment of all included studies is presented in supplementary table 2.

4. Surgical oncology volumes

The total number of performed surgical oncology procedures during the COVID-19 pandemic was 2867, compared to 3895 during pre-pandemic practice (total decrease 26.4%) (Table 1).

Moreover, 614 oncological breast procedures were performed during the pandemic, compared to 612 before the pandemic (total increase 0.3%) (Fig. 2 and Table 1).

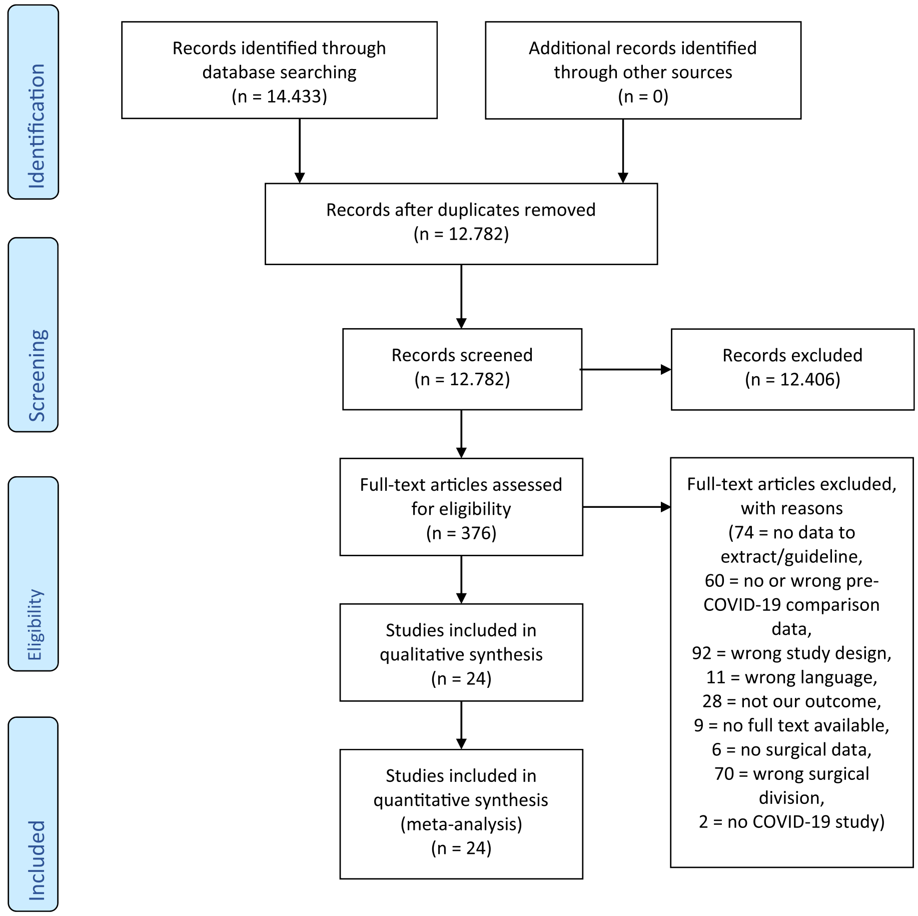

Fig. 1. Flow chart showing literature search and study selection with fourteen relevant studies included.

5. Clinical oncological outcomes

Five studies with a total of 2608 patients included data on pathological ≥ T2 staged tumors [28,36,39,41,43]. No difference was identified in the proportion of ≥T2 in the pandemic group compared to the pre-pandemic group (OR 1.00; 95% CI 0.72–1.38, P = 0.989) (Fig. 3A, Table 2).

Four studies describing 1986 patients included pathological ≥ T3 data [36,39,41,43]. No difference was observed in the number of ≥T3 tumors during the pandemic compared to pre-pandemic practice (OR 0.95; 95%CI 0.69–1.32, P = 0.778) (Fig. 3B, Table 2).

Furthermore, four studies with a total of 1951 patients included data on a pathological ≥ N1 stage [36,39,41,43]. No difference in ≥N1 during the COVID-19 pandemic compared to the pre-pandemic group was observed. (OR 1.01; 95% CI 0.68–1.50, P = 0.964) (Fig. 3C, Table 2).

In addition, five studies describing 1901 patients included the number of major postoperative complications Clavien-Dindo ≥3 during the pandemic compared to the pre-pandemic cohort [19,22,28,34,40]. No significant difference in the number of major postoperative complications was identified (OR 1.55; 95% CI 0.87–2.74, P = 0.134) (Fig. 3D, Table 2).

6. Discussion

The current meta-analysis analyzed the number of performed surgical procedures for oncological pathologies during the COVID-19 pandemic. In total, the number of performed surgical procedures for an oncological pathology decreased (2867 vs. 3895, −26.4%) during the pandemic compared to pre-pandemic practice. In addition, the number of performed surgical procedures for breast cancer remained stable during the pandemic (578 vs. 569, +1.6%). Furthermore, no difference was identified in the proportion of ≥T2, ≥T3, ≥N1 during the pandemic compared to pre-pandemic practice, with OR's 1.00, 0.95, and 1.01, respectively. Finally, the number of major postoperative complications (Clavien-Dindo ≥3) was slightly, however not significantly, higher during the pandemic (OR 1.55, P = 0.134) compared to pre-pandemic performance.

During the COVID-19 pandemic, several guidelines have been established to triage the performance of (surgical oncology) procedures to determine within which time frame surgical procedures should occur. Different triage methods were used for the clinical implementation of non-COVID care, including the stratification of acute, semi-acute, and elective procedures, or by emergency-, urgent-, elective with the expectation of cure and elective with no predictive harmful outcome procedures or by low-, intermediate- or high acuity [1,44–46]. In addition, some guidelines specifically described deferrable- or prioritizing surgical oncology procedures [4,6]. The common denominator in these guidelines was to provide the maximal care capacity for the COVID-19 patient with as little disease progression as possible in non-COVID-19 pathologies. It is essential to investigate whether these guidelines are implemented in daily surgical practice and if short-term clinical outcomes are reported. This enables to determine whether disease progression may occur during possible future changes in operating room capacities, for example, if new pandemics arise.

This current systematic review and meta-analysis showed that the number of performed surgical oncology procedures declined (2867 vs. 3895, 26.4% total decrease) during the pandemic compared to pre-pandemic clinical practice. This is in line with the Dutch Integral Cancer Registration (IKNL), which showed a decrease in the number of

Table 1
Characteristics of the included studies.

Author	Country	Malignancy	Pre-COVID-19 study period	COVID-19 study period	No. of performed surgical procedures pre-COVID-19	No. of performed surgical procedures COVID-19	Difference in percentages	Waiting time in days pre-COVID-19	Waiting time in days COVID-19
Akhtar et al., 2021 [16]	India	Head and neck, GI, hepatobiliary, genitourinary, thorax, breast, sarcoma, skin	April–September 2019	April–September 2020	598	410	−31%	NR	NR
Amoo et al., 2021 [17]	Ireland	Glial tumors	1 March – 31 May 2019	1 March – 31 May 2020	56	60	+7%	2.89	2.39
Araujo et al., 2020 [18]	Brazil	Not specified	March–May 2019	March–May 2020	607	242	−60%	NR	NR
Blache et al., 2021 [19]	France	Gynecology	21 January – 16 March 2020	17 March – 12 May 2020	127	85	−33%	NR	NR
Cadili et al., 2020 [20]	Canada	Breast	16 March – 30 April 2019	16 March – 30 April 2020	99	162	+64%	23	27
Drysdale et al., 2020 [21]	Australia	Upper GI, Breast, colorectal, endocrine	1 April – 19 May 2019	30 March – 17 May 2020	51	44	+0%	14.7	11.7
Fancelllu et al., 2020 [22]	Italy	Breast	1 March – 30 Apr 2019	1 March – 30 Apr 2020	41	42	+2%	46.4	49.1
Hübner et al., 2020 [23]	Switzerland	Major visceral, not specified	3 Feb – 13 March 2020	16 March – 24 April 2020	52	38	−27%	NR	NR
Kiong et al. [24]	USA	Head and neck	23 March – 9 April 2019	23 March – 9 April 2020	111	59	−47%	NR	NR
Leung et al., 2021 [25]	UK	Gynecology	1 January - 12 August 2019	1 January - 12 August 2020	296	289	−2%	NR	NR
McLean et al., 2020 [27]	UK	GI	16 Feb – 15 March 2020	16 March – 15 April 2020	7	9	+29%	NR	NR
Perrone et al., 2021 [28]	Italy	Gynecology	9 March – 4 May 2019	9 March – 4 May 2020	55	51	−7%	NR	NR
Pikety et al., 2022 [29]	France	Gynecology and breast	14 March - 11 May 11, 2019	14 March - 11 May 11, 2020	23	20	−13%	NR	NR
Salzano et al., 2021 [30]	Italy	Head and neck	21 Feb – 25 March 2019	21 Feb – 25 March 2020	101	113	+12%	NR	NR
Santambrogio et al., 2020 [31]	Italy	Hepatocellular	28 Feb – 14 April 2019	28 Feb – 14 April 2020	9	11	+22%	NR	NR
Shah et al., 2021 [32]	USA	Head and neck	February–May 2019	February–May 2020	60	66	+10%	NR	NR
Stevens et al., 2022 [33]	USA	Head and neck	March–July 2019	March–July 2020	79	69	−13%	NR	NR
Subbiah et al., 2021 [34]	India	Head and neck, breast, GI, STS, gynecology and others	October 2019–February 2020	March–July 2020	234	151	−35%	NR	NR
Tan et al., 2021 [35]	Australia	Head and neck	6 August 2019–15 March 2020	16 March - 27 October 2020	33	26	−21%	NR	NR
Vanni et al., 2020 [36]	Italy	Breast	11 March – 30 March 2019	11 March – 30 March 2020	172	203	+18%	56	42
Vanni et al., 2021 [37]	Italy	Breast	30 January - 29 February 2020	1 March - 30 March 2020	39	37	−5%	11.8	12.2
Vissio et al., 2021 [38]	Italy	Breast, CNS, colorectal, lung, ovary, pancreas, prostate, uterus and thyroid	9 March – 8 May 2019	9 March – 8 may 2020	420	372	−11%	NR	NR
Yiğit et al., 2020 [39]	Turkey	Breast, thyroid, colon, gastric, hepatocellular	11 March – 31 May 2019	11 March – 31 May 2020	143	57	−60%	NR	NR
Zhang et al., 2020 [40]	China, South Korea, Iran, Italy	Thyroid	26 Feb – 20 April 2019	26 Feb – 20 April 2020	531	293	−45%	NR	NR
Total difference surgical oncology procedures							−26.4%		
Total difference surgical breast cancer procedures							+0.3%		

COVID-19 = Coronavirus disease 2019, No. = Number, CNS = Central nervous system, GI = Gastrointestinal, STS = Soft tissue sarcomas, UK = United Kingdom, NR = Not reported.

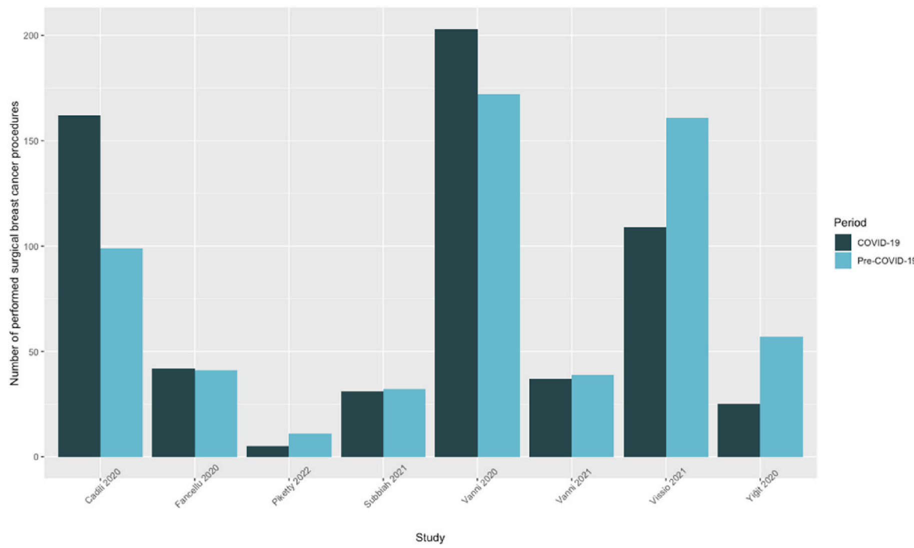

Fig. 2. Bar chart of the number of surgical breast cancer procedures performed during and before the COVID-19 pandemic.

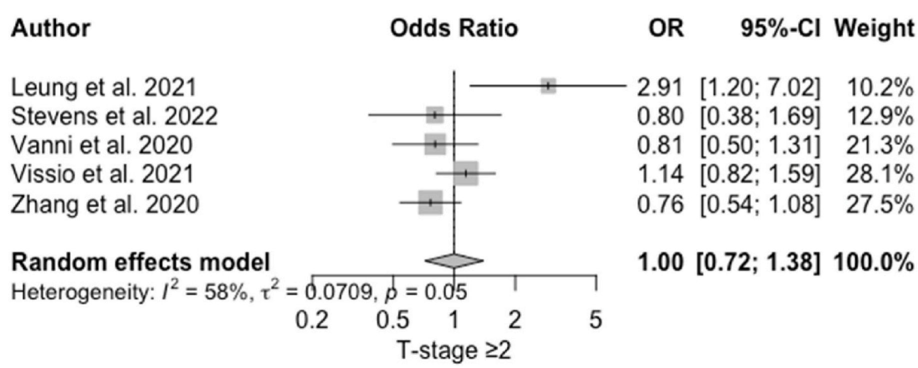

Fig. 3A. Forest plot of the odds ratio of ≥T2 stage during the COVID-19 pandemic compared to the pre-pandemic control group.

Table 2
Odds ratios of oncological outcomes and major postoperative complications during the pandemic compared to pre-pandemic practice. OR = Odds ratio, CI = Confidence interval, T = Tumor, N = Node.

Parameter	OR	95% CI	p-value
≥T2	1.00	0.72–1.38	0.989
≥T3	0.95	0.69–1.32	0.778
≥N1	1.01	0.68–1.50	0.964
Postoperative complications Clavien-Dindo ≥3	1.55	0.87–2.74	0.134

performed surgical oncology procedures during the first pandemic wave in the Netherlands [47]. In contrast to the overall number of performed surgical oncology procedures and the IKNL data, this meta-analysis showed a stable number of performed surgical breast cancer procedures during the pandemic compared to previous pre-pandemic volumes (614 vs. 612, 0.3% total increase). Therefore, this study's decreased number of performed surgical oncology procedures may not be attributed to breast cancer practice. It is possible that, in order to reduce the pressure on healthcare, the operating time freed up by postponed elective surgical procedures was more easily filled by breast cancer procedures, in which patients are discharged faster postoperatively than by complex oncological procedures requiring intensive care unit admission.

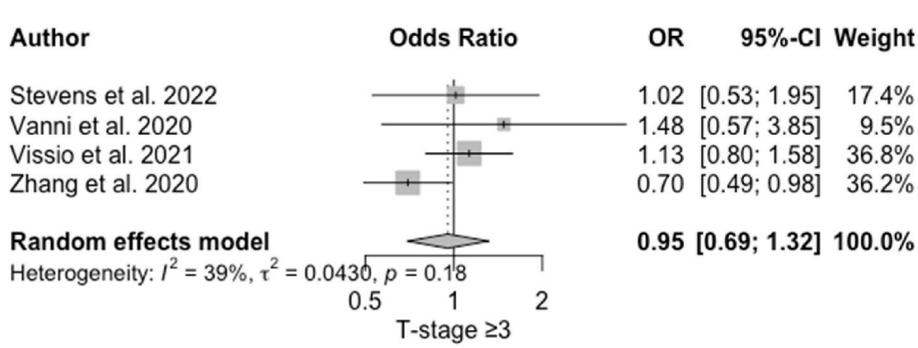

Fig. 3B. Forest plot of the odds ratio of ≥T3 stage during the COVID-19 pandemic compared to the pre-pandemic control group.

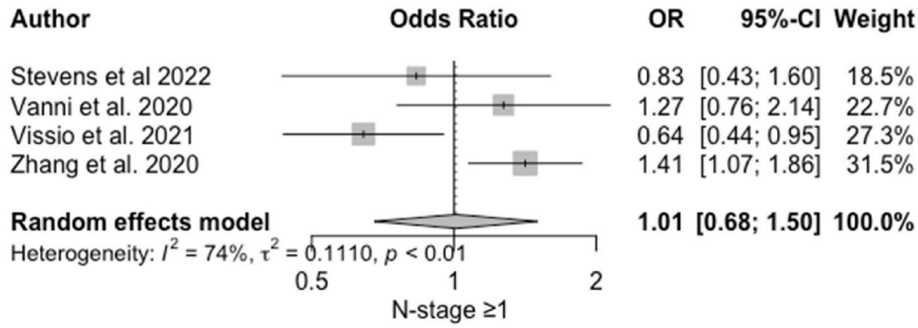

Fig. 3C. Forest plot of the odds ratio of ≥N1 stage during the COVID-19 pandemic compared to the pre-pandemic control group.

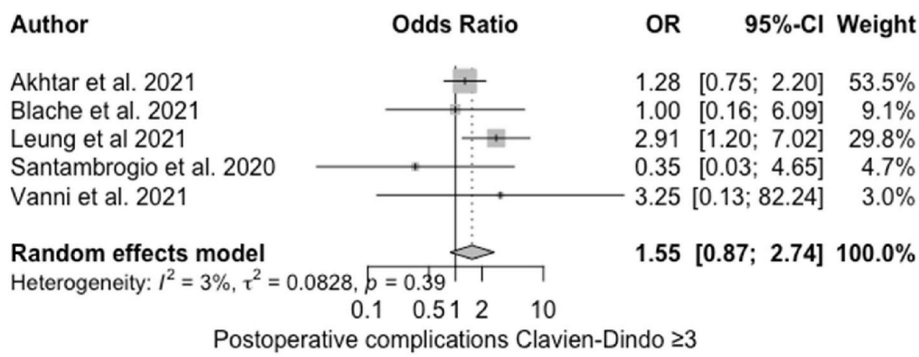

Fig. 3D. Forest plot of the odds ratio of major postoperative complications (Clavien-Dindo ≥3) during the COVID-19 pandemic compared to the pre-pandemic control group.

Moreover, postponement in surgical oncology procedures may or may not lead to disease progression; however, this depends on multiple factors [48–50]. IKNL has estimated that due to stable chemotherapy performances, catch-up in cancer diagnosis, and surgical procedures, enough (non-)surgical patients have received cancer treatment in the Netherlands [47].

This systematic review and meta-analysis included six studies reporting the waiting time between histological- or cytological-examination or diagnosis of cancer and date of performed surgical procedure, or time between surgical consult and surgical procedure. Of these studies, three showed a minimally longer waiting time during the pandemic than before the pandemic (mean difference 2.4 days, range 0.4–4.0). The tumors are not expected to have grown clinically relevant in this short time [51]. Additional data is necessary to inventory each hospital's waiting time since previous literature states that increased waiting time for oncological procedures may lead to a lower overall survival rate [49,52]. Moreover, this meta-analysis showed no significantly increased number of patients presenting with pathological ≥ T2, ≥T3, ≥N1 tumors or major postoperative complications during the COVID-19 pandemic compared to pre-pandemic cohorts. These results may indicate that no disease progression occurred during the COVID-19 pandemic in the included oncological studies, a possible conclusion also seen in a recent Dutch COVID-19 study focusing on stage distribution of colorectal cancers [53]. This may be explained by some solid cancers being years old when noticed and requiring a surgical procedure [54]. However, caution is advised as calculations anticipate diagnostic delays due to the COVID-19 pandemic may increase the number of preventable cancer deaths [55].

This systematic review and meta-analysis has some limitations. First, separating surgical oncology volumes by type of oncology discipline was only possible for breast cancer. In addition, the majority of the breast cancer studies included data from Italy. Therefore, extrapolating the number of performed surgical breast cancer procedures to other countries may be difficult. Further research is necessary to determine the net summary of the number of performed surgical procedures for each country to allow for a more realistic representation of the delayed healthcare. Second, the current meta-analysis is limited by the data's heterogeneity. The COVID-19 pandemic severity differed between countries and regions, leading to heterogenic approach of oncological guidelines. As a result, inevitable variation is observed in chosen pre-pandemic and pandemic phases, chronology and management between the included studies. Specifically, some studies determined the start date of their COVID-19 cohort before the official WHO declaration of the COVID-19 pandemic, which may be explained by the varying incidence of COVID-19 between countries and/or regions [56,57]. Third, this study was unable to review whether the observed reduction in surgical volumes was related to the deferral of surgical procedures due to altered hospital approach or patient-driven avoidance of care. Finally, more research is essential to determine whether people have been treated on time to have well-founded information for possible future pandemics.

In conclusion, this meta-analysis showed a decrease (−26.4%) in the number of performed surgical oncology procedures during the COVID-19 pandemic (3895 vs. 2867). In addition, the number of performed surgical breast cancer procedures remained stable (+0.3%). Moreover, reported short-term oncological staging and major postoperative complications showed no significantly increased disease progression compared to pre-pandemic practice. In the event future pandemics, the performed surgical oncology care during the first wave of the COVID-19 pandemic appears appropriate regarding short-term outcomes. Further research should determine long-term and country-specific clinical outcomes.

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Informed consent

Not applicable.

Data presentation

Research data is available upon reasonable request.

Author contributions

E. de Bock: conception and design, data collection, analysis and interpretation, writing the article, critical revision of the article, E.S. Herman: conception and design, data collection, analysis and interpretation, writing the article, critical revision of the article, O.W. Bastian: conception and design, data collection, analysis and interpretation, writing the article, critical revision of the article, M.D. Filipe: conception and design, data collection, analysis and interpretation, writing the article, critical revision of the article, M.R. Vriens: conception and design, analysis and interpretation, writing the article, critical revision of the article, M.C. Richir: conception and design, analysis and interpretation, writing the article, critical revision of the article.

Declarations of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2022.101859.

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