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Meta-analysis of COVID-19 prevalence during preoperative COVID-19 screening in asymptomatic patients

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ABSTRACT

Objectives Patients with COVID-19 may be asymptomatic and are able to transmit COVID-19 during a surgical procedure, resulting in increased pressure on healthcare and reduced control of COVID-19 spread. There remains uncertainty about the implementation of preoperative screening for COVID-19 in asymptomatic surgical patients. Therefore, this study aims to determine the prevalence of preoperative COVID-19, confirmed by reverse transcriptase PCR (RT-PCR), in asymptomatic patients.

Design Systematic review and meta-analysis.

Data sources Pubmed and Embase databases were searched through 20 February 2022.

Eligibility criteria All COVID-19 articles including preoperative asymptomatic patients were included.

Data extraction and synthesis Two independent reviewers extracted data and assessed risk of bias. Meta-analysis was performed to determine the prevalence of COVID-19 with 95% CI. Moreover, estimated positive predictive value (PPV), negative predictive value, false-positives (FP) and false-negatives were calculated for preoperative asymptomatic patients.

Results Twenty-seven studies containing 27 256 asymptomatic preoperative screened patients were included, of which 431 were positive for COVID-19 by RT-PCR test. In addition, the meta-analysis revealed a pooled COVID-19 prevalence of 0.76% (95% CI 0.36% to 1.59%). The calculated PPV for this prevalence is 40.8%.

Conclusions The pooled COVID-19 prevalence in asymptomatic patients tested preoperatively was 0.76%, with low corresponding PPV. Consequently, nearly three-quarters of postponed surgical procedures in asymptomatic preoperative patients may be FP. In the event of similar pandemics, modification of preoperative mandatory RT-PCR COVID-19 testing in asymptomatic patients may be considered.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Inclusion of all studies on reverse transcriptase PCR (RT-PCR) COVID-19 asymptomatic patients tested preoperatively during the COVID-19 pandemic.
- ⇒ Analyses of COVID-19 prevalence of large population of patients without COVID-19-like symptoms.
- ⇒ Calculation of corresponding positive predictive value, negative predictive value, true positives and false positives for this prevalence.
- ⇒ True positives and false positives could not be determined in asymptomatic patients tested with RT-PCR only since studies excluded patients presenting with symptoms.
- ⇒ Analyses did not include other COVID-19 diagnostic tests besides RT-PCR.

INTRODUCTION

Since the declared COVID-19 pandemic, many countries have experienced peaks in the number of infected patients.[1] As a result of the confirmed COVID-19 cases, restrictive measures were implemented, including postponing (elective) surgical procedures.[2–7] Performing surgical procedures was accompanied by alterations in clinical practice, including introducing preoperative guidelines for COVID-19 screening to minimise the risk of spreading COVID-19.[8–11] While these preoperative guidelines differed in the preferred type of COVID-19 test, they all recommended testing every (surgically admitted) patient.[8–11] As a result, many patients without accompanying COVID-19 symptoms are tested preoperatively.

The majority of the patients with confirmed COVID-19 experience mild influenza-like symptoms, including fever, cough, dyspnoea, sputum secretions, fatigue and malaise.[12 13] However, a significant proportion (15%–25%) of the COVID-19 infected patients may be asymptomatic.[14 15] Since tracheal intubation is an aerosol-generating procedure and COVID-19 has the ability to remain viable and infectious on certain surfaces during a surgical procedure, there may be an increased risk of viral transmission during surgical procedures.[16–18] Consequently, these infected asymptomatic patients may be able to spread the virus to healthcare personnel and or other hospitalised patients.[19–23] Nevertheless, mandatory COVID-19 screening before all surgical procedures requires testing equipment and is time-consuming, leading to additional pressure on hospital staff and overall healthcare and increased costs.[24 25] Ambiguity remains about the necessity and implementation of the testing guidelines for preoperative screening in asymptomatic surgical patients. Therefore, this systematic review and meta-analysis aims to determine the COVID-19 prevalence in asymptomatic patients tested preoperatively and determine the implications for clinical screening by calculating diagnostic, predictive values.

MATERIALS AND METHODS

Search strategy

This systematic review and meta-analysis was performed according to the guidelines' requirements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist for meta-analysis.[26] A systematic literature search was performed in the PubMed and Embase databases, including all articles published before 20 February 2022. Search strategy contained a combination of keywords (and their synonyms), including 'screening,' 'preoperative,' 'SARS-CoV-2'. The complete search strategy is available in online supplemental table 1.

Study selection

After removing duplicates, two reviewers (EdB and MDF) independently screened articles for eligibility using title and abstract. The two authors discussed conflicting judgements until consensus was reached. All articles with asymptomatic patients requiring a surgical or interventional procedure with a high risk of generating COVID-19 aerosols were selected for full article review. In addition, articles from which absolute numbers of true positive (TP), false-positive (FP), true negative (TN) or false-negative (FN) could be derived were included. Subsequently, articles were required to perform COVID-19 screening through symptom screening and reference reverse transcriptase PCR (RT-PCR) test or COVID-19 screening by chest CT and reference RT-PCR test.

Studies were excluded from the systematic review for the following reasons: diagnostic testing in symptomatic patients only; non-human biological sample usage; no English language article, case reports, case series, editorials, commentaries, short communications, letters, review articles, conference abstracts; no full text available. The reviewers (EdB and MDF) reviewed the retrieved full-text articles. Agreement for eligibility was obtained for all articles.

Data extraction and definitions

The following data were extracted from each eligible study: first author's surname, publication year, study period, number of asymptomatic patients, type of surgical division, COVID-19 preoperative screening method, COVID-19 reference test, number of days symptom screening was performed before surgical procedure, number of TP, number of FP, number of TN, number of FN.

CT-scan positive for COVID-19 was defined as COVID-19 Reporting and Data System (CO-RADS) ≥4 or if scored as 'typical COVID-19' or 'indeterminate' according to the European Society of Radiology guidelines and the European Society of Thoracic Imaging.[27 28] Symptom screening included but was not limited to dyspnoea, cough, fever or influenza-like symptoms. Surgical patients were determined 'asymptomatic' if none of the aforementioned symptoms were present. In addition, some studies evaluated high-risk exposures, travel outside the country, or recent contact with a COVID-19 confirmed individual. If studies implemented different preoperative screening protocols due to changes in national screening guidelines, only data from the relevant protocol was retrieved. Postoperative COVID-19 test results were not included in the analysis. The prevalence of positive COVID-19 patients was defined as the percentage of patients who tested positive for SARS-CoV-2 out of all asymptomatic patients tested preoperatively.

Patient and public involvement

We did not seek patient or public comment in designing the study.

Bias assessment

The risk of bias for each eligible study was independently evaluated by the reviewers (EdB and MDF) using the Risk Of Bias In Non-randomised Studies - of Interventions (ROBINS-I) Tool.[29] 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 judgements until consensus was reached. Full assessment criteria can be found in online supplemental figure 1.

Statistical analysis

Meta-analysis was performed using a random effects model to determine the prevalence with 95% CI of asymptomatic COVID-19 positive patients.

Calculation of the estimated positive predictive value (PPV) was established by the following mathematical formula:[30]

$$PPV = \frac{sensitivity\ x\ prevalence}{[(sensitivity\ x\ prevalence)+((1-specificity)\ x\ (1-prevalence))\ ]}$$

Calculation of the estimated NPV was established by the following mathematical formula[30]:

$$NPV = \frac{specificity\ x\ (1-prevalence)}{[(specificity\ x\ (1-prevalence))+((1-sensitivity)\ x\ prevalence)]}$$

According to the WHO guideline, an acceptable sensitivity and specificity rate should be 90% and 99%, respectively,[31] and were used to calculate PPV and NPV with the aforementioned formulas.

The effect of heterogeneity was quantified using I^2, if I^2 >50% or p<0.05, indicating significant heterogeneity across the studies. Meta-analysis was performed to compare the pooled prevalence of all included studies. The statistical analyses were carried out using the *meta* package in the R statistical software (V.4.0.2.).

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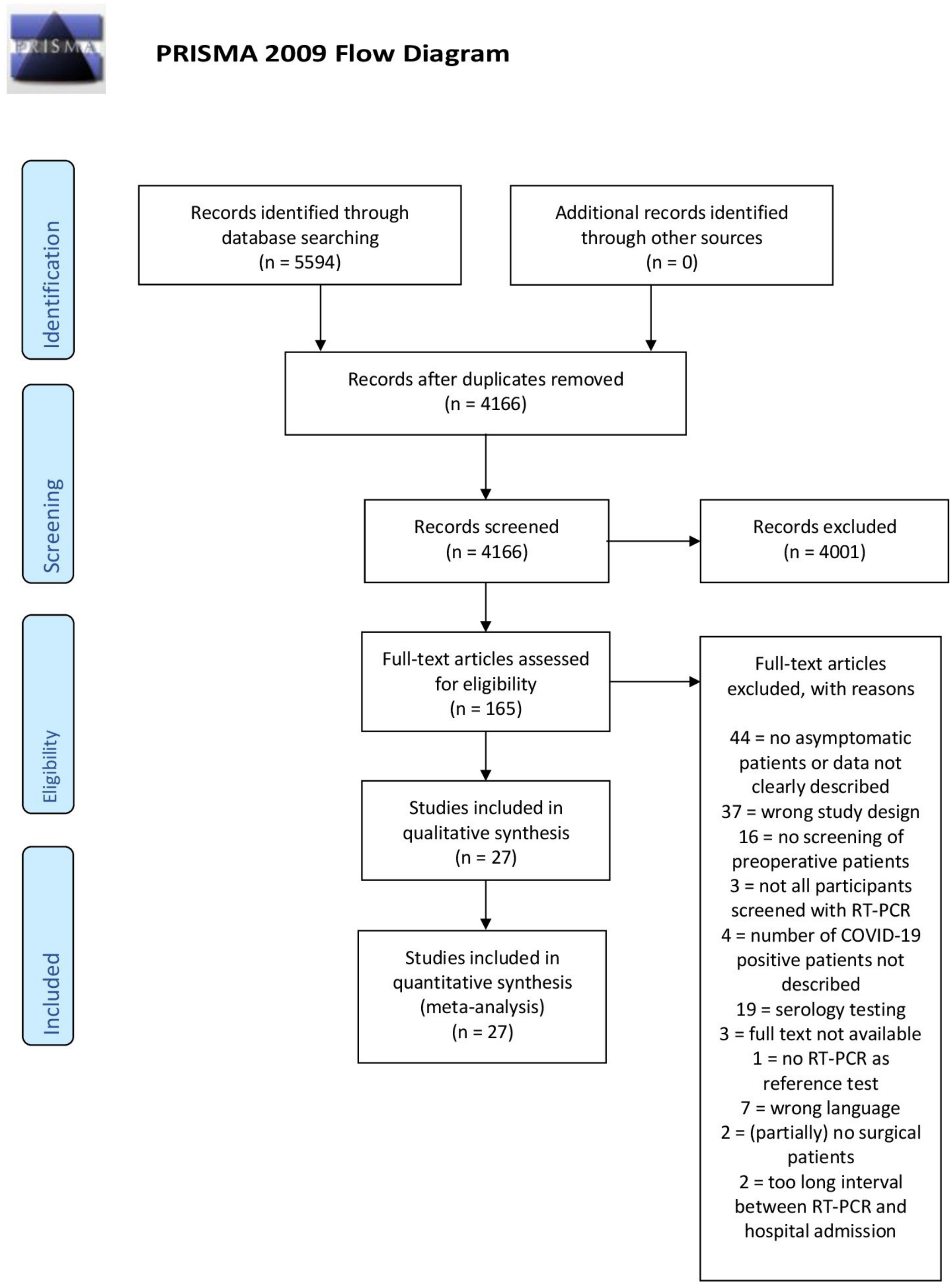

Figure 1 Flow chart showing literature search and study selection with 27 relevant studies included. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RT-PCR, reverse transcriptase PCR.

RESULTS

A total of 4166 articles were identified after duplicate removal. Of these, 4001 were excluded during the titles and abstracts screening, 165 articles were screened in full text (figure 1). Overall, 27 studies were included, 27 256 asymptomatic patients were reviewed, of which 431 patients were tested COVID-19 positive by RT-PCR test. On average, symptom screening was performed less than 2 days before the surgical procedure.

Table 1 summarises the main characteristics of the included studies. All studies presented a COVID-19 screening method of either chest CT, symptom screening and RT-PCR or symptom screening and RT-PCR.[32–58] Symptom screening with RT-PCR as the reference test

Table 1 Characteristics of the included studies on preoperative COVID-19 screening

Author	Country	Study period in 2020	No of asymptomatic patients	Surgical discipline	Evaluated screening method	Reference screening method	TP	FP	TN	FN	Prevalence of COVID-19 (%)	No days symptom-screening before hospital admission
Ap Dafydd *et al*[44]	UK	April 1 - May 31	240	Oncology	Symptom screening and chest CT	RT-PCR	1	8	230	1	0.83	NR
Bloom *et al*[53]	USA	March 30 - April 12	84	Urgent, different disciplines	Symptom screening	RT-PCR	0	0	81	3	3.57	≤2
Blumberg *et al*[54]	USA	March 26 - June 13	1161	Orthopaedic	Symptom screening	RT-PCR	0	0	1155	6	0.52	≤3
Castellvi *et al*[55]	Spain	April 15 - May 4	171	Oncology	Symptom screening	RT-PCR	0	0	171	0	0.00	≤2
Coatsworth *et al*[41]	Australia	June 2 - July 17	3010	Different divisions	Symptom screening	RT-PCR	0	0	3010	0	0.00	NR
Ferrari *et al*[56]	Italy	March 16 - April 17	41	Oncology	Symptom screening	RT-PCR	0	0	41	0	0.00	≤7
Gruskay *et al*[57]	USA	April 5 - April 24	81	Orthopaedic	Symptom screening	RT-PCR	0	0	74	7	8.64	NR
Guerlain *et al*[42]	France	March 25th and May 12th	477	Oncology	Symptom screening and chest CT	RT-PCR	NR	NR	459	18	3.77	0
Gümüs *et al*[32]	Turkey	April 20 - May 31	218	Different divisions	Symptom screening and chest CT	RT-PCR	1	12	203	2	1.38	NR
Gupta *et al*[58]	India	April 18 - May 28	764	Different divisions	Symptom screening	RT-PCR or True-NAT RT-PCR	0	0	762	2	0.26	0
Hendrickson *et al*[43]	USA	April 7 - May 21	1997	Different divisions	Symptom screening	RT-PCR	0	0	1990	7	0.35	0
Kannan *et al*[34]	India	July 16 - August 31	413	Retinal	Symptom screening	RT-PCR	0	0	404	9	2.18	0
Kavanagh *et al*[51]	Ireland	March 1 - June 30	156	Otolaryngology	Symptom screening	RT-PCR	0	0	156	0	0.0	0
Lopes *et al*[45]	Brazil	May – October	1636	Oncology	Symptom screening	RT-PCR	0	0	1534	102	6.23	five and 1
Myles *et al*[46]	Australia	July 15 -August 31	4965	Different divisions	Symptom screening	RT-PCR	0	0	4961	4	0.08	five and 0
Nekkanti *et al*[35]	India	April 18 - June 20	262	Oncology	Symptom screening	RT-PCR	0	0	241	21	8.02	≤2
Patkar *et al*[47]	India	April - September	2108	Oncology	Symptom screening	RT-PCR	0	0	1908	200	9.49	≤2
Puylaert *et al*[33]	The Netherlands	March 20 - April 24	1224	Different divisions	Symptom screening and chest CT	RT-PCR	4	4	1206	10	1.14	0
Ralhan *et al*[36]	India	April 19 - May 29	64	Cardiac	Symptom screening	RT-PCR	0	0	63	1	1.56	0
Singer *et al*[37]	USA	April 7 - May 21	4743	Different divisions	Symptom screening	RT-PCR	0	0	4737	6	0.13	≤2
Singh *et al*[48]	India	September - December	218	Ophthalmology	Symptom screening	RT-PCR	0	0	202	16	7.34	0
Shah *et al*[52]	USA	March 1 - April 30	625	Different divisions	Symptom screening and chest CT	RT-PCR	0	19	605	1	0.16	≤7
Tilmans *et al*[38]	France	March 2 - April 10	30	Different divisions	Symptom screening	RT-PCR	0	0	30	0	0.00	0
Urban *et al*[39]	USA	March 23 - April 17	21	Otolaryngology	Symptom screening	RT-PCR	0	0	20	1	4.76	≤4
Cwalinksi *et al*[49]	Poland	June – July	94	Different divisions	Symptom screening	RT-PCR	0	0	94	0	0.00	NR
Zangrilli *et al*[50]	USA	May 1 - July 21	2329	Orthopaedics	Symptom screening	RT-PCR	0	0	2324	5	0.21	NR
Zahra *et al*[40]	UK	May 4 - June 15	124	Orthopaedic	Symptom screening	RT-PCR	0	0	121	3	2.42	≤5

FN, false-negative; FP, false-positive; NR, not reported; RT-PCR, real time reverse transcriptase PCR; TN, true negative; TP, true positive.

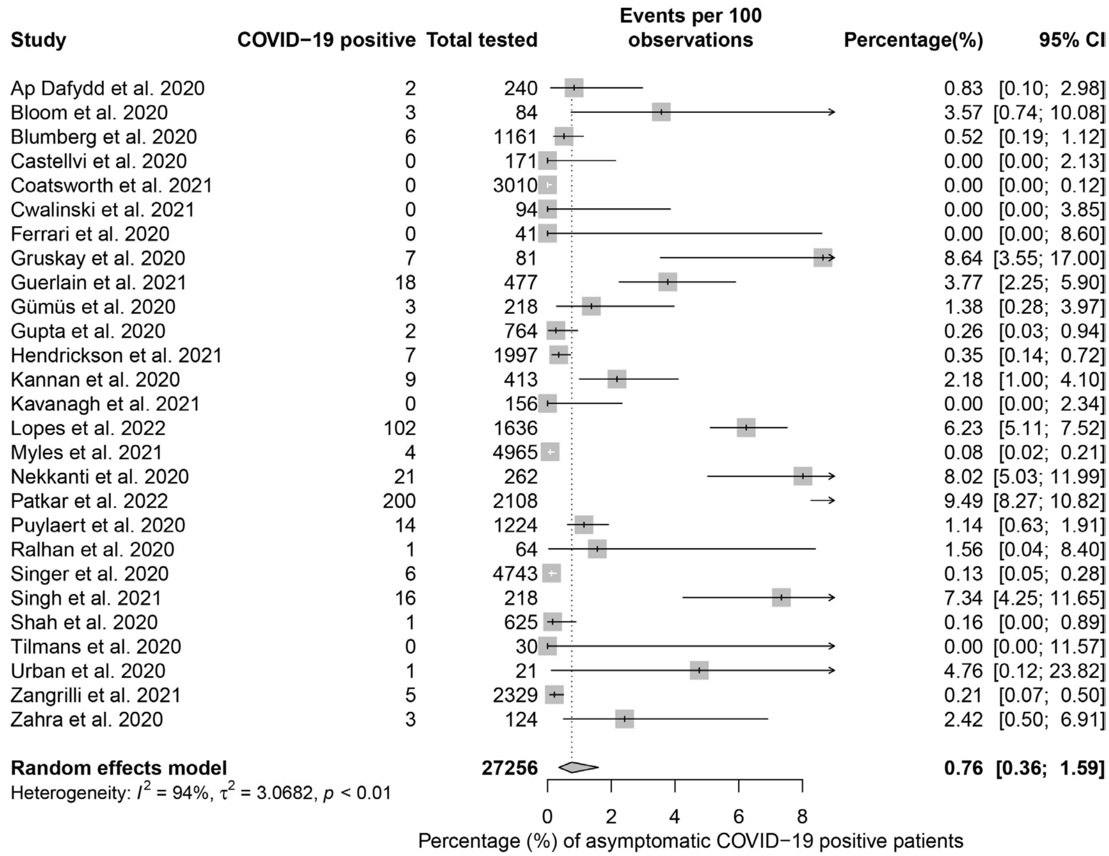

Figure 2 Forest plot of the prevalence (%) of asymptomatic COVID-19 positive patients in the preoperative setting.

was performed in 22 studies.[34–41, 43, 45–50, 53–59] Symptom screening with chest CT and RT-PCR as the reference test was performed in five studies.[32, 33, 42, 44, 52] Most (63%) included studies were published in 2020. In addition, eight (29.6%) studies were published in 2021 and two (7.4%) in 2022 (figure 2). Most studies (85.2%) were conducted during the first wave of the COVID-19 pandemic (table 1).

Table 2 Average PPV, NPV, FP and FN applied to a hypothetical cohort of 100 000 patients with varying COVID-19 prevalence in asymptomatic preoperative patients tested with RT-PCR

COVID-19 prevalence (%)	PPV (%)	NPV (%)	FP (N)	FN (N)
10.00	90.9	98.9	900	1000
9.49*	90.4	99.0	905	949
5.00	82.6	99.5	950	500
1.00	47.6	99.9	990	100
0.76†	40.8	99.9	992	76
0.00‡	0	100	1000	0

*The highest COVID-19 prevalence in our study population in the included studies.
†COVID-19 positive prevalence on average of the 27 included studies in this meta-analysis.
‡The lowest COVID-19 prevalence in our study population in the included studies.
FN, false-negative; FP, false-positive; N, number; NPV, negative predictive value; PPV, positive predictive value; RT-PCR, real time reverse transcriptase PCR.

Prevalence of COVID-19 in asymptomatic preoperative patients

The forest plot in figure 2 shows the pooled prevalence (%) of asymptomatic COVID-19 positive patients requiring a surgical procedure using a random effects model. The overall percentage of our study population was 0.76% (95% CI 0.36% to 1.59%) (figure 2). Moreover, the prevalence of COVID-19 positive asymptomatic surgical patients ranged from 0.00% to 9.49%. In addition, heterogeneity between studies was high (I^2=94%) (figure 2).

PPV, NPV, FP and FN of varying COVID-19 prevalence rates

Table 2 shows the calculated PPV, NPV, FP and FN corresponding with the varying COVID-19 prevalence rates in asymptomatic preoperative patients. Calculated PPV and NPV, taking into account the WHO guidelines for sensitivity (90%) and specificity (99%) with the aforementioned prevalence of 0.76%, were 40.8% and 99.9%, respectively. In addition, estimated FP and FN rates, with the previously mentioned prevalence, were 992 and 76, respectively. The lowest and highest prevalence of COVID-19 positive preoperatively tested asymptomatic patients in the included studies were 0.00% and 9.49%, respectively. The corresponding PPV and NPV with a

9.49% prevalence were 90.4% and 99%, respectively (table 2).

Risk of bias

All studies were classified as overall methodological sufficient quality according to ROBINS-I Tool. Risk assessment of all studies is further described in online supplemental figure 1.

DISCUSSION

This current meta-analysis analysed the COVID-19 prevalence in asymptomatic patients requiring a surgical procedure. In total, 431 asymptomatic preoperative patients were tested SARS-CoV-2 positive by RT-PCR reference test. In addition, the meta-analysis showed a pooled COVID-19 prevalence of 0.76% (95% CI 0.36% to 1.59%) in asymptomatic patients tested preoperatively. Subsequently, with this prevalence, the corresponding NPV and PPV were 99.9% and 40.8%, respectively, with 59.2% of possible FP test results.

During the pandemic, it remained essential to continue and resume surgical procedures. However, caution was advised as 25% of patients may be asymptomatic and are able to transmit SARS-CoV-2, with potentially even greater risk during surgical procedures, which may lead to additional healthcare pressure due to morbidity, increased mortality and decreased control over the SARS-CoV-2 spread.[14 17 18 60] In order to effectively conduct COVID-19 preoperative screening in asymptomatic patients, diagnostic COVID-19 screening methods require specific characteristics, such as low FN rates. Therefore, evaluating sensitivity and NPV is essential to determine the utility of diagnostic methods for preoperative COVID-19 screening in asymptomatic patients. Furthermore, high PPV are essential to determine as well since it represents the potential for FP COVID-19 patients. In addition, rapid test execution and availability of test results are additional important screening features as pressure on healthcare remains high and surgical care may increase in the coming months.[61]

The current meta-analysis showed an overall low pooled prevalence (0.76%, 95% CI 0.36% to 1.59%) of COVID-19 positive asymptomatic preoperative patients. Nevertheless, this indicates that symptom screening without additional RT-PCR testing may lead to viral transmission. This is in line with previous literature stating that symptom screening of surgical patients alone is not sufficient.[62 63] However, a recent review showed that asymptomatic patients are 42% less likely to transmit COVID-19 compared with symptomatic patients.[64] Due to the previously mentioned low COVID-19 prevalence in our study population, the estimated PPV was low as well (40.8%). As a result, almost 60% (59.2%; 992 patients) of COVID-19 RT-PCR positive asymptomatic preoperative patients may be FP. Consequently, the surgical procedures of these patients will be deferred even though they will not spread COVID-19. This (unnecessary) postponement of surgical care may result in clinical deterioration, thereby contributing to additional pressure on healthcare and increasing costs.[65] In addition, the currently used RT-PCR test for preoperative screening is time-consuming, requires a laboratory and additional healthcare providers.

The pressure on healthcare will remain high since the number of surgical procedures to be performed may increase.[61] Therefore, consideration may be given to reviewing the mandatory COVID-19 screening approach of RT-PCR in asymptomatic preoperative patients. Additionally, the current meta-analysis showed a maximum COVID-19 prevalence in preoperatively tested asymptomatic patients of 9.49% with a corresponding PPV of 90.4%. Hence, further research should determine which areas and affiliated hospitals require preoperative COVID-19 testing.

This meta-analysis has some limitations. First, since we used symptom screening in asymptomatic patients as an index test for preoperative COVID-19 screening, TP and FP could not be retrieved. Therefore, diagnostic accuracy evaluation of symptom screening was not possible. Second, our analysis did not include the diagnostic accuracy of other COVID-19 diagnostic tests, such as antigen tests, as our search found no articles on other screening tests in asymptomatic preoperative patients. However, recent studies on the diagnostic accuracy of antigen tests show varying sensitivity rates for detecting COVID-19 in asymptomatic RT-PCR positive patients,[66–69] and a previous study displayed no clinical role for serological testing in asymptomatic patients.[70] Third, the current study did not address possible factors, for example, age, sex, type of surgical procedure, length of hospital stay, period of testing or comorbidities, and different estimates affecting the asymptomatic prevalence of COVID-19 in patients undergoing surgical procedures. However, these factors can most likely be pooled into a meta-analysis once cohorts and/or registries studies are published. In addition, to our knowledge, no research articles have been published to date including these tests in our patient group. Therefore, further research is warranted to explore the possible advantage of these tests. Finally, this meta-analysis was not able to evaluate the possible consequences of (unnecessary) delayed surgical procedures. Further research on surgical outcomes during the COVID-19 pandemic may provide additional information for optimising the surgical approach during a future pandemic.

In conclusion, the pooled prevalence of COVID-19 in asymptomatic preoperative patients was low (0.76%). Since nearly 60% of postponed surgical procedures in asymptomatic preoperative patients may be FP, surgical procedures may be unnecessarily delayed. In the event of similar pandemics, modification of preoperative mandatory RT-PCR COVID-19 testing in asymptomatic patients may be considered.

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and design, data collection, analysis and interpretation, writing the article, critical revision of the article. RKJS: analysis and interpretation, data collection, critical revision of the article. ACK: analysis and interpretation, data collection, critical revision of the article. MRV: conception and design, analysis and interpretation, writing the article, critical revision of the article. MCR: conception and design, analysis and interpretation, writing the article, critical revision of the article, guarantor.

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