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The theoretical mortality risk of an asymptomatic patient with a
negative SARS-CoV-2 test developing COVID-19 following elective
orthopaedic surgery

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Abstract

Aims

The risk to patients and healthcare workers of resuming elective orthopaedic surgery following the peak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has been difficult to quantify. This has prompted governing bodies to adopt a cautious approach that may be impractical and financially unsustainable. The lack of evidence has made it impossible for surgeons to give patients an informed perspective of the consequences of elective surgery in the presence of SARS-CoV-2. This study aims to determine, for United Kingdom population, the probability of a patient being admitted with an undetected SARS-CoV-2 infection and their resulting risk of death; taking into consideration the current disease prevalence, reverse transcription-polymerase chain reaction (RT-PCR) testing and preassessment pathway.

Methods

The probability of SARS-CoV-2 infection with a false-negative test was calculated using a lower-end RT-PCR sensitivity of 71%, specificity of 95% and the UK disease prevalence of 0.24% reported in May 2020. Subsequently, a case fatality rate of 20.5% was applied as a worst-case scenario.

Results

The probability of SARS-CoV-2 infection with a false-negative preoperative test was 0.07% (around 1 in 1,400). The risk of a patient with an undetected infection being admitted for surgery and subsequently dying from COVID-19 is estimated at roughly 1 in 7,000. However, if an estimate of the current global infection fatality rate (1.04%) is applied, the risk of death would be around 1 in 140,000, at most. This calculation does not take into account the risk of nosocomial infection. Conversely, it does not factor in that patients will also be clinically assessed and asked to self-isolate prior to surgery.

Conclusion

Our estimation suggests that the risk of patients being inadvertently admitted with an undetected SARS-CoV-2 infection for elective orthopaedic surgery is relatively low. Accordingly, the risk of death following elective orthopaedic surgery is low, even when applying the worst case fatality rate.

Take home message

- In May 2020, the probability of admitting a patient for elective orthopaedic surgery with SARS-CoV-2 infection and a false-negative preoperative test was 0.07% (around 1 in 1,400).
- The probability of admitting a false-negative patient for elective orthopaedic surgery can be recalculated at any time using the estimated background prevalence in the community

Introduction

The incidence of COVID-19 cases in the United Kingdom is sharply decreasing.[[1]]

Planning to recover surgical services must balance the risks of infection with the requirement for elective surgery in order to reduce the impact on patients' outcomes and quality of life.[[2,3]] Reviewing the available evidence from the peak of the pandemic is discouraging.

A mortality rate of 20.5% was reported in a group of 34 elective surgical patients who developed COVID-19 after being inadvertently admitted during the early stages of the crisis in Wuhan, China. Only seven of the 34 patients underwent orthopaedic procedures, two of the orthopaedic patients required admission to the intensive care unit and subsequently died.[[4]] Recently, the multicentre international COVIDSurg cohort study reported a mortality rate of 18.9% in a group of 280 patients who acquired perioperative COVID-19 infection during admission for elective surgery. The 24 contributing countries employed a pragmatic approach to COVID-19 diagnosis, using a combination of polymerase chain reaction (PCR) (85%), radiological (7.1%), and clinical (6.0%) findings, depending on the resources available in each centre.[[5]] Both studies reported on a highly heterogeneous sample of patients, including, but not limited to cancer sufferers.[[4,5]]

These findings suggest resumption of elective orthopaedics may have a significant mortality risk, however the patients included in these studies received care early in the pandemic within centres across several countries, with no predefined or standardized preoperative testing or risk stratification strategy, at a time when treatment protocols were rapidly evolving. These figures are taken from a period around the peak of the pandemic and will be less relevant as we approach the end of the current COVID-19 crisis.

Screening preoperative patients: Reverse transcription-polymerase chain reaction (RT-PCR)

In order to resume elective orthopaedic surgery, the British Orthopaedic Association (BOA) and NHS England recommend preoperative testing of patients,[[6,7]] however, the sensitivity of the swab test is thought to be between 71% to 98%, meaning up to 29% of infected patients could falsely test negative. [[8]] The specificity has been estimated to be over 95%. [[9]] Early epidemiological studies suggest that 5% to 80% of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections are asymptomatic at any given time. [[10]] In one sero-epidemiological study conducted in the German county of Heinsberg the asymptomatic rate was found to be 22.2%. [[11]] In Iceland, where widespread screening has been employed, only 57% of the individuals who tested positive reported symptoms. [[12]] These findings suggest asymptomatic, pre-symptomatic or sub-clinical patients may evade simple symptom screening and present a risk of transmission to other patients and staff.

Prevalence of the disease in the community

Arguably, the most important risk factor for SARS-CoV-2 infection is the prevalence in the community; as well as its infectivity and, thereby, the incidence of new cases. Due to a mismatch between the testing resources available and the actual number of active cases this is difficult to calculate with certainty. Estimations can, however, be made based on the most recent, representative UK population surveys. The UK Office for National Statistics (ONS) estimated the prevalence of SARS-CoV-2 infection during the period of the 11th May to the 24th May 2020 was 0.24% (95% confidence interval (CI) 0.11% to 0.46%). This was based on random sampling of 18,913 individuals within the community (excluding hospital, care home, and institutional settings). During the same time period the weekly incidence has been estimated to be 0.11% (95% CI 0.06% to 0.16%). [[13]]

Prevalence amongst healthcare workers

Healthcare workers (HCWs) have a higher prevalence of SARS-CoV-2 infection than the rest of the population; the latest figures from May 2020 show that the prevalence in individuals working in patient-facing healthcare was 1.73%.^{[[13]]} A study by the University of Cambridge found that in a sample of 1,032 asymptomatic staff, 31 tested positive (3%), only 17 of whom remained truly asymptomatic (1.6%).^{[[14]]} This is relevant when assessing risk of hospital staff to patient transmission.

We aim to use the most up-to-date data to estimate the risk of patients being admitted for an elective orthopaedic procedure with an undetected SARS-CoV-2 infection and subsequently dying from COVID-19.

Methods

Calculating the risk of missed SARS-CoV-2 infection in elective orthopaedic patients using pre-test probability

Given the reportedly low sensitivity of the PCR test, interpretation of a result will depend not only on the accuracy of the test itself but also on the pre-test probability of the patient having a disease. Clinicians regularly apply the concept of calculating pre-test probabilities in day-to-day practice; this could be derived from hard data such as disease prevalence. Alternatively, clinicians can use their experience to estimate pre-test probabilities based on their interpretation of symptoms, history of exposure, blood tests, and radiological imaging.^{[[15]]} Once a pre-test probability is determined, the risk of a missed infection can then be calculated using Bayes' theorem.^{[[16]]} This is described as the probability of an event, based on prior knowledge of conditions that might be related to the event.^{[[17]]}

Due to the serious nature of the disease and lack of a validated method of quantifying and incorporating the effect of the above influencing factors we decided to include the only quantifiable risk factor (disease prevalence) in our calculation. This may

lead to over-estimation of the pre-test probability of being infected and would present the possible worst-case scenario.

Calculating risk of death

Risk of death from a viral infection within a population can be estimated by the case fatality rate (CFR), which is the number of deaths per number of reported cases, or by the infection fatality rate (IFR), which is an estimate of the fatality rate in all patients with the disease, including those who are asymptomatic or have not been tested. During pandemics, evaluating these figures can be a hazardous exercise.[[18,19]] During the 2009 ‘swine flu’ (H1N1 influenza) outbreak the reported CFR was 0.1% to 5.1%. Subsequently the World Health Organization reported that ‘swine flu’ ended up with an IFR of 0.02%, five times lower than the lowest CFR estimates during the original outbreak. Therefore, it is important to acknowledge that during a pandemic the IFR could potentially decrease five- to ten-fold following final reporting.[[20]] Current data from multiple sources report a CFR for COVID-19 to be between 0.56% to 14%[[1,20-24]] and estimations for the IFR range between 0.3% and 1.3% (Table I).[[11,20,23-26]]

Table I. Reported case fatality rates and estimated infection fatality rate worldwide.

Region/case study	CFR, %	IFR, %
Global	6.3[[21]]	0.38[[20]] to 1.04[[25]]
China	1.38[[24]] to 2.3[[22]]	0.66[[24]]
UK	14[[21]]	0.9[[26]]
Germany	4.7[[21]]	0.36[[11]]*
Iceland	0.56[[20]]	0.3 to 0.56[[20]]
Diamond Princess cruise ship	2.6[[23]]	1.3[[23]]
H1N1 outbreak 2009 - for comparison	0.1 to 5.1[[20]]	0.02[[20]]

*Specific to Gangelt, County of Heinsberg.

CFR, case fatality rate; H1N1, swine flu; IFR, infection fatality rate.

Although wide-ranging CFR estimates are available, it must be noted that patients face the additional risk of undergoing surgery. Therefore, to estimate the risk of mortality in the elective orthopaedic cohort of patients, a worst-case scenario should be adopted. We decided to base our calculation on the CFR reported in elective surgical patients in Wuhan, China (20.5%),[[4]] which is even higher than the CFR in the recent COVIDSurg report (18.9%).[[5]]

Results

Using the available data of prevalence within the community (0.24%)[[13]] to determine the predicted pre-test probability and matching this to the sensitivity and specificity of the SARS-CoV-2 swab test used, the chance of any given patient being admitted for surgery with a false negative result is 0.07%, or around 1 in 1,400. However, it must be noted that this calculation does not take into account the risk of acquiring COVID-19 perioperatively. Equally it does not factor in the relative risk reduction from choosing asymptomatic patients who have been risk stratified, self-isolated and thoroughly pre-assessed by the multidisciplinary team.

The above calculations are based on the estimated disease prevalence in early May 2020 in England and Wales. [[13]] Examples for different levels of prevalence are included below for reference (Table II). Clearly surgeons must be vigilant in interpreting the risks of viral infection with changing prevalence.

Table II. Varying positive predictive value and negative predictive value of severe acute respiratory syndrome coronavirus 2 swab depending on prevalence in population – calculated using a reverse transcription-polymerase chain reaction sensitivity of 71%.

Prevalence in a population, %	PPV at specificity of 95%, %	PPV at specificity of 99%, %	NPV at specificity of 95%, %	NPV at specificity of 99%, %
3.00*	31	69	0.94	0.90
1.00	13	42	0.31	0.30
0.50	6.7	26	0.15	0.15
0.24†	3.3	15	0.07	0.07
0.13‡	1.8	8.5	0.04	0.04
0.05	0.71	3.4	0.02	0.01

*With a 3.00% prevalence, using a test-specificity of 95%, for every 100 people who test positive only 31 actually have the disease. When a test-specificity of 99% is used, for every 100 people who test positive only 69 have the disease.

†Example used in the calculation above, using 0.24% prevalence estimated by Office for National Statistics (ONS) 28th May 2020.[[13]]

‡Alternative example using 0.13% prevalence estimated by ONS 5th June 2020.[[9]]

NPV, negative predictive value; PPV, positive predictive value.

Based upon the worst-case CFR of 20.5% and the calculated risk of 1 in 1,400 pre-symptomatic false negative patients who undergo surgery developing COVID-19, approximately 1 in 7,000 patients undergoing an elective orthopaedic procedure will die of the disease.

The best-case scenario, however unlikely, is that a patient undergoing elective orthopaedic surgery has the same risk of death as a person in the community. If a global IFR of 1.04% is employed as per the recent modelling by Grewell and De Leo[[25]] (one of the higher values, to be cautious) then 1.04% of the 1 in 1,400 pre-symptomatic, false negative patients would die, resulting in a rate of roughly 1 in 140,000 patients undergoing elective surgery who will die from COVID-19.

Discussion

The aim of this study was to determine the risk of a patient being admitted for elective orthopaedic surgery with a missed SARS-CoV-2 infection and their subsequent risk of death. The probability of a patient having a SARS-CoV-2 infection despite a negative test was estimated as 1 in 1,400.

This estimated probability is without calculating the additional positive effect of pre-operative risk stratification, self-isolation, thorough clinical assessment and implementation of several mitigating factors to reduce risk to patients and staff. This analysis may aid surgeon to patient discussion preoperatively during the consenting process when resuming elective orthopaedic surgery. To provide context to the theoretical risk of death, surgeons can also use the background risk of death from an elective orthopaedic procedure for comparison. For example, total knee arthroplasty (TKA) has a 30-day mortality of 0.20% (95% CI 0.17% to 0.24%) or one in 500; and a 90-day mortality of 0.39% (95% CI 0.32% to 0.49%), roughly one in 250.[[27]] In total hip arthroplasty (THA) the 30-day mortality is 0.30% (95% CI 0.22% to 0.38%) or one in 333; 90-day mortality is 0.65% (95% CI 0.5% to 0.81%) or one in 153.[[28]] In addition, one should consider the background risk of death from any cause, for example recent age-standardized mortality rate data from England and Wales shows an average 65- to 69-year-old male has a 1.46% risk of death annually, or one in 68. For females of the same age group this is 0.94%.[[29]] The risks from elective surgery and COVID-19 will be cumulative, nonetheless this will be smaller than the already present, but arguably small, background risk of death from all causes in a given year.

The calculations made thus far have also not taken account of the additional risk of nosocomial SARS-CoV-2 infection acquired from healthcare staff during the hospital admission. This has the potential to be the biggest risk to the patient given the higher prevalence amongst HCWs. Each additional interaction with a member of the healthcare team may potentially present a further risk, which is determined not only by the prevalence within

HCWs but also the transmission rate. Although the Cambridge study reported a high prevalence among HCWs (3%), only seven out of 520 (1.34%) staff working in ‘green zones’ were both asymptomatic and test-positive. ‘Green zones’ were defined as ‘clinical areas without any known or suspected COVID-19 cases’. This illustrates that prevalence is not uniform across all hospital working zones. Furthermore, this study was conducted in April 2020 when the prevalence was high.

Transmission rates between patient-to-patient, staff-to-patient, and vice-versa are difficult to calculate. R_0 is the basic reproductive number, which measures the infectiousness of a disease if left to spread. R_0 is a static number, whereas R_t (alternatively known as R_e or R -effective) is more relevant in a hospital setting as it represents the actual transmission rate at a given time and reflects changes in infectiousness of the virus in response to social distancing measures, mask usage[[30]] and increases in the number of immune HCWs.[[31]] Hospital workers may be less susceptible as suggested in a recent study conducted in New York which found 36% of staff had developed antibodies in one hospital.[[32]] R_t can be further reduced by introducing green pathways with stricter policies[[6]] than those in the ‘green zones’ previously described. This is supported by evidence from a 2010 Cochrane review which showed that the combination of multiple interventions such as hand washing, masks, gloves, and gown use can reduce the risk of transmission of respiratory viral illness by an odds ratio of 0.09 (95% CI 0.02 to 0.35).[[33]]

In our example, the worst mortality figures available for elective surgical patients were used to give a cautious estimate of the likelihood of an asymptomatic, false-negative testing patient being admitted for surgery and subsequently the risk of dying from COVID-19. This figure (20.5%) is around 20 times higher than the highest estimates of mortality from COVID-19 in the community. This disproportionately high mortality rate cannot be explained by the trauma of surgery alone. Likely factors contributing to the high

complication rate include the underdeveloped patient care protocols and professional learning curve faced in dealing with COVID-19 early in the pandemic. The reported sensitivity and specificity of RT-PCR is variable, for the calculated risks presented in this study we chose the lowest rates to present the worst-case scenario.

Our calculations are derived from figures from the most reliable survey study by the ONS at the most relevant time to resuming elective surgery. We are aware that prevalence and incidence numbers are extremely variable during pandemic. Therefore, it is highly likely that the risk may be even further reduced with a reduction in the disease prevalence and incidence by the time elective surgery is resumed (Table II).

Clinicians need to be aware that, as the prevalence of the disease falls, the positive predictive value will decrease leading to patient inconvenience from unnecessary cancellations.[[11]] At a prevalence level of 0.24% and swab-test specificity of 95%, for every 100 people who test positive, only three will have the disease (Table II). The ONS reports that the specificity is likely higher than reported in the literature;[[34]] if a figure of 99.9% is used instead, then for every 100 people who test positive, only 63 will have the disease.

In conclusion, this study provides surgeons with risk estimates of SARS-CoV-2 infection in UK elective orthopaedic patients. This calculation was dependent on estimated disease prevalence in May 2020. It shows that the risk of patients being inadvertently admitted with an undetected SARS-CoV-2 infection for elective orthopaedic surgery is relatively low (1 in 1,400) and the subsequent risk of death may be even lower (1 in 7,000, at worst).

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