



Thoracic Surgery during COVID-19 Outbreak. How High is the Risk for Non Vaccinated Patients?

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Abstract

Background: Despite legislation, guidelines and nudge strategies, a small but not negligible proportion of the population refuses vaccine against COVID-19. The actual risk for non vaccinated patients to undergo a thoracic surgery procedure during COVID outbreak remains undetermined. The aim of the study was to analyze the worst case scenario measuring that risk during the second wave period, when vaccines were not available.

Materials and Methods: Cases of postoperative COVID infection were monitored in the 6 Thoracic Surgery Divisions in Piedmont, Italy, from October to December 2020. Postoperative COVID-19 infection was defined by the presence of a positive quantitative RT-PCR test on nasal swabs found within one month from the procedure. Positive cases were analyzed searching for clinical predictors of symptomatic infection by univariate (Student T test or Mann-Whitney test for continuous variables according to their distribution and Chi square test for categorical variables) and multivariate analysis..

Results: Twenty cases of postoperative COVID infection were identified on an overall population of 466 patients operated on during the considered period (overall incidence 4.2%). Eleven patients were operated for oncological reasons, 3 patients due to pleural infection, and 6 patients for recurrence pleural effusion or pneumothorax with persistent air leak. Infection was asymptomatic in 6 cases and symptomatic in 14 cases. In 3 patients, symptoms occurred after discharge. Five patients died due to consequences of COVID infection (mortality 25%). During the considered period, COVID-19 was responsible of an additional mortality of 1%. Older patients were more likely to develop symptomatic infection.

Conclusion: In the second wave scenario in Italy, the additional overall mortality due to COVID was in the order of 1%. This figure indicates the risk during pandemic outbreak in absence of an effective vaccination and probably overestimates the actual risk. In fact, a large proportion of general population has been immunized since then, reducing viral circulation and exposure of non vaccinated patients.

Keywords: COVID-19; Thoracic surgery; Postoperative complications

Introduction

Despite large-scale vaccination programs against COVID-19 progress worldwide, still a consistent proportion of the population is not immunized yet [1]. Due to the high mortality in patients developing postoperative COVID infection, the STS workforce on critical care recently recommended full vaccination for patients requiring cardiothoracic surgery and at least a single dose of vaccine before time-sensitive procedures [2,3].

As history of vaccination clearly showed, legislation and nudge strategies in order to improve the immunization rate are ineffective in a small but not negligible proportion of the population who refuses vaccine due to ideological reasons or fear of side effects [4]. What if a non vaccinated patient needs a non-cardiac thoracic surgery procedure during COVID outbreak? How to estimate the risk? The answer is difficult because many variables (such as the specific pandemic phase, community

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and in-hospital protection protocols, vaccination rates in general population and caregivers) evolve over time and available data are limited as only few surgical series have been published [5-7].

An estimate of the upper boundary of this risk can be probably obtained retrospectively analyzing the incidence of postoperative COVID infection during the second wave. The specificity of this context was that all patients were routinely tested for COVID at hospital admission (allowing the distinction between pre and postoperative cases) and vaccines were not yet available.

The aim of this study was to define incidence and mortality of postoperative COVID infection in patients who underwent a thoracic non-cardiac procedure during the second Italian lockdown period and in the preceding month in the six Thoracic Surgery Divisions of Piedmont (Italian North-West, 4.4 million inhabitants).

Materials and Methods

At the beginning of November 2020, the Italian Government adopted restrictive measures due to the rising number of COVID-19 cases during the preceding month. At that time, all the six Thoracic Surgery Divisions of Piedmont (S. Luigi Hospital, Orbassano, Città della Salute Hospital, Torino, Giovanni Bosco Hospital, Torino, S. Croce Hospital, Cuneo, Ospedale della Carità, Novara, Alessandria Hospital) decided to monitor the number of postoperative COVID infections in the period October to December 2020.

According to national guidelines, all patients were tested for COVID in the 48 h preceding admission and negative patients were admitted in thoracic wards organized at COVID-free units. After surgery, patients were retested in case of symptoms onset or in case of contact with positive cases. Postoperative COVID-19 infection was defined by the presence of a positive quantitative RT-PCR test on nasal swabs found within one month from the procedure. Once diagnosed, COVID patients were initially isolated and then transferred in a COVID unit or in ICU as needed.

A dedicated 59-field database was designed in order to collect information from patients who developed a postoperative COVID infection. The following variables were collected: Comorbidity, preoperative respiratory function (when available), indication for surgery, performed procedure, postoperative outcome, type of COVID infection (asymptomatic vs. symptomatic), type of symptoms, time of diagnosis, treatment (azithromycin, steroids, remdesivir) and outcome as of March 2021. For patients who developed respiratory failure (defined as the presence of a $paO_2 < 55$ mmHg on air requiring > 24 h of oxygen administration), type of required care was recorded (semi-intensive with continuous monitoring + NIV in the COVID ward or intensive, ICU transfer + NIV or mechanical ventilation).

A comparison between clinical characteristics of symptomatic and asymptomatic cases was performed. Continuous variables were reported according to their distribution (as a mean + standard deviation in case of normal distribution and as median in case of non-normal distribution). Categorical variables were presented as numbers and proportion. Comparisons between groups were performed by Student T test, Mann-Whitney test or Chi-square test as appropriate. Multivariate analysis was planned for significant ($p < 0.05$) factors at univariate analysis.

All patients gave their consent to the use of data for scientific purposes before surgery. Data was de identified, collected and analyzed at the S Luigi Hospital using Stata, version 14 (Statacorp).

The S Luigi Hospital Institutional Review Board reviewed the study and a specific informed consent was waived due to the de identified nature of data (n° 9138, June 18th, 2021). Data were available upon the request of reviewers or editors during the review process and will be shared on reasonable request to the corresponding author.

Results

In the period October to December 2020, 466 patients underwent a non-cardiac thoracic surgery procedure in Piedmont. In twenty of them (4.2%) COVID test resulted positive within a month after surgery. Clinical characteristics of patients are listed in Table 1. Ten patients were operated for oncological reasons, 4 patients due to pleural infection, and 6 patients for recurrence pleural effusion or pneumothorax with persistent air leak.

Six patients were asymptomatic and tested during hospitalization because they were in contact with a positive case during hospitalization. In 11 patients (55%), COVID infection was detected because of symptoms (fever and cough or diarrhea in 5 cases, respiratory failure in 6 cases), and the time of onset ranged from POD0 to POD21. At follow-up in March 2021, three additional cases were detected in which patients developed respiratory symptoms (2 cases) or fever (1 case) early after discharge.

In patients who developed postoperative COVID infection, overall mortality was 25% (5 patients). In patients who were diagnosed during their hospital stay ($n=17$), 3 postoperative deaths occurred after left pneumonectomy, VATS for recurrent pleural effusion and decortication for empyema, all due to severe respiratory failure. Out of the 3 patients who became symptomatic after discharge, 2 deceased. The third patient required 5 weeks of NIV for severe dyspnea associated with diffuse bilateral lung infiltrated and finally recovered. At follow up on March 2021, 15 patients were alive and two of them still required oxygen administration.

Comparing asymptomatic ($n=6$) and symptomatic patients ($n=11$), age was the only clinical factor for which a significant difference was detected (median value 62.5 and 69.5 years respectively, $p=0.05$). Patient who died after COVID infection were older as compared to those who survived but the difference was not significant, due to the exiguity of the cohort (76 vs. 67 years respectively, $p=0.17$).

Comment

It is likely that in the next future a certain, not negligible number of patients non-vaccinated against COVID will require a non cardiac thoracic procedure. In case of surgery during pandemic peak, their risk will range between two extremes: A low risk if the general population is highly immunized and if vaccines are effective against virus variants or an high risk if herd immunity is not reached and vaccines are not effective against variants [8]. Given the fact that the final immunization rate of general population and the occurrence of viral variants are not predictable, only the worst case scenario can be anticipated extrapolating information from retrospective data, which was the aim of this study.

Results from this study showed that without vaccination the risk for patients of developing postoperative COVID infection during the second pandemic wave was in the order of 4%, the same figure recorded during the first wave, despite a probably more precise detection of asymptomatic cases [5]. Mortality in patients who developed COVID infection was in the order of 25%, as expected [9]. These figures suggest a final estimated additional mortality due to COVID of 1%

Table 1: Clinical details of postoperative COVID-positive cases.

Patient	Age	Sex	Surgery	Symptoms/POD	Treatment	Outcome
1	M	63	Sternotomy, thymoma, first COVID infection 3 months before	Respiratory failure/after discharge	Atb, rem, NIV, ICU	
2	M	66	Right lower lobectomy, nsclc	Respiratory failure/2	atb, rem, NIV, ICU	Transferred to rehab
3	M	40	VATS, wedge + talc, pnx	No	Atb, rem, NIV, ICU	
4	M	20	VATS, wedge + talc, pnx	No		
5	M	58	Wedge resection, lung mets	Fever, lung infiltrates/10	NIV, ICU	
6	F	77	Right upper lobectomy, nsclc	Fever/after discharge		
7	M	70	Pleural decortication, empyema	Fever, diarrhea/5	Atb	Discharged on O ₂
8	M	70	Right upper lobectomy, nsclc	Fever/after discharge		
9	F	74	Right lower lobectomy, nsclc	Cough, fever/21		
10	F	56	VATS, wedge res, lung mets	Respiratory failure/after discharge	Atb	COVID ward death
11	F	76	Vats, empyema	Respiratory failure/after discharge	Atb	COVID ward death
12	M	74	Vats, pleural biopsy, pleural nodules	No		
13	M	70	Vats, pleural biopsy, pleural effusion	No		
14	M	80	Vats, pleural biopsy, pleural effusion	Respiratory failure/11	Atb	In hospital death
15	F	58	Vats, empyema	Fever, lung infiltrates/0	Atb	
16	M	82	Left pneumonectomy, nsclc	Respiratory failure/18		In hospital death
17	F	68	Right upper lobectomy, neuroendocrine	Respiratory failure/11	Atb, NIV	
18	F	55	Multiple wedge resections, lung mets	No		
19	M	69	Vats, empyema	Respiratory failure/5	Atb, NIV	In hospital death
20	M	73	Right lower lobectomy, nsclc	No/22		

Table 2: Comparison between asymptomatic and symptomatic postoperative COVID cases.

Variable	Asymptomatic (n=6)	Symptomatic (n=14)	p value
Age (median)	62.5	69.5	0.05
Sex (M)	5 (83.6%)	8 (57.1%)	0.35
Smoke (active)	2 (33.3%)	3 (21.4%)	0.61
COPD	2 (33.3%)	3 (21.4%)	0.61
Comorbidity	2 (33.3%)	7 (50%)	0.64
Oncological disease	2 (33.3%)	9 (64.2%)	0.33
Pleural infection	0	3 (21.4%)	0.52
Major surgery (sternotomy, horacotomy and/or anatomical/multiple lung resection)	2 (33.3%)	7 (50%)	0.64
Other postoperative complications	1 (16.6%)	5 (35.7%)	0.61

in this scenario, which probably overestimates the actual risk. In fact, since our data collection, caregivers have been extensively vaccinated at the beginning of 2021 and immunization of general population started, with a consequent decrease of postoperative symptomatic cases during the third outbreak (February to April 2021). Moreover, efficacy of vaccines against the delta variant, which is at present responsible for more than 80% of COVID cases in Italy, has been proven [10]. The possible occurrence of new variants eluding vaccine protection against them remains unpredictable.

Albeit potentially inaccurate, this estimate becomes probably more precise in those patients who need surgery and did not receive vaccination for medical reasons. In fact, due to their delicate clinical condition in some cases, the impact of postoperative COVID infection could be devastating and they should not probably be operated during outbreak peak if procedure can be postponed. Anyhow, in case of hospitalization, promiscuity with other non-vaccinated patients should be probably avoided in these frail patients.

Focusing on the category of younger patients, only one case of asymptomatic infection was recorded in the present series, suggesting that the risk for young non-vaccinated people is minimal. Nevertheless, caution should be employed in case of surgery during pandemic for several reasons. First of all, during the study period regional guidelines recommended to postpone surgery for benign disease after the end of pandemic peak and this could explain the low number of postoperative infection recorded in the study. Additionally, young patients seems to have been spared during the first three waves of pandemic but, at the time of submission of the paper, the number of cases is increasing in this population and their rate of immunization remains low (in August 2021, complete immunization rate in Piedmont for persons aged 10 to 19 was 17.5% and for those aged 20 to 29 was 43.5%), as compared to general population [11]. Finally, the risk of postoperative COVID infection does not seem to be related to the extent of the procedure, as 50% of postoperative cases in the series occurred after minor surgery (VATS for pleural disease or wedge resection).

There are some limitations in the present study. First, results do not permit to precisely measure the risk of surgery in the next future for non vaccinated patients but figures give an approximate estimate of the upper boundary only. Also, the choice to consider only data from the second wave was arbitrary. This decision was based on the fact that first wave data were imprecise in detecting asymptomatic cases, as COVID testing was not performed as a routine at hospital admission [5]. On the contrary, third wave data were not considered because general vaccination program was in progress, the risk of potential contamination from vaccinated to non-vaccinated individuals was undetermined and first cases of the Delta variant were recorded. However, it is reasonable to assume that progressive vaccination of general population progressively reduced the risk of postoperative infection in non-vaccinated patients. Unfortunately, an exact estimate in case of a new outbreak remains uncertain, as it depends on variables which are unpredictable such as herd immunity, occurrence of variants and efficacy of vaccines against them.

Taking decisions in a context of uncertainty requires a proper balance between forecast capacity and analysis of available data. In case of new COVID outbreak, surgical management of time-sensitive, non vaccinated cases can represent an additional problem for thoracic surgeons. A prospective collection of data would be helpful in order to obtain a more precise estimate of this risk.

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