

The Impact of COVID-19 Infection During the Postoperative Period After Surgery for Ovarian Cancer

NICOLAE BACALBASA^{1,2} and IRINA BALESCU³

¹Department of Visceral Surgery, Center of Excellence in Translational Medicine “Fundeni” Clinical Institute, Bucharest, Romania;

²Department of Obstetrics and Gynecology,

“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania;

³Department of Surgery, “Ponderas” Academic Hospital, Bucharest, Romania

Abstract. *Background/Aim: The COVID-19 pandemic has significantly influenced the management of oncogynecologic patients in regard to time of diagnosis, to delay of treatment, therapeutic strategy and postoperative complications. The aim of the study was to investigate the impact of preoperative SARS-Cov2 infection on the postoperative outcome after debulking surgery for ovarian cancer. Patients and Methods: Between June 2021 and September 2021, 12 patients with antecedents of COVID-19 infection and ovarian cancer were submitted to surgery at “Dr. I. Cantacuzino” Hospital, Bucharest, Romania. Their outcomes were compared to those reported in a similar group of patients submitted to surgery during the same period in the absence of COVID-19 infection. Results: Although preoperative data showed no statistically significant differences between the two groups, intraoperative length and estimated blood loss were higher in the COVID-19 group and so were the postoperative complications, the most commonly encountered ones being reported by wound infection, postoperative hemoperitoneum and pneumonia. However, the differences did not reach statistical significance. Conclusion: Preoperative COVID-19 infection seems to slightly increase the risk of postoperative complications after debulking surgery for ovarian cancer.*

Correspondence to: Nicolae Bacalbasa, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania. Tel: +40 723540426, e-mail: nicolae_bacalbasa@yahoo.ro

Key Words: COVID-19 pandemic, ovarian cancer, debulking surgery.

In March 2020 the World Health Organization declared the COVID-19 infection as a pandemic especially due to its rapid spread and due to the gravity of certain cases (1). The rapid spread of the disease led to a rapid occupation of the available beds in hospitals over the world, necessitating segregated pathways of treatment and dedicated health care professionals in order to impede the cross-infection between patients. Therefore, a rapid lock-down of the sanitary systems occurred leading to a significant delay of establishing the diagnostic and initiation of therapy in a significant number of pathological conditions, oncologic patients being maybe the ones most affected. In order to minimize the risk of contamination, self-isolation became the new standard and patients with non-specific symptoms were encouraged to use telemedicine and on-line medical appointments. Therefore, the physical examination as well as the possibility of performing a basic imagistic evaluation such as vaginal ultrasound significantly decreased; in this context it is well understood that ovarian cancer patients were usually diagnosed at more advanced stages of disease and more extended surgical procedures were needed in order to achieve complete resection (2, 3). Meanwhile, it should not be omitted that COVID-19 infection can be associated with serious pulmonary and cardio-circulatory problems such as respiratory failure, pneumonia, deep venous thrombosis or pulmonary embolism, pneumonia, arrhythmia or other coagulation issues and therefore, a more difficult recovery is expected especially after performing aggressive surgical procedures (4-8). The aim of the current study is to compare the postoperative outcomes of patients submitted to surgery after COVID-19 infection to the ones reported in a similar group of patients in the absence of this event.

Patients and Methods

After obtaining the approval of the Ethics Committee of “Dr. I. Cantacuzino” Hospital, Bucharest, Romania data of patients submitted to surgery between June 2021 and September 2021 were



This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY-NC-ND) 4.0 international license (<https://creativecommons.org/licenses/by-nc-nd/4.0>).

retrospectively reviewed. Among these cases, there were 12 patients diagnosed with advanced-stage ovarian cancer associating antecedents of COVID-19 infection submitted to surgery in this period. Their outcomes were compared to those reported in a similar group of patients diagnosed at similar ages and in similar stages submitted to surgery during the same period, by the same surgical team but in whom there was no evidence of COVID-19 infection. However, at the time of surgery all patients were tested negative for COVID-19 infection while the computed tomography demonstrated the absence of active, evolving pleuro-pulmonary lesions. The mean interval between the last positive test of COVID-19 and surgery was of six weeks (range=4-8 weeks), the time of surgery depending on the severity of the oncologic disease.

Results

The mean age at the time of initial diagnosis was 56 years in the COVID-19 group and respectively 59 years in the non-COVID-19 group ($p=0.92$) while the mean value of cancer antigen 125 (CA125) was of 2,234 U/ml in the COVID-19 group and 1,990 U/ml in the non-COVID-19 group ($p=0.642$). All cases (in both the COVID-19 group and non-COVID-19 group) were diagnosed in advanced stages of the disease (stage IIIC and IV) and were submitted to surgery as first intent treatment. When it comes to the severity of SARS CoV-2 infection, in all cases the patients presented asymptomatic forms or mild symptoms, only two of the 12 cases necessitating hospital in stay. However, none of the cases necessitated admission in the intensive care unit.

When it comes to operative outcomes, surgery with curative intent was intended in all cases and was defined as resection to no residual disease. However, this desiderate was obtained in only seven cases in the COVID-19 group and in eight cases in the non-COVID-19 group. In the remaining cases there were two cases in which microscopic residual disease was achieved in the COVID-19 group and respectively one case in the non-COVID-19 group; meanwhile, macroscopic residual disease was found in three cases in each subgroup. Intraoperative details are presented in Table I. As can be observed in Table I, there was no significant difference in terms of extent of surgery in the lower and respectively upper abdomen as well as in terms of the complexity of resection. Even though, patients in the COVID-19 group experienced a longer intraoperative time (240 min *versus* 200 min, mean value), a higher amount of blood loss (1,400 ml *versus* 1,000 ml, mean value) and a higher number of units of blood (3 units *versus* 2 units, mean value). However, in univariate analysis none of these differences reached statistical significance (operative time – $p=0.331$, blood loss – $p=0.918$, transfused units – $p=0.571$). These data come to demonstrate that patients in the COVID-19 group presented an increased fragility of tissues. Meanwhile, this fragility was also considered to be correlated with the increased trend of intraoperative bleeding (demonstrated through a higher

amount of blood loss and a higher necessity of transfusions among COVID-19 patients. However, although patients with previous COVID-19 infection proved to have more fragile tissues, exhibiting a higher risk of perioperative bleeding, the rates of complete cytoreduction as well as the complexity of the surgical procedures were similar between the two groups.

When it comes to postoperative outcomes, patients in the COVID-19 group reported a slightly increased hospital stay as well as a slightly increased number of postoperative complications, without reaching any statistical significance. Meanwhile, the number of reinterventions was higher among the COVID-19 group, the most commonly encountered indication for re-operation being reported by hemoperitoneum, in two cases. The mean hospital in stay among COVID-19 patients was of 14 days, slightly increased when compared to the one reported in the COVID-19 free group (in which the mean hospital in stay was of 12 days); however, this fact did not reach statistical significance ($p=0.278$). Details of the postoperative outcomes are shown in Table II.

As can be seen in Table II, the most commonly encountered complications were represented by wound infections – in eight cases – five cases among the COVID-19 patients and three cases among non-COVID-19 patients, followed by hemoperitoneum and pneumonia – each in three cases in the COVID-19 patients and respectively in one case in the non-COVID-19 patients. Other reported complications were represented by digestive and urinary leaks, encountered in two and respectively one case among non-COVID-19 patients. However, re-operation was required only in one case, due to the presence of urinary fistula; meanwhile the other two cases diagnosed with digestive leaks were successfully treated in a conservative manner. Similarly to the intraoperative outcomes, during the postoperative period the most significant complication reported after surgery in COVID-19 patients was related to the fragility of tissues and to increased rates of perioperative bleeding. Interestingly, when it comes to the rates of pulmonary complications, they were similar between the two groups.

Discussion

During the COVID-19 pandemic a significant number of patients were affected developing different forms of disease with a wide spectrum of symptoms from completely asymptomatic to severe pneumonia, pulmonary embolism, uncontrollable arrhythmias and even death (1). Meanwhile, due to the sanitary lock-down which took place during this period a significant number of patients had restricted access to the medical services leading to delays in terms of diagnostic and therapy initiation, with tragic consequences especially in oncological cases (2). When it comes to advanced-stage ovarian cancer, guidelines developed during the COVID-19 pandemic propose administration of neoadjuvant chemotherapy

Table I. Intraoperative aspects of patients submitted to surgery between June and September 2021.

Parameter	COVID-19 group	Non-COVID-19 group
Type of resection		
R0	7	8
R1	2	1
R2	3	3
Lower abdominal resections		
Rectosigmoidian resections	6	5
Total/partial cystectomy	3/2	2/3
Right colectomy	3	4
Small bowel resection	4	2
Pelvic lymph node dissection	12	12
Pelvic peritonectomy	10	8
Upper abdominal resections		
Para-aortic lymph node dissection	8	11
Splenectomy	3	1
Atypical liver resection	3	5
Pancreatic resection	1	0
Diaphragmatic resection	2	4
Partial gastrectomy	0	1
Transverse colectomy	1	2
Length of surgery (min, range)	240 min (180-360 min)	200 min (150-320 min)
Estimated blood loss (ml, range)	1,400 ml (600-2,100 ml)	1,000 ml (400-1,800 ml)
Units of transfusion (no, range)	3 units (1-4 units)	2 units (1-4 units)

Table II. Postoperative outcomes among COVID-19 and respectively non-COVID-19 patients submitted to surgery for advanced-stage ovarian cancer between June and September 2021.

Parameter	COVID-19 group	Non-COVID-19 group
Hospital in stay (days, range)	14 (9-21 days)	12 (6-20 days)
Postoperative intensive care stay (days, range)	2 (1-3 days)	1 (1-3 days)
Intensive care readmissions	3/12	2/12
Postoperative complications		
Wound infection	5	3
Postoperative hemoperitoneum	3	1
Pneumonia	3	1
Digestive leak	1	0
Urinary leak	0	1
Re-operations	3 cases - hemoperitoneum	2 cases – hemoperitoneum, urinary leak

followed by maintenance therapy with poly adenosine diphosphate ribose polymerase inhibitors until the moment in which surgery becomes possible (9). Moreover, an even more affected category of patients was the one with COVID-19 infection and in which an advanced oncological issue was diagnosed. In such cases large studies have been conducted in order to determine which is the most appropriate moment for surgery and analyse whether the antecedents of COVID-19 infection significantly influence the postoperative outcomes in such cases (9-12).

An interesting study which was conducted on the issue of postoperative complications after major elective surgery in

active or post-COVID-19 infection has been recently published by Deng *et al.* (10). The study included 5,479 patients who tested positive for COVID-19 and who underwent a surgical procedure: 2,621 patients were submitted to surgery at least 30 days before a positive test for COVID-19 infection, 780 patients were submitted to surgery after 0 to 4 weeks after diagnosis of COVID-19 infection, 445 cases were submitted to surgery at 4 to 8 weeks after the initial diagnosis of SARS CoV-2 infection and the remaining 1,633 patients were submitted to surgery after at least 8 weeks from the initial positive COVID-19 test. The authors demonstrated the fact that pre-COVID-19 patients – submitted to surgery at 0-4 weeks after the initial positive test

– had a significantly higher risk of developing postoperative pneumonia, sepsis and respiratory failure when compared to pre-COVID-19 patients; meanwhile early post-COVID-19 patients (submitted to surgery at 4-8 weeks after COVID-19 infection) reported only a slightly increased risk of developing postoperative pneumonia while late post-COVID-19 patients reported a similar risk of postoperative complications when compared to pre-COVID-19 patients (10).

Another meta-analysis which studied the influence of COVID-19 infection on the postoperative outcomes was conducted by Wang *et al.* and demonstrated that, besides pulmonary complications, another significant issue which should be taken in consideration regards the immune system and impaired immune function which might develop during the early postoperative period (13).

Similarly to the results reported in the literature so far, in our study the most commonly encountered complications after surgery in post – COVID-19 patients were represented by the pulmonary ones; meanwhile, infectious complications such as wound infection were more frequently encountered in the post – COVID-19 group. Interestingly, in our cases another frequently encountered complication which also required re-operation and re-admission in the intensive care unit was represented by the postoperative hemoperitoneum, which, in our opinion is caused by the increased fragility of the tissues in these cases. A similar conclusion regarding the risks of postoperative bleeding in post-COVID-19 patients was demonstrated by Chiariello *et al.* in a study group of 23 patients submitted to cardio-pulmonary bypass with perioperative diagnostic of COVID-19 infection. The authors underlined the fact that post-COVID-19 patients had a significantly higher rate of postoperative bleeding, including a significantly higher rate of re-operation, a higher incidence of postoperative thrombocytopenia, a higher need of postoperative transfusion and a longer period of maintenance of the drainage tubes (14). The pathophysiology is not fully understood but it has been considered that diffuse systemic bleeding can develop due to the cytokine storm which is frequently induced by COVID-19 infection. The increased amounts of circulating cytokines usually conduct to the development of generalised endothelial damage and increased permeability at this level therefore inducing the apparition of diffuse bleeding, vasospasm and multiple organ failure (15, 16). Moreover, a virus directed thrombocytopenia and fibrinolysis has also been incriminated (17, 18); these processes seem to significantly influence the bleeding risks even after minimal surgical procedures such as biopsy procedures (19, 20).

Conclusion

Although COVID-19 infection can cause serious health problems and even death in cases in which a severe form develops, it seems that in asymptomatic cases or in cases

presenting mild symptoms complete recovery can be expected; in this context, cases diagnosed with other severe health problems such as gynaecological cancers can be safely submitted to standard surgical procedures such as debulking surgery. Although a more difficult perioperative outcome is to be expected, it seems that the rates of perioperative complications are similar between COVID-19 and non-COVID-19 patients.

Conflicts of Interest

There are no conflicts of interest to declare regarding this study.

Authors' Contributions

NB performed analysis of data; IB performed literature review.

References

- 1 World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available at: <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020> [Last accessed on March 22, 2022]
- 2 COVIDSurg Collaborative: Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. *Br J Surg* 107(11): 1440-1449, 2020. PMID: 32395848. DOI: 10.1002/bjs.11746
- 3 COVID-19Surg Collaborative. COVID-19Surg Cancer/COVID-19Surg-Cancer Gynaecological Oncology (GO), 2020. Available at: https://globalsurg.org/wp-content/uploads/2020/05/GOCovidSurg_StudySummary_v2.pdf [Last accessed on March 22, 2022]
- 4 Rali P, O'Corragain O, Oresanya L, Yu D, Sheriff O, Weiss R, Myers C, Desai P, Ali N, Stack A, Bromberg M, Lubitz AL, Panaro J, Bashir R, Lakhter V, Caricchio R, Gupta R, Dass C, Maruti K, Lu X, Rao AK, Cohen G, Criner GJ, Choi ET and Temple University COVID-19 Research Group: Incidence of venous thromboembolism in coronavirus disease 2019: An experience from a single large academic center. *J Vasc Surg Venous Lymphat Disord* 9(3): 585-591.e2, 2021. PMID: 32979557. DOI: 10.1016/j.jvsv.2020.09.006
- 5 Fraser E: Long term respiratory complications of covid-19. *BMJ* 370: m3001, 2020. PMID: 32747332. DOI: 10.1136/bmj.m3001
- 6 Chen S, Zhang D, Zheng T, Yu Y and Jiang J: DVT incidence and risk factors in critically ill patients with COVID-19. *J Thromb Thrombolysis* 51(1): 33-39, 2021. PMID: 32607652. DOI: 10.1007/s11239-020-02181-w
- 7 Knisely A, Zhou ZN, Wu J, Huang Y, Holcomb K, Melamed A, Advincula AP, Lalwani A, Khoury-Collado F, Tergas AI, St Clair CM, Hou JY, Hershtman DL, D'Alton ME, Huang YY and Wright JD: Perioperative morbidity and mortality of patients with COVID-19 who undergo urgent and emergent surgical procedures. *Ann Surg* 273(1): 34-40, 2021. PMID: 33074900. DOI: 10.1097/SLA.0000000000004420
- 8 Jonker PKC, van der Plas WY, Steinkamp PJ, Poelstra R, Emous M, van der Meij W, Thunnissen F, Bierman WFW, Struys MMRF, de Reuver PR, de Vries JPM, Kruijff S and Dutch Surgical COVID-19 Research Collaborative: Perioperative

- SARS-CoV-2 infections increase mortality, pulmonary complications, and thromboembolic events: A Dutch, multicenter, matched-cohort clinical study. *Surgery* 169(2): 264-274, 2021. PMID: 33158548. DOI: 10.1016/j.surg.2020.09.022
- 9 Uwins C, Bhandoria GP, Shylasree TS, Butler-Manuel S, Ellis P, Chatterjee J, Tailor A, Stewart A and Michael A: COVID-19 and gynecological cancer: a review of the published guidelines. *Int J Gynecol Cancer* 30(9): 1424-1433, 2020. PMID: 32576608. DOI: 10.1136/ijgc-2020-001634
- 10 Deng JZ, Chan JS, Potter AL, Chen YW, Sandhu HS, Panda N, Chang DC and Yang CJ: The risk of postoperative complications after major elective surgery in active or resolved COVID-19 in the United States. *Ann Surg* 275(2): 242-246, 2022. PMID: 34793348. DOI: 10.1097/SLA.0000000000005308
- 11 Madrazo Z, Osorio J, Otero A, Biondo S, Videla S and COVID-CIR Collaborative Group: Postoperative complications and mortality following emergency digestive surgery during the COVID-19 pandemic: A multicenter collaborative retrospective cohort study protocol (COVID-CIR). *Medicine (Baltimore)* 100(5): e24409, 2021. PMID: 33592888. DOI: 10.1097/MD.00000000000024409
- 12 Gulina M, Novakov IP, Antovic S and Velikova T: Surgical complications in COVID-19 patients in the setting of moderate to severe disease. *World J Gastrointest Surg* 13(8): 788-795, 2021. PMID: 34512902. DOI: 10.4240/wjgs.v13.i8.788
- 13 Wang K, Wu C, Xu J, Zhang B, Zhang X, Gao Z and Xia Z: Factors affecting the mortality of patients with COVID-19 undergoing surgery and the safety of medical staff: A systematic review and meta-analysis. *EClinicalMedicine* 29: 100612, 2020. PMID: 33169112. DOI: 10.1016/j.eclinm.2020.100612
- 14 Chiariello GA, Bruno P, Pavone N, Calabrese M, D'Avino S, Ferraro F, Nesta M, Farina P, Cammertoni F, Pasquini A, Montone RA, Montini L and Massetti M: Bleeding complications in patients with perioperative COVID-19 infection undergoing cardiac surgery: a single-center matched case-control study. *J Cardiothorac Vasc Anesth*, 2021. PMID: 34906382. DOI: 10.1053/j.jvca.2021.11.013
- 15 Tang N, Li D, Wang X and Sun Z: Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 18(4): 844-847, 2020. PMID: 32073213. DOI: 10.1111/jth.14768
- 16 Iba T, Levy JH, Levi M and Thachil J: Coagulopathy in COVID-19. *J Thromb Haemost* 18(9): 2103-2109, 2020. PMID: 32558075. DOI: 10.1111/jth.14975
- 17 Xu P, Zhou Q and Xu J: Mechanism of thrombocytopenia in COVID-19 patients. *Ann Hematol* 99(6): 1205-1208, 2020. PMID: 32296910. DOI: 10.1007/s00277-020-04019-0
- 18 Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS and China Medical Treatment Expert Group for Covid-19: Clinical characteristics of Coronavirus disease 2019 in China. *N Engl J Med* 382(18): 1708-1720, 2020. PMID: 32109013. DOI: 10.1056/NEJMoa2002032
- 19 Altschul DJ, Unda SR, de La Garza Ramos R, Zampolin R, Benton J, Holland R, Fortunel A and Haranhalli N: Hemorrhagic presentations of COVID-19: Risk factors for mortality. *Clin Neurol Neurosurg* 198: 106112, 2020. PMID: 32738585. DOI: 10.1016/j.clineuro.2020.106112
- 20 Degeneffe A, Bruneau M, Spitaels J, Gilis N, De Witte O and Lubansu A: Acute hemorrhage after intracerebral biopsy in COVID-19 patients: report of 3 cases. *World Neurosurg* 141: 157-161, 2020. PMID: 32526365. DOI: 10.1016/j.wneu.2020.06.016

Received January 24, 2022

Revised March 1, 2022

Accepted March 29, 2022