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Review Article

# Considerations for Perioperative Thromboembolic Risk Mitigation in Actively and Recently COVID-19-Positive Patients Undergoing Hand Surgery

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Coronavirus Disease 2019 (COVID) induces a hypercoagulable state causing an increased risk of venous and arterial thromboses. Distal limb and microvascular circulation are critical to the success of many hand surgeries, and patients who are actively or recently infected with COVID may be at a higher risk for perioperative thrombotic events. Little information is available regarding how to handle actively or recently infected COVID patients, including preoperative risk assessment, intraoperative decision making, and postoperative considerations regarding thrombotic risk. Our aim was to review the literature to determine how the hand surgeon can best prepare for and manage the actively or recently COVID-positive patients undergoing hand surgeries.



Nearly 500 million cases of COVID-19 (COVID) have been reported worldwide.[1] In addition, COVID induces a hypercoagulable state with associated risks of venous and arterial thromboses.[2–4] The pathophysiology likely involves endothelial cell dysfunction, platelet activation, and the release of coagulation and inflammatory factors.[5] As coagulopathic conditions increase the risk of peripheral vascular occlusion and distal circulation is critical to the success of many hand surgeries, the unique potential risk of COVID hypercoagulability on hand surgery must be considered.

Although vaccination has changed the course of the pandemic, hand surgeons will likely continue to see a substantial number of patients who have had a recent COVID infection or are actively infected. Although patients with active infection are distinct from those with a recently resolved infection, a paucity of data exists regarding how to distinguish these groups. This article examines both groups as representations of the underlying pathophysiology of COVID, especially as it pertains to inflammation and hypercoagulability.

Little information exists on guiding the hand surgeon on preoperative risk assessment, intraoperative decision making, and postoperative management regarding thrombotic risk in COVID patients. Our purpose was to review the literature for available guidance as to how the hand surgeon can best prepare for and manage COVID-positive patients. Due to the lack of studies purely on surgical patients, we combined the findings from medical and surgical patients.

## *Preoperative considerations*

A February 2022 statement from the American Society of Anesthesiologists states that unvaccinated patients should wait at least 7 weeks from COVID infection until elective surgery due to increased risk of complications.[6] However, evidence on the impact of vaccination on perioperative morbidity remains insufficient; hence, this statement does not have a recommendation for vaccinated patients. Patients continue to receive elective surgery with little attention paid to the timing of a recovered COVID infection. Recent studies in the orthopedic and arthroplasty literature suggest a higher risk of postoperative complications, including venous thromboembolism (VTE), in patients with both preoperative/resolved COVID infections and in those infected with COVID postoperatively.[7–9]

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Performing hand surgery on actively or recently COVID-positive patients who have a greater propensity for clotting demands a thorough preoperative evaluation of additional thrombotic risk factors, including presenting symptomatology and medical history. With increased COVID severity comes a higher risk of associated complications. Leentjens et al[10] classified patients—based on symptomatology and laboratory markers—into three stages of COVID coagulopathy, with stage 1 representing mild symptomatic cases. Although they did not provide specific rates of thrombotic events, increasing stages of COVID are associated with higher coagulation risk and even stage 1 patients are at risk of microthrombi. These data suggest that more severe COVID symptomatology is linked with increased coagulopathy. Therefore, even mild COVID cases with symptoms including fatigue, shortness of breath, low-grade fever, and associated flu-like symptoms are important to identify because they can provide insights into the risk of thrombotic events.

In addition to patients with symptomatic COVID, patients with recently resolved COVID have a higher risk of thrombotic events even if otherwise asymptomatic.[11] Additionally, more recent data have demonstrated that "long COVID" can impact all organ systems and present with diverse symptomatology similar to the acute infection—the most common being residual fatigue or weakness in 63% of the patients at 6 months postinfection.[12,13] These data indicate that potential consequences of COVID infections need to be considered even after acute infection, especially in those with lingering symptomatology.

A recent cohort study of 48 million adults with 1.4 million COVID diagnoses reported an increased incidence of arterial and venous thrombotic events, with an adjusted hazard ratio (aHR) of 21.7 and 33.2, respectively, in the first week after diagnosis.[14] The increased risk of both arterial and venous events declines with time; however, 49 weeks after diagnosis, VTE risk remains elevated 2-fold and aHR of arterial thrombosis is 1.34.[14] The overall absolute increased risks across the entire population for arterial thrombosis and VTE were 0.5% and 0.25%, respectively.[14] Additionally, subgroup analyses revealed that Black or Asian compared with White and people without a history of vascular events compared with those with a history of vascular events had a marginally higher long-term risk of thrombotic events.[14] Literature on urgent surgical revascularization of patients with acute limb ischemia with and without COVID demonstrates a greater risk of thrombosis in patients with COVID versus without (52.1% vs 21.5%) ($P = .004$).[15] Operating on a patient during or after COVID infection and adding another prothrombotic insult to the system may create additional risk, and at minimum should be discussed with the patient before a major urgent or semi-elective procedure.

Elevated C-reactive protein (CRP), D-dimer, interleukin 6 (IL-6), and depleted fibrinogen levels (Table 1) all provide insights into the severity of COVID infection, correlating with the higher risk of complications and mortality.[16–20] Elevated CRP and IL-6 have been linked to systemic inflammatory response syndrome and acute respiratory distress syndrome, respectively.[21] Lower fibrinogen has been associated with increased disease severity in actively infected patients, with one study showing 17 of the 84 patients with critical COVID (20%) having fibrinogen <2g/L compared with only 1 of the 135 patients with moderate disease.[17] D-dimer >1 μg/mL is also associated with greater in-hospital mortality in patients with COVID infection (18.42, 2.64–128.55; $P = .003$).[16] These laboratory data identify patients at higher risk for a perioperative thrombotic event.

Among these markers, D-dimer may be most suggestive of thromboembolic complication risk. In 40 hospitalized patients with an upper respiratory tract infection and arterial thromboembolic complications, Indes et al[22] demonstrated that those with COVID infection had higher D-dimer levels at the time of imaging for suspected arterial thromboembolism than those with negative COVID polymerase chain reaction test (odds ratio [OR] 17.3 vs 1.8; $P = 0.038$). Similarly, Chen et al[23] found that among 15 patients with COVID pneumonia and suspected pulmonary embolism (PE), those with PE confirmed on CT had a significantly higher D-dimer level (median, 11.07 μg/mL; IQR, 7.12–21.66 vs median, 2.44 μg/mL; IQR, 1.68–8.34, respectively, $P = .003$). Li et al[24] explored the utility of biomarkers for predicting the risk of VTE in hospitalized patients with COVID by comparing 104 COVID-positive patients with VTE with 208 COVID-positive disease-severity-matched patients without VTE.[24] They measured fibrinogen level and D-dimer level on admission, and D-dimer increment (D-dimer level on days 4–6 divided by that on days 1–3). They found D-dimer increment >1.5-fold to be the most predictive of VTE in the setting of an active COVID infection.[24]

**Table 1**
Laboratory Value Thresholds That Should Alert the Microvascular Surgeon to Potential Increase Complications in a COVID-19 Positive Patient

| Parameter | Threshold of Concern |
|---|---|
| D-dimer | >1.0 μg/mL |
| CRP | >10 mg/L |
| IL-6 | >25 pg/mL |
| Fibrinogen | <2 g/L |

CRP, C-reactive protein; IL-6, interleukin 6.

How long these laboratory levels remain abnormal after COVID is not clear; however, they are all known to indicate potential coagulation risk, regardless of COVID. Any specific additional COVID-related risk associated with findings from a preoperative coagulation profile has not been clarified. However, abnormal values may encourage the surgeon to consider a potential increased risk and adjust the plan/timing or at least guide preoperative counseling and may guide thromboprophylaxis strategy.

### *Intraoperative considerations*

Therefore, COVID-positive patients undergoing elective or emergency surgery had an increase in perioperative morbidity and mortality up to 28% when compared with propensity-matched COVID-negative counterparts.[25,26] The IMPACT-Restart trial demonstrated a perioperative COVID infection in patients undergoing orthopedic and trauma surgery almost doubled the postoperative mortality adjusted for age, female sex, and hip fracture (aHR 1.89, 95% confidence interval [CI] 1.14–3.12; $P = .014$).[27] Another study demonstrated that patients with recent COVID, defined as 1 to 6 weeks before surgery, or perioperative COVID, defined as 7 days before to 30 days after surgery, are at a higher risk of VTE complications within 30 days of surgery when compared with those without recent or perioperative COVID infection (OR 1.9 [95% CI 1.2–3.3] and OR 1.5 [95% CI 1.1–2.0]), respectively.[11] These findings have guided recommendations to consider nonsurgical management or delaying surgery when possible.[25,26,28]

Part of surgical planning must also consider the risk of general anesthesia (GA). The induction and emergence periods of GA pose the highest risk for deep vein thrombosis (DVT).[29] General anesthesia versus regional/local anesthesia in patients undergoing surgery has been associated with a higher risk of VTE in the 30-day postoperative period in patients both with and without COVID infections (OR 1.47 [95% CI 1.19-1.83]).[11] Additionally, total joint arthroplasty literature has demonstrated a lower incidence of postoperative DVT in patients receiving total intravenous anesthesia versus general or combined spinal epidural anesthesia for

total knee arthroplasty (4.48% vs 15.87 and 14.93, respectively [$P$ 0.05]).[30] Although a much rarer occurrence in patients with upper extremity trauma versus lower extremity trauma, the rate of VTE following upper extremity fractures ranges from 0.95% in the distal radius/ulna to 3.0% in the proximal humerus,[31] representing a clinically significant complication. In patients with a traumatic insult, undergoing potentially lengthy surgery, who are also COVID-positive, and thus, in a hypercoagulable state, the surgeon must have a low index of suspicion for thrombotic complications and consider using a method of anesthesia that mitigates this risk.

Wide-awake local anesthesia no tourniquet surgery (WALANT) is safe and efficacious in hand surgery.[32] When the hand surgeon is planning surgery on a patient at a higher risk of thromboembolism (eg, COVID), using WALANT or regional blockade with sedation as needed for patient tolerance should be strongly considered to eliminate the additional risk of GA. Conventional local anesthesia with an arm tourniquet cuff to 250 mmHg may also be a safe and reasonable alternative; however, it has been associated with more intraoperative pain associated with the tourniquet and the injection and more postoperative pain at 1 and 2 days compared with WALANT.[33] Therefore, WALANT may also reduce any additional thrombotic risk associated with tourniquet use.

Delaying surgery is not always an option. Therefore, it is important to broaden intraoperative considerations to reduce COVID-associated risks. This could include more aggressive anticoagulation and thrombosis prophylaxis, or perhaps, it could include a focus on more judicious dissection out of the zone of injury for vascular repairs, given the higher propensity to clot because this could manifest in a zone of injury broader than expected or with higher likelihood of clot at the anastomotic site. Keen attention to the risks of postinjury edema and congestion and associated challenges to vascular repair or flap coverage are also warranted.

*Postoperative considerations*

Another important consideration is prophylactic anticoagulation. Patients hospitalized with COVID had a nearly 3-fold increase in VTE compared with those without.[24,34] Thromboprophylaxis is effective in reducing in-hospital incidence of VTE with one study showing a reduction of DVT by almost half in hospitalized COVID patients receiving thromboprophylaxis (34% vs 66%, $P$ = .010).[18] Current guidelines recommend DVT prophylaxis in all patients hospitalized with COVID, with unfractionated heparin or low molecular weight heparin generally used as first-line treatment options.[35] However, a strong consensus on an optimal agent and dosing has not been established. One randomized controlled trial evaluated the efficacy and safety of therapeutic dosing with rivaroxaban (20 mg once daily) or enoxaparin (1 mg/kg twice daily) versus prophylactic anticoagulation with enoxaparin or heparin in hospitalized patients with COVID and elevated D-dimer, finding no difference in the primary outcomes; however, increased bleeding was noted in the therapeutic group (relative risk 3.64, 95% CI 1.61–8.27, $P$ = .001).[36] Aspirin has also been posited to reduce COVID severity, suggesting that it may be a prudent prophylactic choice demonstrating decreased rates of mortality at 14- and 30-day post-COVID infection in patients taking preexisting aspirin.[37] Postoperative anticoagulation for these patients merits consideration, given the higher risk for postoperative complications including thromboembolism.

There also seems to be an increased risk of postoperative VTE in patients who become COVID-positive after surgery. Prasad et al[8] found that patients who became infected in the postoperative period had a higher complication rate ratio, inclusive of DVT and PE (2.6, CI 1.9, 3.4). Whenever possible, encouraging COVID exposure risk reduction during the postoperative period may help minimize these issues.

Many of the most severe upper extremity issues seen early in the COVID pandemic were related to venous thrombosis, associated phlegmasia, and then subsequent ischemia. In a crushing injury, the focus is often on any vascular inflow repairs and restoring perfusion; however, it is important to be aware of the possibility for unusually extensive swelling and, in rare cases, considering prolonged postoperative observation or potentially even fasciotomy.[4,38]

## Limitations

Much of the data regarding laboratories and biomarkers of COVID complications are preliminary and have not been validated. This limits the strength of any recommendations. The lack of high-quality trials comparing anticoagulation strategies for COVID-positive patients prohibits firm recommendations on one protocol over another. However, with the current evidence regarding COVID-induced coagulation derangements and knowing our surgical population is already at increased risk of thrombosis by the nature of their injury, perioperative anticoagulation should be strongly considered.

Furthermore, we included COVID complications in medical patients in addition to surgical patients and did not restrict them hand surgery patients; therefore, the generalizability to hand surgery patients may be limited. Additional research is needed in many of the areas we discussed.

## Conclusion

The hand surgeon can take measures to mitigate the risk of perioperative thromboembolic complications in COVID-positive or recently COVID-positive patients. By obtaining an appropriate history and clinical picture complete with laboratory workup, the hand surgeon can better inform the care of the COVID-positive patient. Furthermore, intraoperative and postoperative considerations can be made accounting for the prothrombotic nature of COVID, and perioperative anticoagulation is potentially impactful in preventing thrombotic complications.

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