










Recommendations for the Evaluation and Acceptance of Solid Organ Transplantation Candidates in the Covid-19 Context

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Nothing to declare.

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Abstract: To date, much has been discussed about performing transplants in candidates who test positive for viral testing (e.g., antigen and molecular testing) or recent exposure/condition compatible with Covid-19. Unfortunately, the literature does not yet provide conclusive guidance, and the risk of complications, graft loss, and death must be considered. This paper discusses these points and provides some premises to inform and assist the transplant team's decision.

Descriptors: Solid Organ Transplantation; Covid-19; Tracking; Screening; SARS-CoV-2.

BACKGROUND

According to the American Society of Anesthesiologists (ASA) position document on elective surgeries after Sars-CoV-2 infection, published in late 2020, it is recommended that nonurgent procedures be postponed when possible.¹

Subsequently, the COVID Surg Collaborative Group² in a prospective, multicenter, international cohort study evaluated the impact of Sars-CoV-2 infection on perioperative morbidity and mortality in patients who had Covid-19. An increased perioperative mortality rate was observed in patients undergoing surgery according to the time interval between the procedure and the previous infection. The risk and respective 95% confidence interval were 4.1 (3.3–4.8) for 0–2-week intervals, 3.9 (2.6–5.1) for 3–4-week interval, and 3.6 (2.0–5.2) for 5–6-week interval after Sars-CoV-2 diagnosis; however, surgeries performed seven or more weeks after diagnosis of Sars-CoV-2 infection were associated with a similar mortality risk compared to those without prior Sars-CoV-2 infection. Similarly, patients still symptomatic after \geq seven weeks of Covid-19 had higher mortality than patients with resolved or asymptomatic symptoms.

CANDIDATE SCREENING

All organ transplant candidates must be screened for Covid-19 by clinical history and testing prior to transplantation whenever possible, regardless of the candidate's prior history of Covid-19 and vaccination status, but Sars-CoV-2 infection may not be recognized even with clinical-epidemiological and laboratory screening. Imaging tests may be part of this screening, depending on institutional protocol. Immunosuppression after transplantation as well as thromboembolic and inflammatory phenomena due to infection, even if asymptomatic, may result in increased risk of complications and associated mortality during and after transplantation. Thus, the risk and benefit of proceeding with transplantation should always be weighed.³

Ideally, transplant centers should include molecular testing (nucleic acid amplification testing – NAAT, the best known being reverse transcriptase reaction followed by real time-polymerase chain reaction – RT-PCR) of an upper respiratory tract specimen (e.g., nasopharyngeal swab), evaluation of symptoms, and history of exposure to Sars-CoV-2.⁴⁻⁶ When there is an indication for lung imaging, such as a potential donor with suspected infection, for example, a chest X-ray is usually sufficient for patients who do not have respiratory symptoms, however for those with respiratory symptoms a computed tomography (CT) scan of the chest is more appropriate because of its higher sensitivity.^{7,8}

CANDIDATE ACCEPTANCE CRITERIA FOR TRANSPLANTATION

Candidates with active Covid-19 and/or signs or symptoms of other respiratory diseases should have the transplant postponed in most cases. However, for patients with active Covid-19 or those with positive screening, the optimal time frame for postponing the procedure is not known. It would be most appropriate to wait until all symptoms have resolved and at least one negative molecular test result for Sars-CoV-2. Nonetheless, it is worth noting that some patients may remain with a positive RT-PCR test for viral RNA or viral particles for prolonged periods, even after symptoms have resolved. Thus, a persistently positive PCR test does not necessarily represent active virus. On the other hand, reinfection or escape infection after vaccination can occur in both immunocompetent and, more frequently, immunosuppressed individuals.⁹

Complete resolution of symptoms and a negative NAAT test result for Sars-CoV-2 in a respiratory tract specimen before transplantation aids in controlling the hospital environment and protecting the healthcare team. Some experts recommend two negative RT-PCR tests at least 24 hours apart because of the limited sensitivity (~70%) of each test.^{9,10}

In general, decision making should be individualized, weighing the probability of active or past disease impacting the postoperative outcome versus the risk of death while waiting for another organ to be offered (Table 1). In patients with extreme urgency for transplantation, such as end-stage organ failure for which no substitute therapy is available, the procedure should be considered.^{3,4,10}

Table 1. Recommendations for acceptance of the transplant candidate.

Time since laboratory diagnosis or symptom onset	Clinical presentation of Covid-19	Conduct
< 14 days	Regardless of severity (including asymptomatic with positive test)	Proceed with transplantation only in urgent cases (eg, fulminant hepatitis, heart transplantation in a candidate maintained with a ventricular assist device) In other cases, consider postponing the transplant for at least 4 weeks (ideally 6 weeks) from the clinical or laboratory diagnosis.
> 14–28 days	Asymptomatic infection or mild disease or no pneumonia with resolution of symptoms	Individualized assessment in which the risk of postoperative complications and death resulting from recent SARS-CoV-2 infection should be weighed against the risk of death on the waiting list.
> 14–28 days	Patient with moderate to severe disease	Proceed to transplantation only in urgent cases
> 28- 42 days		Individualized assessment in which the risk of postoperative complications and death resulting from recent SARS-CoV-2 infection should be weighed against the risk of death on the waiting list.
> 42–90 days		Proceed with transplantation
> 90 days		Individualized assessment. The possibility of reinfection should be considered. Decision should take into account time elapsed since the most recent diagnosis of Sars-CoV2 infection.

DIAGNOSTIC TESTS FOR SARS-COV-2 INFECTION

The tests available for the diagnosis of active Covid-19 are viral tests: antigen and molecular tests. Considering the specimens, it can be seen that upper respiratory tract specimens are the most commonly used in the diagnosis of Covid-19 (both for molecular tests such as RT-PCR and antigen tests) and the more appropriate for screening the transplant candidate.⁶

Molecular tests, or NAATs, are generally performed in a laboratory setting. Because of their better performance regarding both sensitivity and specificity, molecular tests are the recommended option for screening candidates and their donors. Among the available options, the RT-PCR is considered the gold standard, because of its higher sensitivity for detection of Sars-CoV-2. Point-of-care (POC) molecular tests such as the ID Now Covid-19 test or Xpert® (Xpress SARS-CoV-2) can also be used as a screening test.^{9,10}

Antigen tests detect the presence of a viral antigen, usually surface protein. Most antigen kits are lateral flow assays, i.e., immunochromatographic. These tests are easy to use and can be self-administered, but are generally less sensitive than NAATs for establishing the diagnosis of Sars-CoV-2 infection.⁹ The sensitivity of antigen tests is often lower than RT-PCR, with higher detection limits and lower sensitivity after D5 of symptom onset. For this reason, they are not seen as good tests for screening; however, if the test result is positive, the result is considered to be diagnostic. A negative result should ideally be confirmed by PCR, in a sequential screening strategy.^{9,11-14}

Taking into account the emergence of viral mutations and the presence of new variants, such as the Omicron variant, the sensitivity of the tests have been analyzed, and in general the *performance* of molecular tests are not affected if multiple genetic targets are used. However, it is possible that, due to the pattern of viral excretion of the Omicron variant, the diagnostic performance of tests carried out in samples from the upper respiratory tract is improved. The antigen tests, similarly, show similar sensitivity among the variants studied so far.¹²

It is worth noting that antibody testing (i.e., serology for Covid-19) is useful for assessing seroprevalence, but not for diagnosing or screening transplant candidates.

AUTHORS' CONTRIBUTION

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AVAILABILITY OF RESEARCH DATA

All data are presented in this article.

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