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VCA-COVID Survey Grp

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VCA in the Era of the COVID-19 Pandemic

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Since its onset in the beginning of 2020, the coronavirus disease 2019 (COVID-19) pandemic has impacted the transplantation community broadly. Indeed, the number of transplantations decreased dramatically and transplantations were temporarily shut down in many localities.[1,2]

The dramatic impact of the COVID-19 pandemic on solid organ transplant (SOT) recipients began to emerge with reports initially from China, Spain, and Italy. The prevalence of COVID-19 in SOT during the first pandemic wave varied geographically, but despite several reports, the effective incidence of the COVID-19 in SOT recipients remains unclear.[2-5] Most relevant, solid organ transplantation (heart, liver, and kidney) rates declined, exposing candidates to an increased rate of waitlist mortality.[1]

Vascularized composite allotransplantation (VCA) is an emerging field of transplantation; approximately 200 to 300 procedures have been performed thus far[6,7] since the first hand transplantation in 1998. VCA (including upper and lower extremity, face, larynx, uterus, penis and abdominal wall transplants) is usually contemplated as life-enhancing rather than life-saving procedures but nevertheless requires lifelong immunosuppression. Although, VCA recipients are exposed to the same risks as SOT recipients, no relevant data have been so far published on the impact of COVID-19 on VCA.

IMPACT OF COVID PANDEMIC ON VCA RECIPIENTS

In order to assess the impact of the COVID-19 pandemic on VCA, a survey was sent in June 2020 (updated

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P.P., J.K., B.B.G., and E.M. designed the study, created the survey, and wrote the manuscript. C.S. analyzed the data and contributed in manuscript preparation. The VCA-COVID survey group participated in the survey and contributed in writing of the manuscript.

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in September 2021) to 29 teams with activities in upper extremity (UET) and face allotransplantation. The survey data were deidentified and as such the study did not need ethics board approval.

Twenty-one centers (72.4%) representing 63 VCA recipients from several countries, including Australia, Europe (Finland, France, Italy, Poland, Spain, Sweden, and United Kingdom), India, Mexico, and the United States responded to the survey.

The survey collected data on recipients who had received a VCA before the pandemic and also on the VCA program and new transplants performed during the pandemic.

The 63 patients included 49 men and 14 women, with a mean age of 46 ± 14 years (range, 13–74) at the time of the survey; they had received unilateral hand transplantation (n = 13), bilateral hand transplantation (n = 26), unilateral arm transplantation (n = 1), bilateral arm transplantation (n = 5), or face transplantation (n = 18). The time between transplantation and the survey ranged from 1 to 21 years. During the pandemic period, the immunosuppressive treatment of the VCA recipients was based on steroids, tacrolimus, and mycophenolate mofetil (MMF) in the majority (61.3%) of cases.

The majority of patients had no comorbidities. A total of 19.4% listed diabetes and arterial hypertension, and 17.7% were smokers.

In the present survey, 7/63 (11.1%) of the VCA recipients developed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (3 face transplant recipients, 3 bilateral, and 1 unilateral UET recipients).

Two COVID19-positive face transplant recipients[8,9] were over 50 years old and both had comorbidities. Their immunosuppressive treatment included tacrolimus and steroids, or tacrolimus, MMF and steroids, respectively. Both were hospitalized, and one of them required assisted ventilation (which denotes severe disease according to the WHO scale). In both cases, the immunosuppression was reduced but not completely stopped. Treatment approaches differed but both patients recovered.[8,9] More details could not be obtained concerning the third face-transplanted patient, a 39-year-old man, who had received a face transplantation 9 years earlier, with an immunosuppressive treatment based on tacrolimus, MMF, and steroids.

The fourth and fifth patients were bilateral UET recipients with an immunosuppressive treatment based on tacrolimus, MMF, and steroids. They were young and otherwise healthy and developed very mild or no symptoms, respectively. They were treated as outpatients. Tacrolimus and MMF were tapered in the fourth patient and the treatment was not modified in the fifth patient.

The sixth patient was a 45-year-old woman, with a bilateral hand transplantation, on tacrolimus, sirolimus, and steroids. Although the patient had received 2 doses of mRNA vaccine she developed gastroenteritis, dehydration and her health declined rapidly. Acute renal failure occurred, requiring dialysis, and her renal function is still recovering. She also developed retroperitoneal bleeding requiring embolization of bleeding lumbar vessels. Her immunosuppressive treatment was tapered.

The seventh patient was 46-year-old, had no comorbidities, and recovered at home without specific treatment or changes in immunosuppression.

None of these patients showed signs of acute rejection after the infection.

To the best of our knowledge, no mortality in VCA recipients due to SARS-CoV-2 infection occurred. It has been reported[3] that COVID-19-related mortality is considerably higher in SOT recipients (ranging from 13% to 30%)[4] compared to the general population (3.4%); however, the fatality rate in SOT recipients remains unclear as the majority of the literature considered only the infected recipients who were hospitalized, ranging widely from 9% to 46% of the total SOT recipients, depending on the studied cohorts.

Thirty-three patients included in this survey received at least 2 doses of vaccine and 7 of them 3 doses on the basis of the strategy of the different countries. Thirty patients received mRNA vaccines and 3 received viral vector vaccines. Only few patients were tested for antibodies and T-cell responses after vaccination with different results. Only the sixth patient developed infection with severe decline of her general condition, even though she had received 2 doses of mRNA vaccine. Prospective studies will help to understand better the long-term efficacy of vaccines to protect those patients at greatest risk for SARS-CoV-2 infection.

IMPACT OF COVID PANDEMIC ON VCA PROGRAMS

The VCA programs of the 21 centers that participated to the survey were placed on hold during the first wave (March–June 2020).

VCAs are not life-saving procedures, therefore, candidates have no waitlist-associated mortality, supporting a more conservative approach. Subsequent to the first wave, only a few, highly selected VCAs were performed. Six cases of VCAs were performed during 2020 up to September 2021, including a face retransplantation in the United States (July 2020) and 2 bilateral hand transplantations in India (August 2020). In December 2020, one bilateral hand transplantation was performed in Sweden, and in January 2021 a bilateral arm transplantation was performed in France. To our knowledge, a successful case of face and bilateral hand transplantation was also performed in August 2020 in the United States.

In all cases, both donors and recipients had a negative polymerase chain reaction test for SARS-CoV-2 before transplantation. UETs received an induction treatment with antithymocyte globulins and a maintenance immunosuppression with tacrolimus, MMF, and steroids as maintenance therapy. The face transplant recipient who had developed chronic allograft deterioration had been highly sensitized when a well-matched graft became available. Both UET were performed in bilateral amputees who had been in a waitlist for several years because of the great difficulty to find a suitable donor. In the UET recipients, the immunosuppressive treatment was not modified, the rehabilitation therapy was performed in an in-patient basis and then they were vaccinated as soon as the vaccines fifth patient available in their countries.

CONCLUSIONS

Compared with other SOT, VCAs are significantly less frequent with recipients usually being younger and with fewer comorbidities.

The management of the VCA recipients grafted before the pandemic was easier compared to SOT recipients

because VCA are not life-saving procedures, consequently, the functional evaluation of upper extremity and face allotransplantations could be postponed; besides, other examinations (ie, blood exams) were performed without moving the patients to the transplantation centers.

The impact of the pandemic on SOT has been enormous affecting potential donors, candidates, and recipients.[10] The pressure of the pandemic on healthcare systems disrupted all transplant programs and may have long-lasting consequences, including the discontinuation of activities in some centers. The few cases of VCA performed after the first wave of the pandemic have had good outcomes and are an encouragement to the VCA community.

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