



Coping with a lack of evidence: living-donor kidney transplantation in the initial phase of the SARS-CoV-2 pandemic

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Summary Due to immunosuppressive therapy, transplant patients are more susceptible to viral and bacterial infections. A potentially deadly new virus haunted us in 2020: SARS-CoV-2, causing coronavirus disease 19 (COVID-19). We analyzed the consequences of this previously unknown risk for our living-donor transplant program in the first year of the pandemic. After the complete lockdown in spring 2020, our transplant center in Linz resumed the living-donor kidney transplantation program from June to September 2020, between the first and second waves of COVID-19 in Austria. We compared the outcomes of these living-donor kidney transplantations with the transplant outcomes of the corresponding periods of the three previous years. From June 4 to September 9, 2020, five living-donor kidney transplantations were performed. All donors and recipients were screened for COVID 19 infection by PCR testing the day before surgery. Kidney transplant recipients remained isolated in single rooms until discharge from hospital. All recipients and donors remained SARS-CoV-2 negative during the follow-up of 10 months and have been fully

vaccinated to date. The number of living transplants in the studied period of 2020 was constant compared to the same months of 2017, 2018, and 2019. Living-donor kidney transplantation can be continued using testing for SARS-CoV-2 and meticulous hygienic precautions in epidemiologically favorable phases of the SARS-CoV-2 pandemic. Donors and recipients should be carefully selected and informed about risks and benefits.

Keywords Laparoscopic versus open living kidney transplantation · Single-center-study · SARS-CoV-2 · Protective measures · Pandemic

Main novel aspects

1. Single-center clinical strategy for a living-donor kidney donation program in the absence of high-level evidence treatment.
2. Comparison of living kidney transplantation during the SARS-CoV-2 pandemic to the former 3 years.
3. Strict protective measures have allowed the safe resumption of our living-donor kidney transplantation program.

Introduction

Living-donor kidney transplantation during the pandemic of a potentially deadly new virus, SARS-CoV-2, has become challenging in most aspects.

SARS-CoV-2 is a single-stranded positive-sense RNA virus belonging to the *Coronaviridae* family that causes fever, muscle pain, headache, loss of taste or smell, diarrhea, predisposition to hypercoagulability, multisystem inflammatory syndrome in healthy children, and long covid syndrome; it is potentially deadly [1].

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Table 1 Donor and recipient demographics June–September 2020

	Recipients	Donors
Age, years, median	47	58
Sex, female/male	1/4	4/1
Genetically related/genetically unrelated	4/1	4/1
Median eGFR at donation	–	92.4 ml/min
Mild hypertonia	–	2/5
Hospital stay, median	–	6
BMI median	–	28.2 kg/m ²

Infection is a common complication after kidney transplantation, and one of the most frequently infected organs is the respiratory system. Cross-reactivity after respiratory viral infection can cause acute rejection in recipients [2].

At the beginning of the pandemic, starting with the complete lockdown in Austria in March 2020, the national transplant activity was reduced for patient safety in this unknown situation. It was difficult to assess whether patients are particularly at risk immediately after transplantation due to immunosuppression. In Austria, the transplant programs for kidneys were therefore temporarily suspended. The transplantation of other organs was temporarily decided on the basis of individual case analyses [3].

The aim of the current study is to report our clinical strategy for coping with the threat of the pandemic in the absence of high-level evidence for the nexus of kidney transplantation and SARS-CoV-2. Furthermore, we compare the outcome of the living-donor transplantations in our center during the time period after the first lockdown in 2020 with the same months of the previous 3 years.

Materials and methods

After the complete lockdown in spring 2020, our transplant center in Linz decided to continue the living-donor kidney transplantation program under strict conditions in May 2020.

Measures regarding SARS-CoV-2

Donors and recipients were tested by nasopharyngeal PCR test 24 h prior to donation; results were available within 4–6 h. Antigen tests were performed daily 2 weeks before the hospital stay and donors were in self-isolation. Also, serological specific antibody detection for SARS-CoV-2 was performed prior to donation. Recipients were isolated in single rooms during their hospital stay.

All patients were informed about the risks of transplantation during the SARS-CoV-2 pandemic and provided written informed consent for the procedure despite the risk of SARS-CoV-2 infection. Recipients had no relevant underlying diseases and age ranged from

Table 2 Donor and recipient demographics June–September 2017, 2018, 2019, 2020; *P*-value (2020 vs. 2017–2019)

	2017	2018	2019	2020	<i>p</i> -value
Age, years, donors	53	51	52	58	0.720
Age, years, recipients	45	51	32	47	0.689
Related/unrelated	2/2	2/3	4/2	4/1	–
Median GFR donors	99.3	114.8	103.2	92.4	0.652
Mild hypertonia	–	–	–	2/5	–
Hospital stay, days	7.3	6	6.8	6	0.586
BMI median, kg/m ²	28.7	27.1	27.6	28.2	0.733

44 to 58 years; 4 out of 5 donors and recipients were related.

Data collection and outcome measures

All living-donor kidney transplantations from June to September 2020 were included in this retrospective analysis and their outcomes, any COVID-19, and vaccination statuses were followed until June 2021 (range 10–12 months). Demographic data of donors and recipients, intraoperative data and postoperative outcomes, SARS-CoV-2 infections, and later vaccinations were analyzed. We compared these data from June to September 2020 with the living-donor transplantations during the same time period of the 3 previous years. Pre-nephrectomy donor data documented were age, body mass index (BMI, kg/m²), pre-existing arterial hypertension, kidney size, history of smoking, graft side, scintigraphic left and right renal function, and number of arteries and veins. Operative times such as time of anastomosis and operation, warm and cold ischemia, arterial reconstructions, unusual venous anatomy, conversions, and postoperative complications were analyzed.

Donor age at nephrectomy; relationship between donor and recipient; laparoscopic versus open nephrectomy; duration of hospital stay; postoperative creatinine; complications such as conversions, reoperations, and interventions; and long-term follow-up of donors was listed.

For recipients, age, gender, individual number of prior kidney transplantations, arterial reconstructions, ABO incompatibility, and rejections were documented.

Immunosuppressive regime

Our standard immunosuppression regimen is a combination of prednisolone, tacrolimus, and mycophenolate mofetil following induction with basiliximab. All patients undergoing living-donor kidney transplantation in this initial phase of the pandemic received this standard immunosuppression without adaptation regarding potential viral infection.

Table 3 Intra- and postoperative data of donors and recipients June–September 2017, 2018, 2019, 2020; *P*-value (2020 vs. 2017–2019)

	2017	2018	2019	2020	<i>p</i> -value
Operation time	173	179	166	165	0.659
Warm ischemia	127	142	132	117	0.636
Anastomosis time	36	24	25	25	0.391
Arterial reconstruction	–	1	–	1	–
Cold ischemia	60	54	61	74	0.679
ABO incompatible	1	1	1	1	–
2nd transplantation	1	–	1	1	–
1a–3a follow-up creatine mg/dl, donor	1.23	1.24	1.28	1.22	0.621
Complications, donor	–	–	2	–	–
Graft loss, recipient	1	–	–	1	–

Surgical technique

All laparoscopic living-donor nephrectomies (LDN) were performed by an intraperitoneal approach, with four trocars placed pararectally. The graft was removed with an endobag via a Pfannenstiel incision. Open donor nephrectomy was used to harvest right kidneys by an oblique incision in the upper right quadrant. Vessels were secured by clamps and sutures; in laparoscopy by use of vascular staplers. Surgical devices were sealing instruments and caustic ticks.

Statistical analysis

Outcomes of the period from June to September 2020 were compared with the same periods of the previous 3 years. Categorical variables were reported as frequencies and proportions, and continuous data as median, minimum, maximum and range. Fisher's exact test was used to compare 2020 to 2017–2019.

Results

From June 4, 2020, until September 9, 2020, five living-donor kidney transplantations were performed. The number of living-donor transplantations in 2020 ($n=5$) was constant compared with the same period in 2017 ($n=4$), 2018 ($n=5$), and 2019 ($n=6$). In 2020, the median recipient age was 47 years (range 26–54), the donors were a median of 58 years old (range 39–68). 80% male recipients versus 80% female donors were observed, four of five (80%) were related.

The median pre-donation eGFR (estimated glomerular filtration rate) was 92.36 ml/min (range 75.3–105.7). Two donors had mild hypertonia (40%), treated with medication. The median hospital stay for donors was 6 days, median BMI amounted to 28.2 kg/m² (range 26.7–35.2). Details are presented in Table 1.

Comparing the corresponding time periods of 2020 with 2017–2019, donor age ranged between 51 and 58 years. The age of recipients is more variable,

between 32 and 51 years. The majority of donor/recipient pairs were related (80%). Most donors were parents or married couples.

Median GFR ranged between 92.2 ml/min and 114.8 ml min. Only two of all reported donors (10%) in the 4 years had mild hypertension treated by medication. Median BMI was between 27.1 and 28.7 kg/m², the mean length of stay between 6 and 7.3 days. (Table 2).

In 2017 four left LDN, in 2018 five left LDN, and in 2019 five left LDN and one right open donor nephrectomy (ODN) were performed; in 2020 three right ODN and two left LDN were performed.

The mean operating time in the 4 years was between 165 and 179 min, the warm ischemia between 117 and 142 s. The time of anastomoses was similar in 2018, 2019, and 2020, with 24 and 25 min, respectively. In 2017 it was longer, with 36 min, although causes could not be determined. Cold ischemia lasted between 54 and 74 min, depending on the beginning of the implantation in the neighboring operating room. Arterial reconstructions had to be performed twice for accessory renal arteries or two arteries (10%). From 2017 to 2020, there was one ABO incompatible (ABOi) transplantation every year. Most recipients had their first transplant; three patients obtained their second graft (Tab 3).

The mean donor creatinine in the follow-up ranged between 1.22 mg/dl and 1.28 mg/dl. No donor had postoperative kidney dysfunction, and no one developed mild hypertension after kidney donation. There were no smokers in the cohort.

Two donors had a revision in 2019, one due to subcutaneous hematoma after a Pfannenstiel incision and one an intraoperative hematoma. There was no need for blood replacement in the series. An intraoperative complication with conversion was not observed.

A recipient transplanted in 2017 developed rejection due to a systemic hematological disease after 3 years because of reduced immunosuppression. In 2020, 3 days after arterial reconstruction, two arteries that were anastomosed from the side had a thrombotic occlusion with subsequent loss of organ. Thus, there were two graft losses in 20 transplants in the observed period (10%) (Tab. 3).

One donor developed a myelodysplastic syndrome within the control period.

All recipients and donors remained COVID-19 negative during the follow-up of 10 months. Thereafter, all were vaccinated with mRNA-based vaccines (Spikevax/Moderna or Comirnaty/Pfizer-BioNTech). None of the living-kidney recipients died.

Follow up SARS-CoV-2

During the follow-up, patients remained asymptomatic and were tested by nasopharyngeal PCR or serological tests that resulted negative for anti-SARS-

CoV-2 antibodies. None of the donors or recipients had contracted COVID 19 by June 2021, and all recipients and donors have now been vaccinated three times with Spikevax or Comirnaty. None of the living kidney recipients died.

Discussion

In 2020, 672 organ transplantations were carried out in Austria. That is a decrease of almost 7% according to the Transplantation Report 2020 published by Gesundheit Österreich GmbH [3]. This decline was caused by the effects of the COVID 19 pandemic and mainly affected kidneys and heart transplantations [3].

Of the 335 kidney transplantations, 44 were from living donors. Especially at the beginning of the pandemic, it was difficult to assess whether patients were particularly at risk immediately after transplantation due to the severe immune deficiency. The transplantation programs for kidneys were therefore temporarily suspended throughout Austria. The transplantation of other organs was temporarily decided on the basis of individual case analyses [3]. Since then, the number of donors and transplantations has levelled off at a slightly lower level than before the pandemic. On average, the waiting time for a kidney from a deceased donor amounts to 36.4 months [3, 4].

In patients after transplantations, compared to the general population, respiratory viral infections occur not only in the cold months, but throughout the whole year, and the postoperative incidence of respiratory infections, especially 1–6 months post transplantation, including pneumonia, is higher. This process can determine an acute rejection in recipients [5–7].

Living kidney donors are a healthy population, eager to help their loved ones, undergoing all testing strategies, and even putting themselves in free isolation 14 days prior to donation [4, 8, 9]. New studies and data show that a COVID 19 infection mostly results in mild viral infection symptoms with good recovery in donors [10].

Recipients aged >60 years with multiple diseases have shown high mortality rates, up to 75% [7, 11]. Therefore, only younger ones without former diseases were chosen.

In this retrospective single-center study, we described our outcomes during the initial period of the pandemic. From the beginning, preventive measures were necessary and updated in daily routine.

An adjustment process was carried out. Screening for COVID 19 symptoms in every patient admitted for donation and transplantation, testing with a nasopharyngeal swab PCR test 24h prior to donation, use of FFP 2 masks in all hospital facilities, restrictive visitation to the transplant department, and social distancing for donors and recipients were priority [4, 6, 8, 12]. In addition to these measures, which were pro-

vided for hospitals in Austria in general, we isolated our recipients in single rooms.

The strength of this study is that we report and analyze the measures taken in the initial phase of the pandemic. The task was to continue living-donor kidney transplantation in an unassured setting without scientific evidence or censored practice rules. The newly developed protective measures have allowed safe resumption of our living-donor kidney transplantation program. The limitation of our study is its retrospective nature and the relatively small number of participants. Larger studies with longer follow-up are needed to confirm the results. Donors and recipients should be carefully selected. They must be informed about all risks [5, 6, 8, 13].

Strict protective measures have allowed the safe resumption of our living-donor kidney transplantation program; therefore, it should be continued. Donors and recipients should be carefully selected. They must be informed about all risks.

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Conflict of interest N. Roth, C.S. Rösch, A. Krause, M. Kalteis, W. Enkner, M. Haller, D. Cejka, R. Függer, and M. Biebl declare that they have no competing interests.

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