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Research article

Kidney function, future health costs, and quality-adjusted life-years in kidney transplant recipients transplanted during the SARS-Cov-2 lockdown in Denmark – An observational study

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ABSTRACT

Background: It is unknown whether lockdown due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may affect both clinical outcome in kidney transplant recipients and health care economics in Denmark.
Methods: We compared kidney transplant data at a tertiary university hospital before and during the lockdown period from March 13, 2020 until March 31, 2021, as well as kidney transplant data from Scandiatransplant for entire Denmark. Outcome variables included fall of plasma creatinine during the first postoperative day, and graft function three months posttransplant. We calculated the quality-adjusted life-years (QALYs) and costs which were caused by the lockdown recommendations.
Findings: The portion of living donation kidney transplantation was largely reduced during the lockdown period compared to before the lockdown: AB0-incompatible living donation declined from 14% to 7% ($P < 0.01$), and AB0-compatible living donation declined from 34% to 20% ($p < 0.01$).
In entire Denmark during the lockdown period 78 living donor kidney transplants out of 268 kidney transplants (29%) were performed, whereas there were 878 living donor kidney transplants out of 2218 kidney transplants (39%) before the lockdown ($P = 0.01$).
The observed reduction of living donor kidney transplants and consecutive reduction of graft survival will cause a loss of 5.04 QALYs.
The additional costs in kidney transplant recipients who received a kidney transplant during the lockdown period will be 277,298 EUR.
Interpretation: SARS-CoV-2 lockdown period largely reduced living donation kidney transplants which will lead to reduced QALY as well as higher costs in kidney transplant recipients.

1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has posed major challenges in every aspect of healthcare. Kidney transplant recipients (KTRs) were thought to be especially vulnerable to severe SARS-CoV-2 infections and mortality because they are immunosuppressed. Initial studies showed mortality rates ranging from 20% to 32% [1, 2, 3], and SARS-Cov-2-associated acute kidney injury in 52% [3]. At the start of the pandemic, it was uncertain, how to practice kidney transplantation in patients with end-stage kidney disease during this challenging period [4, 5, 6].

Denmark was one of the first countries in Europe which responded to the rise of SARS-CoV-2 cases with a lockdown that was announced to officially begin March 13, 2020 [7]. The Danish health authorities issued a statement recommending a halt to all surgical procedures that were safe to postpone [8]. Kidney transplantation with living donation was an example of a procedure deemed to be safe to postpone, while donation from deceased, brain-dead donors was not [8].

According to lockdown recommendations, kidney transplantation was continued on tertiary university hospital (Odense University Hospital, Odense, Denmark). However, contact to kidney transplant recipients were kept to a minimum, and fast discharge was encouraged.

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Upon discharge, tele-communication through phone calls was the encouraged method of follow-up, and in-person consultation was undergone only if the treating specialist deemed it necessary.

The effects of the lockdown recommendations and changes of care during hospitalization and to follow-up of newly transplanted patients are unknown. Furthermore, it is unknown whether the recommendations to halt to all surgical procedures that were safe to postpone may have effects on end-stage renal failure patients on the waiting list for kidney transplantation. We therefore hypothesized that the lockdown recommendations may have affected kidney transplantations.

The objective of the present investigation was to compare the characteristics of kidney transplant recipients who were transplanted during and before the SARS-Cov-2 lockdown period at tertiary university hospital. We evaluated whether the lockdown may affect medical and clinical outcome in kidney transplant recipients. In addition, we investigated the changes to the type and number of transplants performed in entire Denmark during the lockdown period and evaluated the effects of lockdown recommendation on future quality-adjusted life-year (QALY) and health economics.

2. Methods

2.1. Participants of the general study and design of the case-control study

This observational study included cases and controls from incident kidney transplant recipients at the Odense University Hospital, Odense, Denmark, a tertiary university hospital for a region of approximately 1.2 million inhabitants (Danmarks Statistik. Population statistics). Patients were recruited for the ongoing Molecular Monitoring after Kidney Transplantation (MoMoTx) study. Study data were prospectively collected from January 1, 2011, until June 30, 2021. Details from the MoMoTx study have previously been published [9, 10]. The study protocol was in accordance with the ethical standards of the Declarations of Helsinki and Istanbul. Its registration identifier at ClinicalTrials.gov is NCT01515605. The study was approved by the local ethics committee (Den Videnskabsetiske Komite for Region Syddanmark, Projekt-ID: 20100098). Written informed consent was obtained from all patients before entry into the study. Exclusion criteria were age below 18 years or missing consent.

In December 2019 coronavirus disease 2019 (Covid-19) emerged in Wuhan City, Hubei Province, China [11]. In Denmark, the official nationwide lockdown started March 13, 2020 [7,8], which included the closure of universities, restrictions for number of people assembling in public areas, and the recommendation that all surgical procedures, which were safe to be postponed, should be avoided [8]. Most restrictions were retracted until March 31, 2021.

During the lockdown period in Denmark from March 13, 2020, until March 31, 2021, a total of 67 patients were screened for inclusion into the MoMoTx study. Seven patients were excluded from the present investigation, because three patients did not receive a transplant because of severely calcified arteries, one with missing consent, two had graftectomies shortly after transplantation, and one patient died. The present study contained 60 cases. During the control period, i.e., from January 1, 2011 until December 31, 2020, a total of 533 kidney transplant recipients were screened. Five patients were excluded from the present investigation, because four had graftectomies shortly after transplantation, and one patient died. Thus, the present study contained 60 matched controls out of 528 kidney transplant recipients.

Cases were adult kidney transplant recipients who were transplanted at the Odense University Hospital during the SARS-CoV-2 lockdown period, from March 13, 2020 until March 31, 2021. Controls were adult kidney transplant recipients who were transplanted at the Odense University Hospital in the period from January 1, 2011 until December 31, 2020. Controls were matched to cases according to donor type (i.e., AB0-blood-type-incompatible living donation, AB0-blood-type-compatible living donation, and donation after brain death), kidney transplant recipient gender, and age (within 5-year intervals). If several putative matching controls were available, we chose the most recent kidney transplant recipient.

2.2. Data collection

We collected data from electronical medical record review. Data included recipient age, gender, biochemical characteristics, donor type (AB0-blood-type-incompatible living donation, AB0-blood-type-compatible living donation and donation after brain death), plasma creatinine levels on the day before and after kidney transplantation, comorbidities, cause of kidney disease, number of blood tests, and time until removal of ureteral stents which had routinely been placed during transplantation.

The outcome variables were delayed graft function, which was defined according to United Network for Organ Sharing at least one dialysis session within one week after transplantation [12]; estimated glomerular filtration rate (eGFR) one month after transplantation, as calculated according to the Chronic Kidney Disease Epidemiology Collaboration equation [13], bacterial infections requiring hospitalization within three months posttransplant, which was defined as the presence of relevant symptoms and biochemical - or microbiological evidence of a bacterial disease or alleviation of symptoms following use of antibiotics, urological complications posttransplant requiring hospitalization, e.g., need for ureteral stenting or nephrostomy.

The sample size was calculated to be 23 with a power of 0.80; standard deviation of eGFR one month after transplantation derived from preliminary studies, 18 mL/min/1.73m^2; and assuming a clinical meaningful difference of eGFR of 15 mL/min/1.73m^2.

2.3. Ethical considerations

The MoMoTx study has been approved by the local ethics committee (Den Videnskabsetiske Komite for Region Syddanmark, Projekt-ID: 20100098), and the study protocol is in accordance with the ethical standards of the Declarations of Helsinki and Istanbul. Its registration identifier at ClinicalTrials.gov is NCT01515605. Permission for data processing was acquired from the Danish data protection agency (journal nr.: 18/18718).

2.4. Statistical analysis

Continuous data are presented as median and interquartile range (IQR). Frequency counts were calculated for categorical data. For comparative statistics in the case-control analysis, we used non-parametric Mann-Whitney U test to compare continuous data, and Fisher's exact test to compare categorical data.

Data were analyzed using GraphPad prism software (version 6.0, GraphPad Software, La Jolla, CA) and Stata (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.)

2.5. Investigation of transplant procedures in Denmark

Data concerning the number of transplantations and donor type was gathered from Scandiatransplant, the organ exchange organization for the countries Denmark, Finland, Iceland, Norway, Sweden and Estonia [14]. Quarterly, Scandiatransplant publishes freely accessible data concerning organ transplantation from all transplant centers in Denmark, including Aarhus University Hospital (Aarhus), Rigshospitalet (Copenhagen) and Odense University Hospital (Odense).

The lockdown period in Denmark was defined as the second, third and fourth quarter of 2020, as well as the first quarter of 2021. We calculated the average number of kidney transplants performed per month and the ratio of living donation and donation after brain death per year, results are displayed as mean and standard deviation (SD). The yearly ratio of living donation and donation after brain death during the

lockdown period in Denmark was compared to the yearly ratio obtained before the lockdown period using one-sided t-test.

We estimated the number of recipients who will require dialysis within five years post transplantation using recent patient and allograft survival data from the Danish Nephrology Society Registry Annual Report 2017 [15] both for recipients with living donation and recipients with donation after brain death and calculated costs and quality-adjusted life-year (QALY). To determine QALY, we used utility values for transplantation and hemodialysis from a Scandinavian population provided by Sennfält et al. [16]. Costs for transplantation and dialysis have been published by Jensen et. al [17].

2.6. Role of the funding source

The funder had no role in the writing of the manuscript or the decision to submit it for publication. The funder had no role in data collection, analysis, or interpretation; trial design; patient recruitment; or any aspect pertinent to the study. There was no payment for writing this article by a pharmaceutical company or other agency.

The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

3. Results

3.1. Characteristics of kidney transplant recipients who were transplanted during compared to before the SARS-Cov-2 lockdown period

We analyzed data from 584 incident kidney transplant recipients from the ongoing, prospective MoMoTx study, 60 cases were transplanted during lockdown period from March 13, 2020, until March 31, 2021; whereas 524 controls had been transplanted before the lockdown, i.e., from January 1, 2011 until December 31, 2020. The clinical and biochemical characteristics of kidney transplant recipients are shown in Table 1.

Age, gender, and underlying cause of kidney disease were not significantly different between kidney transplant recipients who were transplanted during and before the lockdown, which indicates that patients with end-stage kidney disease were consistent during and before lockdown.

Deceased donation kidney transplantation was more frequent during the lockdown period (73.3% vs. 52.7%; $P < 0.01$), whereas living donation kidney transplantation was largely reduced during the lockdown period (i.e., AB0-incompatible living donation (6.7% vs. 13.6 %; $P < 0.01$); AB0-compatible living donation (20.0% vs 33.7 %, $P < 0.01$).

Plasma creatinine concentrations before transplantation and on the first postoperative day were not significantly different between in kidney transplant recipients who were transplanted during and before the lockdown. In contrast, the relative fall of plasma creatinine on the first postoperative day was significantly lower in kidney transplant recipients who were transplanted during compared to before the lockdown (median, 0.27; IQR, 0.13–0.52; vs. median, 0.40; IQR, 0.18–0.58; $P = 0.03$). Since the relative fall of plasma creatinine is known to be lower in recipients with donation after brain death compared to living donation, that result can be attributed to the higher portion of deceased donation kidney transplantation during the lockdown period.

Kidney function, i.e., eGFR four weeks posttransplant, tended to be lower in kidney transplant recipients who were transplanted during compared to before the lockdown (median, 39.9 mL/min/1.73m^2; IQR, 28.9–52.9; vs. median, 45.3 mL/min/1.73m^2; IQR, 32.6–56.9; $P = 0.11$).

Furthermore, kidney transplant recipients who received the transplant during the lockdown period had significantly lower hospital stay (median, 7 days; IQR, 7–9; vs. median 8 days; IQR, 7–12; $P < 0.01$). Table 1 summarizes the data for comparisons.

Table 1. Baseline characteristics of kidney transplant recipients who were transplanted during the lockdown period from March 13, 2020, until March 31, 2021 and those who were transplanted before the lockdown from January 1, 2011 until December 31, 2020. Data are shown as median [IQR] for continuous data and frequency (%) for categorical data. For comparative statistics, Mann-Whitney U was used for continuous data and Fisher's exact test for categorical data.

	Lockdown (n = 60)	Before lockdown (n = 528)	P-value
Age (years)	54 [41–65]	51 [41–61]	0.15
Male sex, N (%)	43 (72%)	348 (65%)	0.42
Donor type, N (%)			**< 0.01**
AB0-compatible living donation	4 (6.7%)	72 (13.6%)	
AB0-incompatible living donation	12 (20.0%)	178 (33.7%)	
Donation after brain death	44 (73.3 %)	278 (52.7%)	
Underlying cause of kidney disease, N (%)			0.22
1. Glomerulonephritis	17 (28%)	188 (36%)	
2. Diabetic nephropathy	7 (12%)	78 (15%)	
3. Hypertensive nephropathy	14 (23%)	67 (17%)	
4. Hydronephrosis	1 (2%)	26 (5%)	
5. Cystic disease	10 (17%)	80 (15%)	
6. Cancer	0	7 (1%)	
7. Unknown	11 (18%)	82 (14%)	
History of, N (%)			
Hypertension	16 (27%)	75 (14%)	**0.01**
Diabetes mellitus	7 (12%)	95 (18%)	0.20
Cardiovascular disease	6 (10%)	80 (15%)	0.07
BMI (kg/m2)	24.9 [22.7–27.7]	26.0 [23.6–30.3]	**0.01**
Plasma creatinine before transplantation (μmol/L)	675 (543–910]	713 [548–890]	0.77
Plasma creatinine first postoperative day (μmol/L)	469 [363–628]	410 [281–604]	0.08
Absolute fall of plasma creatinine on the first postoperative day	161 [80–416]	277 [116–422]	0.11
Relative fall of plasma creatinine on the first postoperative day	0.27 [0.13–0.52]	0.40 [0.18–0.58]	**0.03**
Estimated GFR 4 weeks after transplantation (ml/min/1.73m^2)	40 [29–53]	45 [33–57]	0.11
Length of hospital stay (days)	7 [6.5–9]	8 [7–12]	**0.01**

Bold value indicates $P < 0.05$.

Table 2. Clinical and laboratory characteristics of kidney transplant recipients according to time of transplantation. Cases were transplanted during the lockdown. i.e., March 12, 2020 to March 30, 2021). Controls were transplanted before January 1, 2020 and matched to cases according to donor type, gender, and age (within 5-year interval). If not otherwise specified continuous data are presented as median [IQR] and categorical data as number (percent).

	Cases	Controls	P-value
Recipient age (years)	55 [41–66]	55 [41–66]	0.90
Recipient gender male, N (%)	43 (72%)	43 (72%)	1.00
Body weight (kg)	77.5 [65.7–86.0]	79.1 [71.1–90.8]	0.16
Body mass-index (kg/m^2)	24.9 [22.6–27.6]	26.7 [23.6–29.7]	**0.01**
Recipient history of -, N (%)			
Hypertension	44 (73%)	51 (86%)	0.10
Diabetes mellitus	7 (12%)	10 (17%)	0.60
Cardiovascular disease	6 (10 %)	7 (12%)	1.00
Cause of kidney disease, N (%)			0.66
Glomerulonephritis	17 (28%)	20 (33%)	
Diabetes mellitus	7 (12%)	10 (17%)	
Hypertension	14 (23%)	9 (15%)	
Hydronephrosis	1 (2%)	3 (5%)	
Polycystic kidney disease	10 (17%)	9 (15%)	
Cancer	0	1 (1.67%)	
Other/Unknown	11 (18%)	8 (13%)	
Dialysis vintage (months)	12 [1.5–33]	8 [3–23]	0.23
Type of dialysis, N (%)			0.24
Hemodialysis	25 (42%)	33 (55%)	
Perotinealdialysis	23 (38%)	15 (25%)	
Preemptive transplant	12 (20%)	12 (20%)	
Immunosuppressives, N (%)			
Basiliximab	49 (82%)	51 (85%)	0.80
Thymoglobuline	11 (18%)	7 (12%)	0.44
Corticosteroids	15 (25%)	16 (22%)	0.82
Tacrolimus	60 (100%)	60 (100%)	-
Mycophenolatmofetil	60 (100%)	60 (100%)	-
Donor age (years)	64 [37–65]	56.5 [53–69]	0.96
Number of human leukocyte antigen mismatches	3 [2–4]	3 [2–5]	**0.03**
Cold ischemic time for deceased donors (hours)	11 [8–15]	15 [10–19]	**0.04**
Number of blood tests performed during hospitalization	17 [15–21]	17 [14–22]	0.55
Days until ureteral stent was removed (days)	15 [14–17]	22 [15–34]	**0.01**
Days of hospitalization	7 [7–9]	8 [7–10]	0.10
Plasma creatinine before transplantation (μmol/L)	676 [543–910]	678 [541–843]	0.85
Plasma creatinine on the first postoperative day (μmol/L)	469 [363–628]	482 [300–668]	0.87
Absolute fall of plasma creatinine on the first postoperative day	161 [80–416]	215 [85–396.5]	0.97
Relative fall of plasma creatinine on the first postoperative day	0.27 [0.13–0.52]	0.29 [0.17–0.49]	0.67
Delayed graft function, N (%)	7 (12%)	10 (17%)	0.60
eGFR four weeks after transplantation (ml/min/1.73m^2)	39 [29–53]	44 [34–55]	0.24
Three-month follow-up, median (range)			
Number of re-hospitalizations	1 [0–6]	1 [0–5]	0.85
Bacterial infections	0 [0–3]	0 [0–5]	0.80
Urological problems	0 [0–2]	0 [0–3]	0.33

Bold value indicates $P < 0.05$.

3.2. Case-control study

Now, we evaluated whether the lockdown may affect medical and clinical outcome in kidney transplant recipients. Table 2 shows clinical and laboratory characteristics in 60 cases of kidney transplant recipients who were transplanted at the Odense University Hospital and participated in the MoMoTx study during the SARS-Cov-2 lockdown period from March 13, 2020 until March 31, 2021, and in 60 controls of kidney transplant recipients, who were transplanted at the Odense University Hospital and participated in the MoMoTx study before the lockdown, i.e., in the period from January 1, 2011 until December 31, 2020. Controls were matched to cases according to donor type (i.e., AB0-blood-type-incompatible living donation, AB0-blood-type-compatible living donation, and donation after brain death), kidney transplant recipient gender, and age (within 5-year intervals).

Compared to matched controls the cases had similar causes of end-stage kidney disease, comorbidities, time on dialyses (dialysis vintage), and immunosuppressive treatment. Compared to matched controls the cases tended to have less human leukocyte antigen mismatches, lower cold ischemic time for deceased donors, but higher body mass index. More importantly, the absolute and the relative fall of plasma creatinine on the first postoperative day, the portion of delayed graft function, as well as kidney function, i.e., estimated glomerular filtration rate, four weeks after transplantation were similar in cases and controls, indicating

Table 3. Comparison of outcome in patients transplanted during and before the lockdown according to donor type. Data is presented as median [IQR] unless otherwise specified. The groups were compared using Mann-Whitney U test. eGFR = estimated glomerular filtration rate.

Variable according to subgroups	Cases	Controls	P value
Length of stay (days)			
ABO incompatible living donation	8 [7–10.5]	7.5 [6.5–8.5]	0.62
ABO compatible living donation	7 [6–8]	8.5 [6.5–11]	0.14
Donation after brain death	7.5 [7–9]	8 [7–10]	0.22
Number of blood tests performed within hospitalization			
ABO incompatible living donation	24 [19–27.5]	16 [14–30]	0.62
ABO compatible living donation	16 [15–17.5]	17 [14–28]	0.86
Donation after brain death	18 [15–21.5]	17 [14–21]	0.50
Plasma creatinine before transplantation (μmol/L)			
ABO incompatible living donation	911 [607–1180]	732 [639–832]	0.68
ABO compatible living donation	817.5 [594–998]	692 [522–876]	0.40
Donation after brain death	644.5 [524–825]	678 [529–843]	0.69
Plasma creatinine on the first postoperative day (μmol/L)			
ABO incompatible living donation	458 [350–647]	328 [209–560]	0.48
ABO compatible living donation	410 [218–495]	287 [220–541]	0.88
Donation after brain death	487 [391–651]	510 [381–691]	0.58
Absolute fall of plasma creatinine on the first postoperative day			
ABO incompatible living donation	452 [257–534]	404.5 [272–430]	0.68
ABO compatible living donation	445 [259–550]	429 [234.5–487]	0.67
Donation after brain death	122 [61–248]	157 [52–279]	0.87
Relative fall of plasma creatinine on the first postoperative day			
ABO incompatible living donation	0.45 [0.31–0.53]	0.55 [0.33–0.67]	0.68
ABO compatible living donation	0.57 [0.41–0.70]	0.56 [0.40–0.63]	0.93
Donation after brain death	0.17 [0.09–0.38]	0.23 [0.08–0.35]	0.74
Delayed graft function, N (%)			
ABO incompatible living donation	0	1 (25%)	1.00
ABO compatible living donation	2 (17%)	0	0.47
Donation after brain death	5 (11%)	9 (20%),	0.38
eGFR day 29 after transplantation (ml/min/1.73m^2)			
ABO incompatible living donation	40 [22–44]	56 [35–74]	0.22
ABO compatible living donation	56 [39–67]	55 [44–61]	1.00
Donation after brain death	33 [26–48]	40 [29–49]	0.40
Days until removal of ureteral stent			
ABO incompatible living donation	15 [14–18]	20 [17–23]	0.20
ABO compatible living donation	15 [13–16]	25 [13–45]	0.05
Donation after brain death	15 [14–17]	21 [16–33]	**0.01**

Bold value indicates $P < 0.05$.

that the transplant procedure was not affected during the lockdown period. The number of blood tests performed during hospitalization was similar in cases and controls. Finally, the time scheduled for ureteral stent removal was shorter in cases (15 days [14, 15, 16, 17]) compared to controls (22 days [15–34]; $p = 0.01$), which can be attributed to the fact that competing surgical procedures had been halted during lockdown.

Table 3 shows that these findings could be confirmed in all three transplant groups, i.e., ABO incompatible living donation, ABO

Table 4. Mean number of kidney transplantations performed per month in Denmark during and before the lockdown. The lockdown period in Denmark was defined as the second, third and fourth quarter of 2020, as well as the first quarter of 2021 to transplant center and donor type. Data were calculated from freely accessible data, which are provided by Scandiatransplant. http://www.scandiatransplant.org/.

Transplantat period	Transplant center	Total number of transplants per month (N)	Transplantation after brain death per month (N)	Transplantation after living donation per month (N)
During lockdown periode	Aarhus	9	6	3
	Copenhagen	8	6	2
	Odense	6	4	2
	Total	23	16	7
Before lockdown periode	Aarhus	8	5	3
	Copenhagen	8	5	3
	Odense	6	3	3
	Total	22	13	9

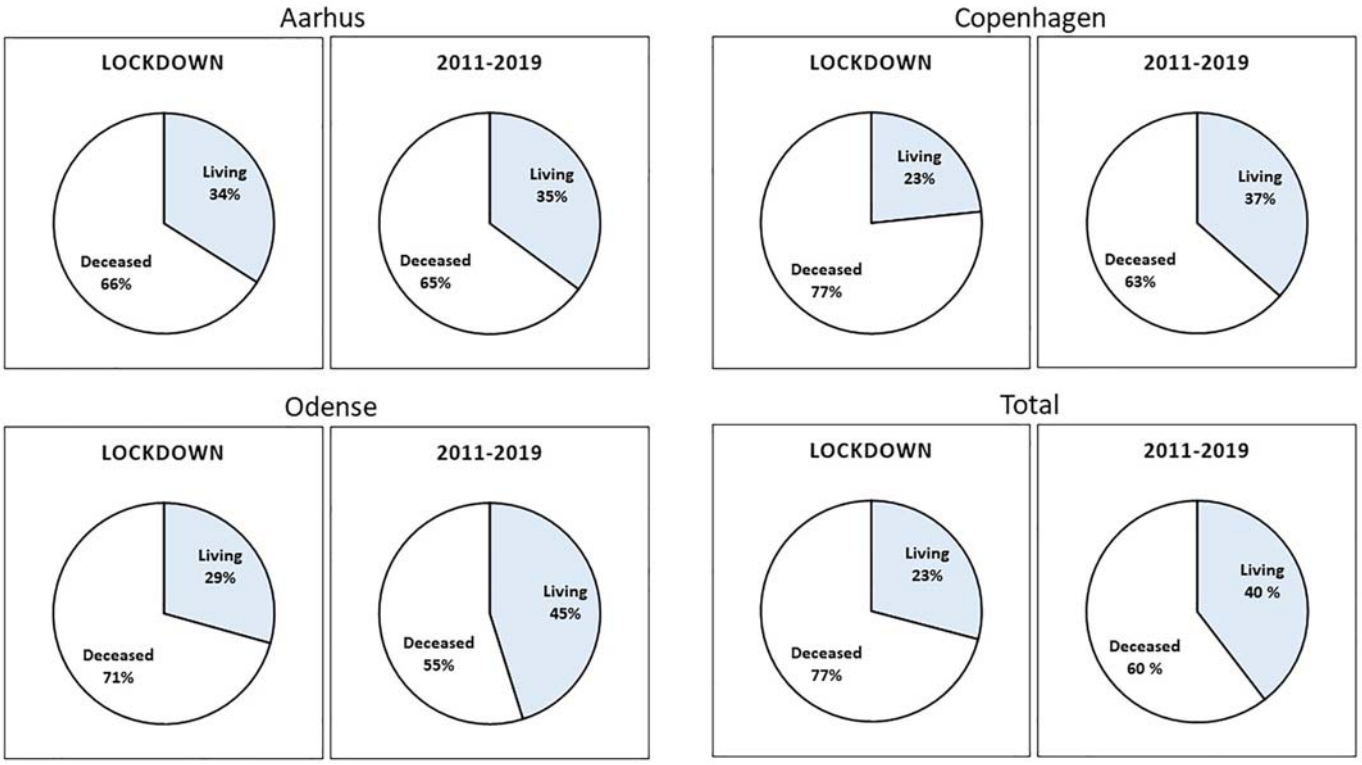

Figure 1. Ratio of living and deceased kidney transplantation in Denmark according to transplant center (i.e., Aahus, Copenhagen, Odense, Total) and time of transplantation (i.e., Lockdown = the secound to fourth quarters of 2020, and the first quarter of 2021; 2011–2019 = transplantation performed in the entire years 2011–2019). Data are available from Scandiatransplant. http://www.scandiatransplant.org/.

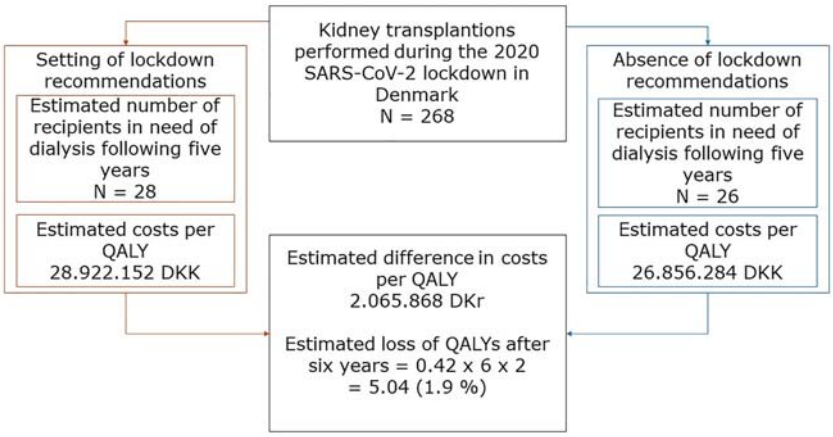

Figure 2. Schematic illustration of the expected consequences of the SARS-CoV-2 lockdown in Denmark on kidney transplant survival. Quality adjusted life-year (QALY) calculations were performed using utility values derived from reference (16), costs per QALY were calculated according to values derived from reference (17). DKK = Danish krone.

compatible living donation, and donation after brain death, supporting that the lockdown did not change medical and clinical outcome in kidney transplant recipients.

3.3. Transplant procedures in entire Denmark

In total 268 patients received a kidney transplant during the lockdown period in Denmark, whereas there were 2218 kidney transplantations during the period of 2011–2019. This amounts to a mean number of 23 kidney transplants per month (SD, 4) during the lockdown period and 22 kidney transplants per month (SD, 2) before the lockdown (Table 4). The proportion of living donor kidney transplants decreased during the lockdown period in all transplant centers in Denmark (Figure 1). During the lockdown period 78 living donor kidney transplants out of 268 kidney transplants (29%) were performed, whereas there were 878 living donor kidney transplants out of 2218 kidney transplants (39%) before the lockdown ($p = 0.01$).

According to the annual report of the Danish Nephrology Registry from 2017, 5-year survival on patients transplanted with the first renal graft from 2010 to 2014 was 95% for living donor kidney transplants and 88% for donation after brain death [15]. The 5-year death censored graft survival was 93% for living donor kidney transplants and 87% for donation after brain death [15]. Since our case-control study showed that the lockdown did not change medical and clinical outcome in kidney

transplant recipients these data may be extrapolated for kidney transplant recipients who received a graft during the lockdown period. According to expected 5-year death censored graft survival, 23 kidney transplant recipients with donation after brain death, as well as 5 kidney transplant recipients with living donation who received a graft during the lockdown period will require dialysis again after five years.

In the absence of the lockdown recommendations, 161 patients could have received a kidney transplant with donation after brain death, as well as 107 patients could have received kidney transplant with living donations. According to expected 5-year death censored graft survival, 20 kidney transplant recipients with donation after brain death, as well as six kidney transplant recipients with living donation would require dialysis again after five years.

3.4. Economic consideration of kidney transplant under lockdown

From an economic perspective the additional two patients in dialysis as a consequence of the lockdown would have implications for future cost of dialysis and future QALYs. Previous studies have reported that the total expected cost (discounted value) of dialysis per patient for 6-year period is 1,032,934 DKK using 2012 currency [17]. Hence, due to the lockdown recommendations, the additional expected cost difference would correspond to 2,065,868 DKK (277,298 EUR) after five years.

Furthermore, patients in dialysis have reduced quality of life compared to transplanted patients. The utility value has been reported to be 0.86 for kidney transplant recipients and 0.44 for patients requiring dialysis [16]. Consequently, the lockdown has caused an expected loss equivalent to 0.42 QALYs per patient per year after 5 years. In relation to the previous study of the cost-effectiveness of kidney transplantation, which used a six-year time horizon [17], the total additional loss of QALYs would be 5.04 after five years because of the lockdown. That is, the observed 10% reduction of kidney transplant recipients with living donation and consecutive reduction of graft survival causes 1.9% reduction of QALYs for kidney transplant recipients who received a kidney transplant during the lockdown period. These findings are illustrated in Figure 2.

4. Discussion

In this two-part study, we evaluated the effects of the SARS-CoV-2 lockdown recommendations on the specialized care of incident kidney transplant recipients. Firstly, we compared cases with kidney transplantations during the lockdown period with matched controls transplanted before lockdown and investigated effects on clinical and medical outcomes. Secondly, using data from the organ exchange organization Scandiatransplant, we explored the changes to the number and type of kidney transplants performed during and before lockdown, and the implications on QALY and costs.

4.1. Clinical and medical outcomes

We observed that lockdown recommendations largely reduced living donation kidney transplantation. This finding at our tertiary university hospital could be confirmed analyzing transplant data from all transplant centers in Denmark. A reduction of living donation kidney transplantation was also been reported in other countries [4].

Living donation kidney transplantation had been classified as elective by the Danish health authorities [8] This recommendation was designed to lessen the burden on health care providers, materials such as respirators and intensive care spots and overall logistics, and to provide the possibility of resource allocation to a potential increase in SARS-CoV-2 patients [8]. Furthermore, concern for the well-being of living donors in the kidney transplantation community also played a role in the reduction of living donation kidney transplantation [4]. Finally, the media coverage of the pandemic and the focus on self-isolation might have dissuaded possible living donors from donation.

Next, we observed that clinical characteristics were not significantly different between kidney transplant recipients who were transplanted during and before the lockdown. It is well known that living donation kidney transplantation is beneficial because it rapidly reduces toxic waste products in patients with end-stage kidney disease and normalizes disturbed water- and electrolyte balance. In line with a decreased portion of living donation kidney transplantation we noticed that the relative fall of plasma creatinine during the first postoperative day was lower during the lockdown period.

Our case-control study showed that medical and clinical outcome in kidney transplant recipients was not affected by lockdown recommendations. These findings could be confirmed in all three transplant groups, i.e., ABO incompatible living donation, ABO compatible living donation, and donation after brain death. In this prospective observational study, selection bias was limited by including controls according to prespecified criteria.

4.2. Transplantation in Denmark and economic aspects

Although the monthly average number of kidney transplantations did not decrease due to the lockdown, the proportions of living donation decreased across all transplantation centers in Denmark. Living kidney donations are associated with better patient- and graft survival outcome compared to donation after brain death (15), consequently an unintended consequence to the restrictions could be an earlier return to dialysis for a higher proportion of those transplanted during the Lockdown. As our results show, this will increase the costs in kidney transplant recipients by almost 300,000 EUR. In addition, kidney transplant during the lockdown recommendations may decrease QALY by approximately 1.9%.

5. Conclusion

The SARS-CoV-2 pandemic and subsequent lockdown recommendations have strained many aspects of health care. To the best of our knowledge, this is the first report showing that the SARS-CoV-2 lockdown recommendations may affect future QALY and costs in kidney transplant recipients transplanted during the lockdown periods.

Declarations

Author contribution statement

Qais W. Saleh and Martin Tepel: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Lone Grønbæk, Christian Kronborg and Jørgen T. Lauridsen: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

The clinical trial described in this paper was registered at Clinical-Trials.gov under the registration number NCT01515605.

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