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Should Thorax Thin-Section Computed Tomography Be a Standard Diagnostic Procedure in the Evaluation of Potential Kidney Transplant Recipients? Lessons Learned From the COVID-19 Pandemic

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ABSTRACT

Background. Kidney transplant is the preferred treatment for most patients with end-stage renal disease. Because dialyzed patients often have significant comorbidities or multimorbidities, they should be carefully evaluated before being waitlisted for transplant. The COVID-19 pandemic presents a major challenge for surgery, including transplant surgery. Owing to a fear of COVID-19 symptoms occurring in lungs, thin-section computed tomography (TSCT) became a standard evaluation technique in potential kidney transplant recipients before surgery.

Methods. The aim of the study was to evaluate the rationale and usefulness of TSCT in deceased donor kidney transplant during the COVID−19 pandemic. All adult patients who underwent deceased donor kidney transplant between May 1, 2020, and December 15, 2021, were included in the study. Potential kidney transplant recipients who were admitted to the Department of General, Vascular**,** and Transplant Surgery at the Medical University of Warsaw in Warsaw, Poland, were tested for COVID-19 (CovGenX rapid test); blood chemistries were performed; dialysis was performed (if needed); and, on a negative reverse transcriptase polymerase chain reaction test**,** HRCT was performed.

Results. From May 2020 until the end of December 2021, 54 patients were transplanted; however, 7 patients were disqualified after TSCT and consulted with a pulmonary specialist. Disqualification from kidney transplant accounted for 13% of the potential kidney allograft recipients.

Conclusions. Despite the possibility of overdiagnosis by TSCT, TSCT should be considered a standard evaluation technique in potential kidney transplant recipients. Potential kidney transplant recipients must be periodically reassessed given the prolonged wait time for a donor kidney and the significant number of comorbid conditions in this patient population. However, more data with longer follow−ups are needed to prove or disprove the rationale to use TSCT in transplant surgery.

KIDNEY transplant is the preferred treatment for most patients with end-stage renal disease (ESRD). A successful kidney transplant not only mitigates the mortality and morbidity, but it also improves quality of life relative to chronic dialysis. Because dialyzed patients often have significant comorbidities or multimorbidities, they should be carefully evaluated before being waitlisted for transplant. The evaluation ought to be efficient and cost-effective [1,2]. Assessment of lung disease pretransplant per the 2020 Kidney Disease

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Improving Global Outcomes (KDIGO) guidelines includes chest imaging in all transplant candidates (level of evidence 2C) and pulmonary function testing in candidates with impaired functional capacity, respiratory symptoms, or known pulmonary disease (level of evidence 1C). Chest computed tomography (CT) for current or former heavy tobacco users (≥30 pack-years) is suggested per local guidelines and chest radiograph for other potential kidney transplant recipients (level of evidence 2C) [3]. However, data on the evaluation of potential transplant candidates with pulmonary disorders are limited [1,2]. All patients, not only potential transplant candidates, should discontinue smoking [4] because it increases the risk of allograft loss and patient death. It has been reported that a 25-pack-year smoking history at the time of transplant is associated with a 30% higher risk of allograft failure when compared to nonsmokers or past smokers [5]. Importantly, the prevalence of serious pulmonary diseases, including chronic obstructive pulmonary disease (COPD) and lung cancer is significantly higher in ever-smokers than in never-smokers [6,7]. The COVID-19 pandemic presents a major challenge for surgery, including transplant surgery [8]. Using the Scientific Registry of Transplant Recipients data in the United States, Boyarsky et al [9] reported the decline in new listings and deceased donor kidney transplants, particularly in states with higher per-capita confirmed COVID-19 cases. Similarly, the number of waitlist deaths was higher than expected in the states with the highest COVID-19 burden.

In the United Kingdom, the Royal College of Surgeons of England published general surgery guidance on COVID-19 [10], and the Royal College of Radiologists issued a statement on the use of chest CT to screen for COVID-19 in preoperative patients [11]. It is agreed that transplant candidates should be screened for COVID-19 before surgery [12], and history of symptoms and exposure, physical examination, chest imaging, and a reverse transcriptase polymerase chain reaction (RT-PCR) test for COVID-19 are prerequisites. At the University of Washington Medical Center, potential recipients were screened for COVID-19 risks with at least a chest radiograph, and most of them had a chest CT; donors were similarly screened [13]. In our center, we performed a rapid RT-PCR test (CovGenX) of an upper respiratory tract specimen (nasopharyngeal swab) and if the test resulted negative, a chest thin-section computed tomography (TSCT) followed. The aim of the study was to evaluate the rationale and usefulness of TSCT in deceased donor kidney transplant during the COVID−19 pandemic.

MATERIALS AND METHODS

All 62 adult patients who were evaluated for deceased donor kidney transplant between May 1, 2020, and December 15, 2021, were included in the study and followed up until December 30, 2021. We analyzed the medical data from the Polish Transplants Registry waiting list (https://rejestrytx.gov.pl/tx/) to obtain demographic data (age, sex, cause of end-stage kidney disease, mode of dialysis, dialysis vintage, etc), as well as data related to imaging, endoscopy studies, and all required consults; also, we checked the data validity. Sixty-two potential kidney transplant recipients were admitted to the Department of General, Vascular, and Transplant Surgery at the Medical University of Warsaw in Warsaw, Poland, and they were tested for COVID-19 (rapid RT-PCR test, CovGenX); blood chemistries were performed; dialysis was performed (if needed); and, on a negative RT-PCR test, TSCT was performed before elective transplant surgery. All of the 62 patients had a negative RT-PCR test for COVID-19. All tomography examinations were performed with 64-row multidetector computed tomography scanners (Optima CT660 CT Scanner, GE Healthcare, Chicago, Ill, United States). Studies were performed without intravenous contrast medium administration using the following settings: 120 kVp, 150-300 mAs, pitch 0.938-0.984, and a reconstruction interval of 1.25 mm. Acquisition of continuous 0.623-mm thick sections was started at peak inspiration and was performed in the cranio-caudal direction. The image data were reconstructed with a high spatial frequency algorithm and analyzed at a window width (WW) of 1500 Hounsfield units (HU) and a window level (WL) of 600 HU. As transplant is a standard procedure performed at the hospital, additional ethical approval was not required. Content of each informed consent was approved by an ethical hospital board. However, special additional informed written consent for transplant during the pandemic, besides surgery, was obtained. Physical examination and investigation for the following symptoms were performed: cough, dyspnea, fevers, chills, chest pain, fatigue, headaches, body aches, rhinorrhea, sore throat, conjunctivitis, anosmia, dysgeusia, altered mental status, nausea or vomiting, abdominal pain, and diarrhea. All of the 62 patients were negative for these symptoms, including 8 patients who were disqualified on the basis of TSCT. The immunosuppresion protocol was written up by a consulting nephrologist before transplant surgery. In the case of a doubtful TSCT, a pulmonary specialist consultation was requested, and then it was followed by a decision on whether to proceed or disqualify a patient from transplant.

From May 2020 until the end of December 2021, 54 patients were transplanted. Eight patients were disqualified after TSCT and underwent consultation with a pulmonary specialist owing to relevant pathologies found in the chest imaging after thorough examination of all available data, including previous thorax CT scans or chest radiographs. Disqualification from kidney transplant accounted for 15% of the potential kidney allograft recipients. After a negative pulmonary consultation, another potential recipient was chosen and evaluated for possible transplant following the same procedure (RT-PCT COVID-19 test, physical examination, and TSCT). All of the potential recipients had a chest radiograph performed at the time of evaluation before being waitlisted; only two patients had previously done TSCT which results provided in the transplant registry. Overall, in our cohort there were no pathologies detected on the chest radiograph, except for 1 patient with pleural thickening and subpleural fibrotic changes in the upper parts of the lungs. All the TSCT data are presented in Table 1. In Table 2 we present laboratory data and pulmonary consultation if it was present for the disqualified patients. Figure 1 presents the TSCT at the time of hospital admission for kidney transplant. After imaging and pulmonary consultation, the potential recipient was disqualified (patient 7 in Table 2).

DISCUSSION

Because we were obligated to use TSCT to detect changes suggestive of COVID-19 in the lungs to prevent transplant in patients with possible infection, it appeared that we did detect several pathologies, which were not present and all of them unrelated to COVID-19 on the standard chest radiographs. Previously we reported our preliminary data from May 2020 to December 2020 about the underlying role of TSCT and the issue of disqualification of 5 potential kidney transplant

Table 1. Clinical characteristics of patients and follow-up

Patient (Age, Sex)	Cause of ESRD	Dialysis Vintage	Chest Radiograph While on Waiting List	TSCT at Time of Qualification	Follow-Up
Patient 1 (59, female); current smoker	IgA nephropathy	1 mo	Pleural thickening and subpleural fibrotic changes in the apex of the right lung; less pronounced in the left apex.	Fibrotic lesions with bronchiectasis in the apical and apicoposterior segment of the right upper lobe, less pronounced fibrotic changes in the apical segment of the left upper lobe. Massive pleural thickening in the posterior part of the left pleural cavity. Nodule up to 4 mm in segment 5 of the left lung.	Initiated 12-mo chemoprophylaxis with isoniazid. Suspended from waiting list.
Patient 2 (40, male)	IgA nephropathy	46 mo	Normal CXR with no relevant abnormalities.	Cavitating subpleural nodule 13-14 mm in the apical segment of the right lung (in differential consider pulmonary TB and nontuberculous mycobacterial pulmonary disease).	Adequate diagnostic procedures were ordered. No acid-fast bacilli in sputum bronchoalveolar lavage. Suspended from waiting list.
Patient 3 (64, female); current smoker	Diabetic nephropathy after liver transplant	14 mo	The cardiomediastinal silhouette and pulmonary vasculature are within normal limits in shape and size. The lungs are clear of focal airspace disease pneumothorax or pleural effusion.	Pleural effusion up to 35 mm, in the right pleural cavity with thickening of the parietal and visceral pleura (up to 2.5 mm) in the lower third of the chest. Compression atelectasis of the right lower lobe. Subpleural consolidation 24 × 8 × 34 mm with irregular margins in the apical segment of the left lower lobe. Calcification 7 mm in diameter in the lateral basal segment of the right lung. Several small pulmonary nodules up to 2 mm in both lungs.	Death from COVID-19 pneumonia 2 mo later.
Patient 4 (50, female)	GN membranoproliferative (treated with CPD, MMF, CsA)	14 mo	Normal CXR with no relevant cardiopulmonary abnormalities.	Nodular lesion 27 × 17 mm in the upper quadrant of the left breast 27 × 17 mm—breast tumor? No enlarged lymph nodes in left axilla (the maximal diameter up to 8 mm).	Breast cancer after surgery, chemotherapy, on hormonal therapy. Suspended from waiting list.
Patient 5 (61, male); former smoker	Unknown	12 mo	The lungs are normally inflated. Peribronchial thickening in the lower parts of both lungs. Otherwise, no relevant abnormality.	Irregular consolidation 13 × 6 × 11 mm in the lower part of the right upper lobe surrounded by several small peribronchial nodules—mucous-filled small peripheral airways? Peribronchial infiltrates?	TSCT on November, 25, 2021. Small fibrotic changes in the lower left lung and median part of the right lung. Active on waiting list.
Patient 6 (55, male)	Diabetic nephropathy (type 2 diabetes)	60 mo	Normal CXR with no relevant abnormalities.	Bilateral pleural effusion, up to 72 mm on the right side and up to 24 mm on the left side. Consolidations in the adjacent lung regions that require differentiation, primarily between compression atelectasis and pneumonia.	Suspended from waiting list.
Patient 7 (32, male)	Hypertensive nephropathy	16 mo	Normal CXR with no relevant abnormalities.	Bilateral, patchy, ground-glass opacities and confluent consolidations with centrilobular distribution mainly seen in the upper lobes and apical segments of the lower lobes.	Suspended from waiting list.
Patient 8 (45, male)	Glomerulonephritis (no biopsy)	27 y	Numerous calcified opacifications in the course of secondary hyperparathyroidism −metastatic pulmonary calcification.	An azygos lobe. Localized, ill-defined patchy ground-glass opacities with accompanying reticulonodular pattern in subpleural areas of the right upper lobe (anterior segment) and lateral basal segments of both lower lobes.	Suspended from waiting list.

CPD, cyclophosphamide; CsA, cyclosporine A; CXR, chest radiograph; ESRD, end-stage renal disease; GN, glomerulonephritis; MMF, mycophenolate mofetil; TB, tuberculosis; TSCT, thin-section computed tomography.

Table 2. Basal Clinical and Laboratory Data at Admission to the Department of General, Vascular, and Transplant Surgery at the Medical University of Warsaw in Warsaw, Poland

Patient (Age, Sex)	COVID-19 RT-PCR Test at Admission	Symptoms of Infectionat Admission	C-Reactive Protein (mg/dL)	White Blood Cell Count (x$10^3/\mu$L)	Platelet (x$10^3/\mu$L)	Fibrinogen (mg/dL)	Pulmonary Consultation
Patient 1 (59, female); current smoker	Negative (Gen N2 and Gen E)	Negative	0.3	5.52	182	345	Owing to presence of cirrhotic and fibrotic changes on the top of the right lung, further work is required before transplant.
Patient 2 (40, male)	Negative (Gen N2 and Gen E)	Negative	13.4	8.42	276	347	Owing to the suspected inflammatory focus of TBC and mycobacteriosis origin, more detailed diagnostics is warranted, and the patient should be suspended from transplant.
Patient 3 (64, female); current smoker	Negative (Gen N2 and Gen E)	Negative	Not done	Not done	Not done	Not done	Owing to the suspicion of TBC in the right lung and other pathologies, a lack of previous diagnostics, and the necessity to perform bronchoscopy with further work-up, the patient was disqualified and discharged to the HD unit of origin without complete laboratory results.
Patient 4 (50, female)	Negative (Gen N2 and Gen E)	Negative	5.6	8.35	330	Not done	Not done.
Patient 5 (61, male); former smoker	Negative (Gen N2 and Gen E)	Negative	0.6	6.88	165	330	Owing to the presence of irregular nodule of uncertain origin (inflammatory?) and lack of previous imaging studies for comparison, further work-up is required and the patient was disqualified.
Patient 6 (55, male)	Negative (Gen N2 and Gen E)	Negative	5	6.16	254	499	Despite normal inflammatory parameters, inflammation in the lung could not be excluded with certainty; therefore, the patient should not be qualified at this moment for transplant.
Patient 7 (32, male)	Negative (Gen N2 and Gen E)	Negative	0.7	8.04	179	356	Owing to diffuse peripheral focal peribroncheal consolidation in TSCT and lack of previous imaging studies to compare and exclude predominantly inflammatory change (ie, TBC), the patient was disqualified.
Patient 8 (45, male)	Negative (Gen N2 and Gen E)	Negative	11.1	8.38	164	314	The whole image is uncertain and requires the differential diagnostics mainly between inflammation of fungal, opportunistic origin and bronchoalveolar hemorrhage. Further urgent pulmonary diagnostic is needed in the HD unit of origin before transplant.

HD, hemodialysis; RT-PCR, polymerase chain reaction; TBC, tuberculosis; TSCT, thin-section computed tomography.

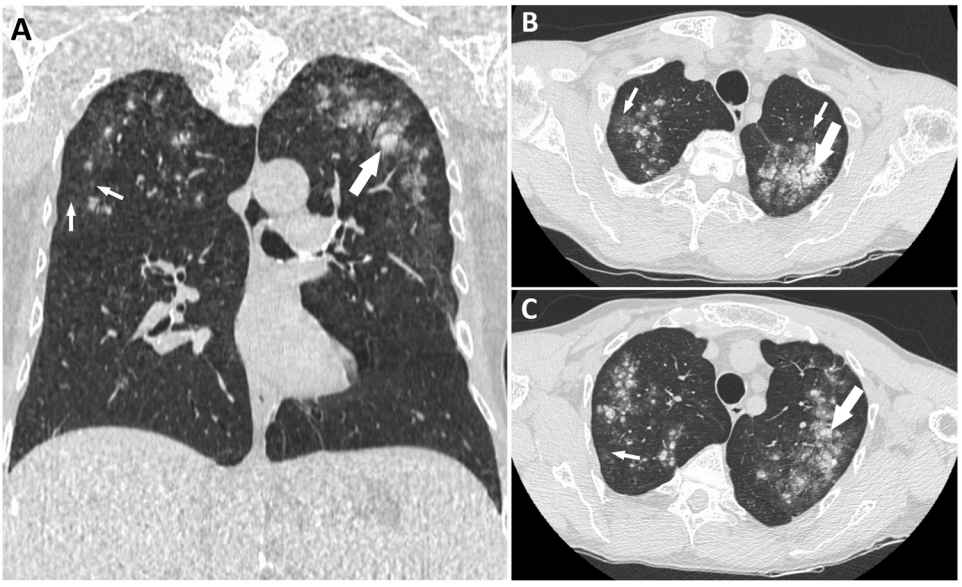

Fig 1. Computed tomography scans (soft tissue window) of a 32-year-old patient showing bilateral, patchy, ground-glass opacities (small arrows) and confluent consolidations (large arrows) with centrilobular distribution mainly seen in the upper lobes and apical segments of the lower lobes. **(A)** Anterior-posterior peojection. **(B and C)** Cross-sectional projection of upper and lower lobes.

recipients [14]. Here, we present data from 2 years (2020 and 2021) of transplant activity during the COVID-19 pandemic with follow-ups of disqualified potential recipients. In general, there are limited data in published literature on the use of TSCT as an imaging study prior to transplant. At the University of Washington Medical Center, chest CT was used to rule out COVID-19 infections in some kidney donors [13], whereas at the Jackson Memorial-Miami Transplant Institute in Miami, Florida, kidney transplant recipients were evaluated for symptoms of COVID-19 and underwent RT-PCR tests and chest radiographs [15]. At Baylor College of Medicine in Houston, Texas, transplant candidates required a negative SARS−CoV2 nasopharyngeal swab and normal chest CT for COVID−19 before transplant surgery [16]. The authors of the study stressed that chest CT in asymptomatic patients who were admitted for solid organ transplant had low specificity for COVID−19 and should be interpreted with caution [17]. KDIGO guidelines recommend a chest radiograph in general and CT in selected cases (heavy smokers) during evaluation for kidney transplant. KDIGO transplant guidelines were prepared before the pandemic and published in April 2020, therefore they did not deal with COVID-19 screening [3]. A chest radiograph is cost-effective and easy to perform; however, it has its limitations. If there is a doubt after a chest radiograph, TSCT is used to clarify the pathology. It provides more information than conventional CT and standard chest radiographs. Chetan et al [18] determined retrospectively the incidence of possible COVID-19−related lung changes on preoperative screening CT for COVID-19 and how their findings influenced decision-making. They evaluated 156 consecutive patients having imaging prior to urgent elective surgery and 283 patients having acute abdominal imaging. Lung findings were categorized according to the British Society of Thoracic Imaging guidelines [19]. RT- PCR testing, management, and outcomes were determined from the electronic patient records. Their study included 25 patients undergoing renal transplant. They found CT abnormalities suggestive of COVID-19 in 13 (8%) patients from the elective surgery group. Only 3 patients had positive RT-PCR for COVID-19. There were 3 patients scheduled for transplant in this group. All of them, despite a negative RT-PCR for COVID-19 and being asymptomatic, were suspended from the transplant waiting list for 14 days. One patient subsequently received a renal transplant 25 days after the initial operative date. Moreover, in 28 (18%) patients, preoperative CT studies identified an alternative disease warranting further action, such as metastatic disease, bacterial infection, and nasogastric tube misplacement. In our group, none of the patients tested positive for COVID-19 and there were no CT abnormalities suggestive of COVID-19 that were detected. The same group of authors performed a retrospective study of the potential renal transplant recipients who had undergone chest CT screening for COVID-19 from March 27, 2020 to June 9, 2020 [20]. They assessed 74 chest CT examinations as a part of a Trust retrospective audit of 68 patients, with 57 patients reported as normal, 7 patients reported as indeterminate, 3 patients reported as classic or probable COVID-19, and 7 patients reported as non−COVID-19 (4 patients with fluid overload and 3 patients with an infection). As a result, 8 of 9 patients were suspended from the transplant waiting list because of classic or probable COVID-19 or indeterminate results for COVID-19. Only 1 patient had a positive COVID-19 PCR test (the initial result was reported as indeterminate by 1 nonthoracic cross-sectional radiologist and was reported negative [other infection] by 2 thoracic radiologists). Of interest, there was a 48.15% overall agreement among the 3 raters (the original report and re-review).

We are fully aware that our present study has several limitations. First, this was a retrospective study, and the data were reliant on documentation within clinical notes. Second, there are inter- and intrareader variability in lung findings reported by radiologists and pulmonologists on duty. Our sample size was relatively small; however, we could not find a larger sample size of patients undergoing kidney transplant in the published literature. The study follow−up time was more than 1 year. On the basis of our study and the scarce data available from the published literature, we are fully aware that the utility of any preoperative chest CT, including TSCT, needs to be balanced with the potential harm of a delayed operation or disqualification and suspension from the transplant active waiting list. In addition, while considering chest CT in the diagnosis of COVID-19, it may not appropriate. It is unknown whether the CT findings are related to detecting COVID-19 or other diseases of the patients. The detection of potential fluid overload from end-stage renal disease may overlap with the detection of COVID-19; similarly, vasculitis may present as ground-glass opacity [21], which occurred in one of our patients. This patient cohort is also more susceptible to bacterial infection and other comorbidities or medication effects, which may challenge interpretation. In addition, with the more widespread availability of the rapid RT-PCR test and its increased use in screening, it still remains to be demonstrated when preoperative chest imaging in transplant surgery will be of value. However, although specific, RT-PCR testing has a reported sensitivity of only 60% to 70% [22]. Meanwhile, the relatively high incidence of other findings warranting further action, for example malignancy or tuberculosis, needs to be considered. Additionally, we have to consider that with a normal chest radiograph, we may miss important pathology resulting in fatal outcomes after transplant, in particular with an induction regimen. Therefore, this decision warrants close discussion between the surgical, radiology, pulmonology, and transplant physician teams working together. However, Tsakok et al [20] stated that National Institute for Health and Care Excellence (NICE) guidelines [23] do not routinely request chest CT scans to screen for COVID-19 in patients with no symptoms. Similarly, Weiss et al [12] recently recommended against routine thoracic CT scans for COVID-19 screening for potential deceased organ donors (strong recommendation; low certainty of evidence).

CONCLUSIONS

We showed that deceased donor kidney transplant could be safely performed during the COVID−19 pandemic. Despite the possibility of overdiagnosis, TSCT should be considered as standard imaging technique in potential kidney transplant recipients. Potential kidney transplant recipients must be periodically reassessed, given the prolonged wait time for a donor kidney and the significant number of comorbid conditions among this patient population. However, more data, including longer follow−up, are needed to prove or disprove the rationale to use TSCT in pretransplant evaluation. There is a paucity of high-quality evidence to guide decisions around deceased donation assessments and the management of solid organ transplant recipients and waitlisted patients.

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