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Whole Body CT Imaging in Deceased Donor Screening for Malignancies

Jacobus W. Mensink, MD,[1,2] Robert A. Pol, MD, PhD,[3] Wijmtje N. Nijboer, MD, PhD,[1] Michiel E. Erasmus, MD, PhD,[4] Jeroen de Jonge, MD, PhD,[5] Kirsten M. de Vries, MSc,[2] Michel F. van der Jagt, MD,[6] Niels P. van der Kaaij, MD, PhD,[7] Marcel C.G. van de Poll, MD, PhD,[8,9] Ian P.J. Alwayn, MD, PhD,[1] and Andries E. Braat, MD, PhD[1]

Background. In most western countries, the median donor age is increasing. The incidence of malignancies in older populations is increasing as well. To prevent donor-derived malignancies we evaluated radiologic donor screening in a retrospective donor cohort. **Methods.** This study analyzes the efficacy of a preoperative computed tomography (CT) scan on detecting malignancies. All deceased organ donors in the Netherlands between January 2013 and December 2017 were included. Donor reports were analyzed to identify malignancies detected before or during organ procurement. Findings between donor screening with or without CT-scan were compared. **Results.** Chest or abdominal CT-scans were performed in 17% and 18% of the 1644 reported donors respectively. Screening by chest CT-scan versus radiograph resulted in 1.5% and 0.0% detected thoracic malignancies respectively. During procurement no thoracic malignancies were found in patients screened by chest CT compared with 0.2% malignancies in the radiograph group. Screening by abdominal CT-scan resulted in 0.0% malignancies, compared with 0.2% in the abdominal ultrasound group. During procurement 1.0% and 1.3% malignancies were found in the abdominal CT-scan and ultrasound groups, respectively. **Conclusions.** Screening by CT-scan decreased the perioperative detection of tumors by 30%. A preoperative CT-scan may be helpful by providing additional information on (aberrant) anatomy to the procuring or transplanting surgeon. In conclusion, donor screening by CT-scan could decrease the risk of donor-derived malignancies and prevents unnecessary procurements per year in the Netherlands.

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Organ transplantation improves quality of life and increases life expectancy of patients with end-stage organ failure but is limited by a shortage of available organs. In the Netherlands and in most European countries, the waiting list for organ transplantation increases. The number of available organs is relatively stable over the past years, but the median donor age is increasing.[1] To increase the amount of available organs extended criteria donors are being used, taking a risk on inferior results achieved compared with normal organ donors.[2] For example, by increasing donor age selection criteria, organ quality may decrease and the risk of malignancy in the donor increases.[3] In case of an active malignancy, the patient is often not eligible for organ donation, depending on type and location of the tumor.[4] Despite extensive donor screening, donor-derived malignancies have been reported.[5–8] Other incidental findings which may exclude

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[1] Department of Surgery, Division of Transplantation, Leiden University Medical Center, Leiden University, Leiden, The Netherlands.

[2] Department of Organ and Tissue Donation, Dutch Transplant Foundation, Leiden, The Netherlands.

[3] Department of Surgery, Division of Transplantation, University Medical Center Groningen, Groningen University, Groningen, The Netherlands.

[4] Department of Cardiothoracic Surgery, University Medical Center Groningen, Groningen University, Groningen, The Netherlands.

[5] Department of Surgery, Division of Transplantation, Erasmus Medical Center, Rotterdam University, Rotterdam, The Netherlands.

[6] Department of Surgery, Division of Vascular and Transplant Surgery, University Medical Center St. Radboud, Nijmegen University, Nijmegen, The Netherlands.

[7] Department of Cardiothoracic Surgery, University Medical Center Utrecht, Utrecht, The Netherlands.

[8] Department of Surgery, Maastricht University Medical Center, Maastricht University, Maastricht, The Netherlands.

[9] Department of Intensive Care Medicine, Maastricht University Medical Center, Maastricht University, Maastricht, The Netherlands.

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Author contributions

A.E.B., I.P.J.A., and J.W.M. participated in research design. J.W.M. participated in data collection. A.E.B., R.A.P., and J.W.M. participated in data analysis. All authors participated in construction and critical revision of the article.

Correspondence: J.W. Mensink, MD, Department of Surgery, Division of Transplantation, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands. (j.w.mensink@hotmail.com).

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organs from transplantation are hepatic steatosis or cirrhosis, pancreatic fibrosis, renal atrophy, or extensive bilateral lower lobe atelectasis. Some benign and incidental findings, such as a single uncomplicated kidney cyst or mild hepatic steatosis, are usually no objection for transplantation.[4] For assessing donor suitability, different characteristics are taken into account, such as medical history, cause of death, demographic characteristics, laboratory tests, and imaging studies. The following imaging studies are part of the current protocol in donor screening in the Eurotransplant (ET) Region; abdominal ultrasound (US), chest radiograph, and occasionally bronchoscopy.[4] In the event of an inconclusive result, additional tests may be performed such as histopathologic examination.

An alternative for standard donor screening by chest radiograph and abdominal US is to perform a computed tomography (CT) scan of chest and abdomen. Malignancies have a higher probability of being detected with a CT-scan compared with a chest radiograph or abdominal US alone. The risk of donor-derived malignancies in organ transplantation can never be excluded completely, but prevention should be pursued given the very poor prognosis in the recipients when transmission has occurred with a <50% 2 year survival in certain malignancies.[7] A potential downside of increasing the number or frequency of medical imaging is the risk of creating uncertainty by incidental findings.[9–11] Incidental findings such as a simple renal, thyroid, or hepatic cyst might not be a contraindication to refrain from transplantation but could unnecessary delay or even abort the donation procedure. And by performing chest/abdominal CT-scans the costs of donor screening will in all likelihood increase slightly. A recent case with a donor-derived malignancy drew a lot of negative media attention in the Netherlands.[8] Therefore, the aim of this study is to analyze the added effect of abdominal and thoracic CT scans in the prevention of donor-derived malignancies.

MATERIALS AND METHODS

Data Analysis

In this retrospective analysis, all patients reported to ET as organ donor in the Netherlands between January 1, 2013 and December 31, 2017 were included. Baseline characteristics were collected from the ET Network Information System from ET and Organ Procurement Information database from the Dutch Transplant Foundation. Donor reports were analyzed for any change in organ allocation outcome based on results of radiologic diagnostics or malignancies found during organ procurement. Reported donors without any documented medical imaging were excluded from the analysis. When both imaging modalities were documented (thoracic CT-scan and chest radiograph or abdominal CT-scan and abdominal US), the donor was included in the CT-scan group. If no CT-scan was reported, the donors were included in the chest radiograph only or abdominal US only group. When a (possible) malignancy was detected by imaging, the donor report was analyzed. If the (possible) malignancy was detected by abdominal US or chest radiograph, the donor was included in standard imaging group. If the (possible) malignancy was detected by the CT-scan alone, the donor was included in the CT-scan group.

Statistical Analysis

To assess the distribution of the data histograms as well as Shapiro-Wilk tests were used. Differences in categorical data were assessed by using the Chi-Square test. To compare skewed continuous data the Mann-Whitney U was used. $P < 0.05$ was considered statistically significant. Continuous data were presented as mean ± SD and categorical data as absolute number (%) unless otherwise stated. For statistical analysis IBM SPSS Statistics for Windows was used (IBM Corp. Released 2016. Version 24.0. Armonk, NY).

RESULTS

Data Analysis

A total of 1644 organ donors were reported of which 1546 donors were approved for donation of at least 1 organ. This resulted in 1316 donor procurements leading to 1270 effectuated donor procedures of which at least 1 organ was transplanted. Donor characteristics stratified for thoracic and abdominal imaging are presented in Table 1 and Table 2. Chest CT-scans or radiographs were performed in 274 (17%) and 996 (61%) of the 1644 potential donors, respectively. Of the 274 potential donors with a thoracic CT-scan, in 207 (75%) potential donors a chest radiograph was made as well. Abdominal CT-scans or USs were performed in 296 (18%) and 1197 (73%) of the 1644 potential donors, respectively. Of the 296 potential donors with an abdominal CT-scan, in 114 (40%) potential donors an abdominal US was made as well. In 374 (23%) donors no thoracic and in 154 (9%) donors no abdominal radiologic screening was documented and hence were excluded from the analysis. Of all reported DCD donors, 984 of 1005 (98%) were type III DCD donors. Euthanasia (according to the Dutch law) was performed in 9 of 1005 (1%) donors (DCD type V) and 12 of 1005 were type I or type II DCD donors. The type I and II DCD donors were evaluated for kidney donation alone during a clinical trial. As shown in Tables 1 and 2, more CT-scans were performed in young donors and in the CT-scan group trauma was the most common cause of death. Of all donors with trauma as cause of death, 6 of 300 donors (2.0%) were diagnosed with a malignancy during procurement. A chest- or abdominal CT-scan was performed in 55% and 52% of all these donors, respectively. Of the donors with a nontraumatic cause of death, 23 of 1344 donors (1.7%) were diagnosed with a malignancy before or during procurement. A chest- or abdominal CT-scan was performed in 14% and 12% of all these donors, respectively. In 286 (17%) organ donors, only the kidneys were procured.

Thoracic and Abdominal Screening

Screening by an additional chest CT-scan versus chest radiograph only resulted in, respectively, 1.5% and 0% detection of (possible) thoracic malignancies (Table 3). During procurement, no additional thoracic malignancies were found in donors screened by chest CT compared with 0.2% in the chest radiograph only group. Screening by abdominal CT-scan versus US resulted in, respectively, 0.0% and 0.2% detection of (possible) abdominal malignancies (Table 3). During procurement, in 1.0% of the potential donors additional abdominal malignancies were found in donors screened by abdominal CT-scan compared with 1.3% in the US only group. Notably, 3 hearts and 5 lungs were already transplanted by the thoracic transplant team, while later on an abdominal malignancy was detected during abdominal organ procurement. Of these donors, no abnormalities were seen on the chest radiograph

TABLE 1.

Donor characteristics of reported donors, stratified for thoracic imaging

	Chest CT-scan	Chest radiograph	*P*
Number of reported donors	274 (17%)	996 (61%)	
Female	115 (42%)	466 (46.8%)	0.156
Age	49.6 (17.2)	53.0 (14.5)	0.027
Cause of death			
CVA	77 (28%)	581 (58%)	<0.001
Trauma	125 (46%)	102 (10%)	<0.001
Other	72 (26%)	313 (31%)	0.101
DCD donation	158 (58%)	559 (56%)	0.649
Kidney-only procurement	37 (14%)	128 (13%)	0.776

CT, computed tomography; CVA, cerebrovascular accident; DCD, donation after circulatory death.

TABLE 2.

Donor characteristics of reported donors, stratified for abdominal imaging

	Abdominal CT-scan	Abdominal US	*P*
Number of reported donors	296 (18%)	1197 (73%)	
Female (%)	106 (36%)	562 (47%)	0.001
Age	49.0 (18.3)	54.2 (14.4)	<0.001
Cause of death			
CVA	85 (29%)	651 (54%)	<0.001
Trauma	148 (50%)	135 (11%)	<0.001
Other	63 (21%)	411 (34%)	<0.001
DCD donation	182 (61%)	712 (60%)	0.529
Kidney-only procurement	57 (19%)	200 (17%)	0.298

CT, computed tomography; CVA, cerebrovascular accident; DCD, donation after circulatory death; US, ultrasound.

TABLE 3.

Number of (possible) malignancies detected before and during procurement

	Before procurement	During procurement
Chest CT-scan	4 (1.5%)	0
Chest radiograph	0	2 (0.2%)
Abdominal CT-scan	0	3 (1.0%)
Abdominal US	2 (0.2%)	15 (1.3%)

CT, computed tomography; US, ultrasound.

or abdominal US before procurement. No CT-scan was performed in these donors. The malignancies of the donors were diagnosed after procurement of the thoracic organs and during or after transplantation of the thoracic organs in the recipients. In the Netherlands, first the thoracic organs are being procured by the thoracic transplant surgeons. After this, the abdominal organs are procured by a certified procurement surgeon, not necessarily being a transplant surgeon. To minimize the cold ischemic time, most of the time the recipient of the heart or lungs is being prepared for transplantation while procurement of the abdominal organs is not yet finished and the results of the pathology are not known. With a mean follow-up of 2 years, no donor-derived malignancy was reported in these transplanted patients.

Malignancies Detected Before and During Procurement

Tables 4 and 5 show all (possible) malignancies detected before and during procurement. Not every suspected finding was biopsied before procurement. The thoracic abnormalities were detected by chest CT-scan only and not by chest radiograph. The abdominal abnormalities were detected by US only or US and CT-scan, as shown in Table 4. Of the possible thoracic malignancies detected before procurement, 2 abnormalities could not be biopsied for histopathologic examination. Histopathologic evaluation of the other 2 thoracic abnormalities showed 1 malignant and 1 benign finding. The abdominal US of donor 5 (Table 4) showed multiple hypoechoic lesions with a possible halo sign. The CT-scan performed after the US confirmed multiple lesions with enhanced uptake of arterial contrast without evidence for wash-out in the venous phase. The most likely diagnosis was focal nodular hypertrophy or hepatic adenomatosis, but metastases could not be excluded completely. A perioperative biopsy showed focal nodular hypertrophy and the organs could be transplanted safely. The abdominal US of donor 6 (Table 4) showed an interlobular cysts of which the biopsy resulted in a renal cell carcinoma. If a malignancy was detected during procurement, all procedures were canceled, except for the already procured thoracic organs as explained before.

DISCUSSION

This study shows the potential benefit of extended radiologic screening in deceased organ donation. Screening by CT-scan decreased the percentages of perioperative detection of tumors, from 0.2% to 0% for thoracic CT-scans, and from 1.3% to 1.0% for abdominal CT-scans. This resulted in a relative risk reduction of 30% for perioperative detection of malignancies by thoracic and abdominal screening with CT-scan. Interestingly, in the traumatic younger patients, more often a CT-scan was performed. But the malignancies detected by CT-scan before procurement (Table 4) were all in nontraumatic patients. This could be explained by the fact that younger donors have an increased risk for trauma as cause of death and a decreased risk for malignancy. Furthermore, the evaluation of a CT-scan made for screening in trauma patients is more focused on traumatic injuries, so malignancies could be missed during the initial evaluation. Implementing CT-scan in the standard donor screening protocol could prevent ~7 unnecessary procurement procedures in 5 years in the Netherlands. To detect 1 abdominal or thoracic malignancy, 235 CT-scans must be made. In this donor cohort, 3 hearts and 5 lungs were already transplanted by the thoracic transplant team when later on a malignancy (lung, renal or pancreas carcinoma) was found by the abdominal organ procurement team. It is to be expected that this could have been prevented if an additional CT-scan had been performed. And despite the apparently good outcome in these cases until now, such risks must be avoided at all times. Besides careful surgical evaluation of the thoracic and abdominal cavity, we suggest a CT-scan could be of additional value. Some possible malignancies detected during screening by chest radiograph, abdominal US or CT-scan turned out to be no malignancy after all. Therefore it is of utmost importance to assess the abnormalities by histopathologic evaluation. In 2016, Tache et al[12] published the results of their study to analyze the role of chest/abdominal CT-scan in donor selection and preoperative

TABLE 4.

Type and location of (possible) malignancies detected before procurement

#	Suspected anomaly	Imaging made	Detected by	Pathology	Outcome
1	Suspected lung nodules	Chest-CT	Chest-CT	No biopsy taken	No procurement
2	Suspected lung nodules	Chest-CT and chest radiograph	Chest-CT	No biopsy taken	No procurement
3	Suspected lung nodules	Chest-CT	Chest-CT	Biopsy during procurement, no malignancy	Organs transplanted
4	Suspected lung nodules	Chest-CT and chest radiograph	Chest-CT	Biopsy during procurement, lung carcinoma	No procurement
5	Liver abnormalities	Abdominal US and abdominal CT	Abdominal US and abdominal CT	Biopsy during procurement, no malignancy	Organs transplanted
6	Kidney abnormalities	Abdominal US	Abdominal US	Biopsy before procurement, renal cell carcinoma	No procurement

CT, computed tomography; US, ultrasound.

TABLE 5.

Type and location of malignancies detected during procurement

#	Affected organ	Imaging made	Detected by	Pathology confirmed
1	Lung	Chest radiograph	Procurement	Adenocarcinoma; primary
2	Lung	Chest radiograph	Procurement	Adenocarcinoma; metastases
3	Spleen	Abdominal CT-scan	Procurement	Lymphoma
4	Pancreas	Abdominal CT-scan	Procurement	Neuroendocrine tumor
5	Liver	Abdominal CT-scan (haemangioma seen)	Procurement	Hepatocellular carcinoma
6	Kidney	Abdominal US	Procurement	Renal cell carcinoma
7	Kidney	Abdominal US	Procurement	Multiple benign tumors, not transplantable due to quality
8	Kidney	Abdominal US	Procurement	Renal cell carcinoma
9	Kidney	Abdominal US	Procurement	Renal cell carcinoma
10	Kidney	Abdominal US	Procurement	Renal cell carcinoma
11	Kidney	Abdominal US	Procurement	Renal cell carcinoma
12	Kidney	Abdominal US	Procurement	Renal cell carcinoma
13	Kidney	Abdominal US	Procurement	Renal cell carcinoma
14	Liver	Abdominal US	Procurement	Liver metastases
15	Large intestine	Abdominal US	Procurement	Colon carcinoma
16	Small intestine	Abdominal US	Procurement	Neuroendocrine tumor
17	Enlarged abdominal lymph nodes	Abdominal US	Procurement	Malignancy not to be excluded
18	Pancreas	Abdominal US	Procurement	Malignancy not to be excluded
19	Pancreas	Abdominal US	Procurement	Pancreas carcinoma
20	Pancreas	Abdominal US	Procurement	Pancreas carcinoma
21	Pancreas	Abdominal US	Procurement	No malignancy

CT, computed tomography; US, ultrasound.

planning of the organ procurement strategy in brain dead organ donors. Organ procurement was not performed in 22 (24%) donors because of general contraindications, in 12 of 22 cases additional findings (diffuse thromboatheromatous disease, 1 hydatid cyst and 10 possible malignancies) detected by a CT-scan alone, were reason to refrain from the donor procedure. Of the 68 potential organ donors accepted for donation, 11 organs (16%) were not procured based on CT-findings alone. Aberrant vascular anatomy was detected in the hepatic or renal vasculature in 10% and 28% of the patients, respectively. The study concluded with a strong recommendation to further implement donor screening by use of a chest and abdominal CT-scan.[12] In 2017, Bethier et al performed a prospective study to assess the role of whole body CT-scan for determining morphologic suitability for organ donation in brain dead patients.[13] Radiologic findings of CT-scans were compared with perioperative findings and/or the result of histopathologic analysis of biopsy specimens. The study concluded that during procurement 4 of 12 lesions, of which biopsies were obtained during procurement, were not visible during procurement but had been detected by CT-scan preoperatively. Vascular anatomic variants were seen in the hepatic or renal vasculature in 8% and 33% of the potential donors respectively. By providing anatomical information to the surgeon, identifying relevant lesions not immediately visible intraoperatively and effectively identifying anomalies as contraindication to donation, this study also confirms the value of extended screening by use of a CT-scan.[13] In a retrospective study, Bozovic et al analyzed the outcome of extended imaging in 110 potential lung donors.[14] All chest radiograph and (in-)complete CT examinations were collected and reviewed from a donation perspective. In 13 potential donors a complete chest CT-scan was performed and in 29 CT examinations of other body parts included a part of the lungs as well. Compared with the chest radiograph group, more relevant information for lung transplantation was obtained in the CT group. These findings consisted of anatomic variations and organ size of importance for preoperative planning, pulmonary edema that may be suitable for ex vivo reconditioning, emphysema, aspiration, lymphadenopathy due to systemic disease, infections or malignancies. Even more important, pulmonary emboli and malignancies were identified before procurement, both absolute contraindications for lung donation. Some of the findings, such as sarcoidosis or anatomical

variants, could be of importance for heart transplantation as well. Based on all findings this study suggests a more prominent role of CT in the screening of deceased lung donors.[14]

In modern surgical practice, no major abdominal surgery is planned or performed without adequate radiologic imaging. The criteria and considerations for the screening of living donors is for a large part comparable with deceased donor screening.[4] Screening of living kidney donors with a CT-scan provides the surgeon with precise preoperative anatomy of the kidney, thus reducing the risks and complications associated with the procurement procedure and identifying preoperative factors that might even preclude living kidney donation.[15,16]

A possible disadvantage of applying more extensive imaging is the risk of incidental findings and false-positive errors, resulting in unnecessary cancelation of the donation procedure before the implication of the findings are properly assessed. In 2005 Beinfeld et al showed a sensitivity between 63% and 94% and a specificity between 63% and 93% to detect malignancies by nonenhanced CT-scans, resulting in false negative and false positive errors, respectively.[17] Because not every detected abnormality was sent for histopathologic evaluation in this study, no false negative or positive errors can be calculated. Development of uniform guidelines on how to deal with incidental findings in deceased donor screening is crucial. Nonetheless, the evolution and development of imaging modalities over the last couple of decades is extensive. Although image modalities are sophisticated, continuous improvement and refinement are expected to further diminishing the harmful effects and errors.

The risk of acute kidney failure as result of contrast-induced nephropathy could be addressed as a negative effect of extended donor imaging by enhanced CT-scans. However, recent studies in high risk patients (estimated Glomerular Filtration Rate 30-59 mL/min) showed no difference in contrast induced nephropathy between prophylactic and nonprophylactic hydrated group. None of the 660 patients required hemodialysis within 35 days after administration.[18] Donors eligible for kidney donation are patients with an adequate creatinine clearance, thus being less at risk compared with patients with a known kidney disease and impaired kidney function.[19] In the last years, a change in practice has occurred within the transplant community, resulting in an increase of using contrast media enhanced examinations.[20] Although caution is still advised, the effects are much less severe than was previously assumed.

In 2018, the reimbursement by health insurance companies in the Netherlands for chest radiograph, abdominal US, enhanced chest, and abdominal CT-scan was €42, €117, €183, and €194, respectively.[21] Calculating extra reimbursements for CT-scans of all reported donors results in ~€66 000 per year. Performing a CT-scan only in potential donors with age ≥45 years would cost €53 250 per year. In this donor cohort, the youngest donor diagnosed with a malignancy before or during procurement was 45 years old. We acknowledge these data consists of really small numbers and does not justify setting any age limit, but generally speaking older donors do have an increased risk on malignancy. If only focusing on malignancy screening, as performed in this study, it could be a possibility to only perform a CT-scan in older donors. If more information is needed on organ anatomy and vasculature, no age limit should be set. From an ethical perspective, if less invasive ways are available to assess donor suitability and organ quality, this cannot be ignored before organ procurement. Considering the poor prognosis of donor-derived malignancies, all efforts should be made to prevent this. Furthermore, by identifying possible contraindications before procurement, it shortens the duration of a donation procedure and hereby decreases the emotional burden for the relatives of the donor. With increasing healthcare expenses and shortage of specialized personnel, it is of utmost importance to utilize these scarce resources. If contraindications are known before procurement procedure, it could save energy, time and money by canceling the procurement procedure.

This study has a few limitations that need to be addressed. First, this retrospective Dutch donor cohort has many missing data on aberrant vascular anatomy and subsequent outcomes after procurement. Radiologic imaging was made for clinical purposes, often not evaluated for donor screening and subsequently not systematically reevaluated for anatomical and vascular variances. Although these data would be a valuable addition to this study, several previous studies have already addressed this topic and its clinical relevance on transplant outcome.[12–16] Second, there is a difference between the percentage of malignancies published in studies on deceased donor screening (7%–11%) and our cohort of Dutch reported donors.[12–14] Before reporting a potential donor to ET, the transplant coordinator performs an in depth analysis of the medical report of the potential donor. Donors with a known active malignancy were likely not to be reported to ET and thus excluded for donation. Previous studies on deceased donor screening included all brain dead patients admitted to the Intensive Care Unit, and this selection bias could partially explain the difference between the reported percentages. Another possible explanation for the difference in the percentage of malignancies detected in this study could be the result of kidney-only donation. During procurement of kidney-only donors, the thoracic organs are not exposed and evaluated. If not detected by chest radiograph, thoracic malignancies could be missed during procurement of the kidneys. Third and last, studies performed on CT-imaging in deceased donor screening lack a control group for comparison. No studies are available that compared conventional screening with CT-scans and the corresponding perioperative findings. Nonetheless, previous studies and our study showed relevant findings by a CT-scan, probably not detected by conventional imaging.[12–14] With increasing incidence of obesity in the general population, abdominal US screening capacities might be limited by donor weight.[22]

This study shows an increased detection of malignancies by CT-scan before organ procurement compared with the standard radiologic screening. If a CT-scan would have been made of all potential organ donors, 7 unnecessary procurements could be prevented in the Netherlands in the last 5 years. Another potential benefit could be the additional information on (aberrant) vasculature, organ size, and quality. In conclusion, screening by CT-scan results in an increased detection of malignancies before procurement by 30%, thereby increasing patient safety for the recipient and decreasing the risk on donor-derived malignancy.

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