EJT European Journal of Transplantation

2025;3:86-98
DOI: 10.57603/EJT-1801

ORGAN TRANSPLANTATION FROM DONORS WITH MALIGNANCIES: RISK ASSESSMENT AND CLINICAL OUTCOMES

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Summary

Background. Using organs from donors with malignant diseases raises concerns about transferring cancer to recipients, requiring careful risk assessment and monitoring. This paper aims to analyze the risk of cancer transmission in recipients of solid organ transplants (SOT) from donors with malignancies in Italy.

Methods. This is a retrospective review of all deceased donors and recipients of solid organ transplants recorded in the Italian Transplant Information System (SIT) between January 1, 2016, and December 31, 2024. Donor and recipient characteristics were examined, including the donor's oncological risk category, determined based on national guidelines and second opinions. Cancer transmission was classified as proven, probable, possible (or suspected), or excluded based on previous evidence.

Results. During the study period, 32,307 transplants were performed from 12,962 donors, with a total of 1,360 transplants (4.2%) from 747 donors (5.7%) who had at least one malignancy. In 712 donors (5.5%), the diagnosis was made during procurement, while in 34 donors (0.2%), it was discovered after transplantation, and in only one case (0.008%), it was an occult condition. Cancer transmission was confirmed in 4 recipients (0.03%), suspected in 44 (0.33%), and ruled out in 13 (0.1%). The per-transplant risk of cancer transmission was 0.012% for the overall cohort of recipients (4/32,307), and 0.29% among recipients of donors with malignancies (4/1,360). The fatality rate of donor-transmitted cancers was 0.006% (2/32,307) in the overall transplant cohort, and 0.14% (2/1,360) in the group of recipients with donors who had malignancies.

Conclusions. With proper risk assessment, second-opinion consultation, and post-transplant surveillance, organs from donors with malignancies can be used safely, expanding the donor pool without significantly increasing recipient cancer risk. Vigilant national reporting and standardized protocols are essential for reducing transmission risk.

Key words: donation, transplantation, malignancy, safety, risk

Abbreviations

CCRC: clear-cell renal carcinoma
CNS: central nervous system
CNT: Italian National Transplant Center
CT: computed tomography
dCD: Donation after Circulatory Death

Received: November 7, 2025
Accepted: November 14, 2025

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How to cite this article: Peritore D, Testa S, Donadio R, et al. Organ transplantation from donors with malignancies: risk assessment and clinical outcomes. EJT 2025;3:86-98. https://doi.org/10.57603/EJT-1801

DBD: donation after brain death
DOC: donor with occult cancer
DTD: donor transmitted cancer
ECD: extended criteria donor
EDQM: Council of Europe Guide to the Quality and Safety of Organs for Transplantation
HLA: human leukocyte antigen
ITT: Intention to treat
NHSBT: National Health Service Blood and Transplant
SIT: National Transplant Information System
PRCC: papillary renal cell carcinoma
UNOS: United Network for Organ Sharing
WHO: World Health Organization

INTRODUCTION

Organ transplantation is one of the most outstanding achievements in modern medicine, providing survival and a better quality of life for patients with end-stage organ failure. However, the ongoing gap between organ demand and supply remains a global challenge, resulting in long waiting times and deaths on waiting lists-issues that affect all types of organs to some extent. In Italy in 2024, 4,276 transplants were performed, while the number of patients on the waiting list (ITT, intention-to-treat) reached 13,306. Mortality rates varied from 1% to 6%, with an average waiting time of 4 to 20 months depending on the organ type (Tab. I).

This historical and global imbalance has driven ongoing efforts to develop strategies to increase organ supply-by expanding the number of donors (such as through DCD, Donation after Brain Death, or ECD, Extended Criteria Donors) and by improving the efficiency of organ use (for example, through machine perfusion systems or other static cold storage methods). Specifically, to raise the total number of donors, the age limit for donation has been gradually raised, and donors with early-stage cancer are now also considered. Since tumour incidence increases with age, implementing more refined donor screening systems has become essential. These systems can utilize advanced diagnostic tools to exclude transmissible malignancies while considering the practical feasibility and time constraints of the donation process. However, some neoplastic diseases may bypass detection during donor evaluations and are only discovered later, sometimes during organ retrieval, after transplantation, or postmortem. These rare cases have provided valuable insights into the biological behavior of specific tumours in transplant recipients under immunosuppressive therapy, thereby increasing confidence in the potential use of organs from donors with certain malignancies.

In this context, the potential transmission of neoplastic disease during organ transplantation can be either expected to varying degrees or accidental (i.e., unintentional events). The more urgent the need for transplantation in a particular recipient, the greater the risk that may be justifiably accepted; therefore, risk assessment must consider both donor- and recipient-related factors [1].

Historically, any neoplastic disease was considered an absolute contraindication to organ donation due to the risk of donor-transmitted cancer (DTC). However, evolving evidence has demonstrated that, under certain conditions, the transmission risk is minimal and manageable [2,3]. Current recommendations – based on registries such as Eurotransplant, the National Health Service and Blood Transplant (NHSBT), and the United Network for Organ Sharing (UNOS) – suggest that selected donors with a history of low-grade, fully treated tumours or those with long-term remission may be considered for donation with appropriate risk stratification [4]. The Italian National Transplant Center (CNT) and regional transplant networks have increasingly adopted protocols that incorporate oncological risk assessment into the donor selection process. This approach is supported by multidisciplinary decision-making processes, which involve transplant surgeons, pathologists, oncologists, hematologists, and coordinators, to maintain a balance between donor utilization and recipient safety [5].

This study retrospectively examines Italy's national experience with organ transplantation from donors with malignancies between 2016 and 2024. It describes epidemiological features, oncological profiles, recipient outcomes, and — among donors with potentially transmissible

Table I. Transplants, waiting lists, average waiting times, and mortality in Italy in 2024.

Organ	Transplants	Waiting list (ITT)	Average waiting time for transplant (months)	Waiting list mortality
Heart	413	1,218	10.7	3.9%
Lung	174	485	8.4	6%
Liver	1,691	2,768	3.7	3.3%
Kidney	2,031	8,571	20.2	1.9%
Pancreas	35	264	7.6	0.8%
Total	**4,276**	**13,306**	**12.0**	

malignant neoplasms — investigates any cases of tumour transmission to recipients, both when organ use was intentional (based on a low estimated risk) and when malignancy was incidentally discovered after transplantation. Additionally, it compares Italian data with international literature to evaluate similarities and differences in donor management and follow-up policies [6,7].

MATERIALS AND METHODS

Donor risk stratification according to National guidelines

In Italy, the first national guidelines for donor risk assessment were issued in 2001. These guidelines, developed by the CNT in collaboration with experts in infectious, neoplastic, hematological, and immunological diseases, are regularly updated. They provide recommendations on diagnostic tests to be performed on donors – helping local procurement coordinators – and on the use of donors with potentially transmissible diseases, thereby guiding transplant centers in their clinical decisions.

The Italian guidelines, along with the Council of Europe Guide to the Quality and Safety of Organs for Transplantation (EDQM, 2023) and international registries (Eurotransplant, NHSBT, UNOS) [8], categorize the risk of transmitting neoplastic disease into several levels, considering not only the donor's condition but also the recipient's clinical status. This approach promotes personalized decision-making regarding the use of donor organs [9].

A donor is considered to be at standard risk when their evaluation shows no factors that could lead to disease transmission to the recipient. Conversely, if the evaluation identifies factors indicating a risk of disease transmission that outweighs the potential benefits of the transplant, the donor is deemed unsuitable due to an unacceptable level of risk. The non-standard risk category includes two subgroups: non-standard, negligible risk donors who have factors that might lead to disease transmission, but the diseases are either easily treatable if transmitted or do not significantly affect graft or patient survival compared with standard-risk donors. Non-standard, acceptable risk donors are those with factors that indicate a potential disease transmission risk, requiring specific restrictions or recommendations. In such cases, organ use may be justified if the recipient's clinical condition or the ability to effectively manage a potential transmission makes the risk–benefit ratio favorable.

From an oncological perspective, within solid organ transplantation, the acceptable risk category can be further divided into acceptable-low risk (< 4% risk of transmission): donors with low-grade malignant neoplasms with limited potential for local or distant recurrence after curative surgery or five years of documented and uneventful follow-up. Acceptable-high risk (4-10% risk of transmission): donors with high-grade malignant tumours, potentially metastatic or diagnosed at an advanced stage, where – even after radical treatment – the likelihood of recurrence or progression remains high. In such cases, a disease-free period of at least 5-10 years, accompanied by written documentation of follow-up, is required. Organs from these donors may be considered for recipients in severe clinical conditions or those with an urgent need, provided the clinical-surgical team justifies the potential benefit despite the increased risk of transmission.

For any acceptable-risk donor, regardless of the recipient's condition, organs are only used after explicit multidisciplinary evaluation, and the use of the organ requires informed consent. At the time of waiting list registration, recipients must sign a dedicated information form acknowledging this possibility, and a second, case-specific informed consent must be obtained immediately before transplantation.

In addition to the national guidelines, the Italian Transplant Network has established a 24/7 national expert second-opinion system, which provides case-specific consultations for complex or unlisted conditions, ensuring consistent and safe donor management across transplant centers [10]. The goal is to validate risk assessments, confirm histopathological findings, and suggest additional investigations – such as morphological and/or immunophenotypic analysis of bone marrow and/or peripheral blood – that could clarify the diagnostic question, while ensuring national consistency in donor eligibility decisions. Donors are accepted only if the malignancy is considered standard risk or non-standard but acceptable, based on histological grade, remission interval, and the absence of metastasis or systemic involvement [11]

Study design and population

A retrospective observational study was conducted by analyzing all donors with a history or current condition of malignant neoplasia from January 1, 2016, to December 31, 2024, using data collected through the mandatory reporting forms of the National Transplant Information System (SIT). Each tumour was categorized according to primary site and histological diagnosis based on the World Health Organization (WHO) classification.

For the current study, three donor categories were identified: 1) those whose malignancy diagnosis was available during the procurement process; 2) incidental cases where the donor's malignancy was diagnosed after transplantation of one of the procured organs; and 3) donors with occult cancer (DOC). The collected donors' characteristics included date of donation, sex, age, time of diagnosis, past versus active disease, organ/site, histology (if available), and the number and types of transplanted organs.

The risk classification, according to national guidelines, and the phase of the donation process at which it was assigned, were also recorded. The frequency of second-opinion consultations during the risk assessment process was also analyzed. For donors with more than one malignancy, the category (i.e., diagnosis during procurement versus incidental) and risk strata were based on the more aggressive tumour. The collected recipient characteristics included sex and age, native disease, date of transplantation, and follow-up data, such as graft function status and occurrence of post-transplant malignancies. Based on available donor, tumour, and recipient data, transmission was defined according to Ison et al. into proven, probable, possible (suspected), and excluded [12].

Data analysis

Data was collected from the SIT, Italy's national IT infrastructure established under Italian Law No. 91 (April 1, 1999), as part of the National Health Information System. The SIT manages comprehensive data on organ and tissue donation and transplantation activities across the country, ensuring traceability and transparency throughout the donation, procurement, and transplantation processes. It also records patient waiting lists, consent declarations for post-mortem donation, activity reports on donation and transplantation, and post-transplant follow-up data for all recipients, including deaths caused by brain injury. Additionally, SIT gathers and monitors reports of serious adverse events and reactions related to organs and tissues.

The National Institute of Health validated all data collected during the creation of the national database. These data were then, where necessary, first classified, then organized and processed in a spreadsheet, and reviewed retrospectively using Microsoft Excel, version 365 (Microsoft Corporation, Redmond, WA, USA) with multivariable pivot tables. A descriptive analysis was performed to explore the data's distribution and the relationships between variables through graphs and summary statistics (mean, median, range). No inferential statistical analysis was conducted, given that the study was purely descriptive.

RESULTS

Transmission category

Between 2016 and 2024, a total of 12,962 donors were used, with 882 (6.8%) having a history of current or previous neoplastic disease, 34 (0.2%) donors with incidental post-procurement diagnosis, and one (0.008%) DOC.

Donor with a history or current malignancy

A total of 900 neoplastic lesions were identified; 725 (80.6%) were malignant or low-grade malignancies, 81 (9.0%) were benign, and 94 (10.4%) lacked a specific histological diagnosis. These 725 malignancies occurred in 712 donors (5.5%), with 699 donors (5.4%) having a single malignancy and 13 donors (0.1%) having two. In four of these cases, one malignancy was diagnosed incidentally after procurement. Out of 712 donors with malignancies, 415 (58.3%) were male and 297 (41.7%) were female. Donor ages ranged from 4 to 97 years, with a median age of 73 years. The age distribution was as follows: 0-17 years (3 donors, 0.4%), 18-39 years (22, 3.1%), 40-59 years (107, 15%), 60-79 years (369, 51.8%), and 80 years or older (211, 29.6%). During the study period, the average annual percentage of donors with a malignant neoplasm was 5.49% (range, 4.62-6.26%). Out of 725 malignancies, 223 (30.8%) were active and identified during donor procurement, while 502 (69.2%) were pre-existing.

Sites and types of donor malignancies

Most malignant neoplasms were from the male reproductive system (129, 18.1%), followed by the urinary system (127, 17.8%), integumentary system (117, 16.4%), central nervous system (CNS) (106, 14.9%), gastrointestinal tract (94, 13.2%), female reproductive system (74, 10.4%), endocrine system (43, 6%), hematopoietic system (11, 1.5%), respiratory system (9, 1.3%), and musculoskeletal system (2, 0.3%). The prostate was the most frequently affected organ, accounting for over 17% of all malignancies and nearly all lesions of the male reproductive tract (94.6%). The urinary bladder was the next most common site, with 65 cases (9.1%), followed by the kidney, with 59 cases (8.3%).

Renal tumours were primarily clear-cell carcinomas (CCRC) in 39 cases (5.5% of total neoplasms; 66.1% of renal tumours) and papillary carcinomas (PRCC) in 13 cases (1.83% of total neoplasms; 22% of renal tumours).

All malignancies of the integumentary system were cutaneous; 83 (70.9%) were basal cell carcinomas, 27 (23.07%) were squamous cell carcinomas, and 7 (6%) were melanomas.

In the CNS, meningioma was the most common lesion, accounting for 58 cases (54.72%), followed by glial tumours, primarily astrocytomas (8, 7.55%), oligodendrogliomas (8, 7.55%), and glioblastomas (9, 8.49%).

The gastrointestinal system accounted for 13.2% of all malignancies, with the main sites being the colon (51.1%), stomach (20.2%), and pancreas (11.7%). There were nine intraductal papillary mucinous neoplasms (IPMNs), representing 1.3% of all tumours and 81.82% of pancreatic malignancies.

Within the female reproductive system, the most affected organs were the uterus (50% of system-specific and 5.2% of total tumours) and the ovary (40.5% and 4.2%, respectively).

Thyroid carcinomas (35 cases, i.e., papillary in 28, follicular in 2, mixed in 5) accounted for 81.4% of endocrine tumours and 4.9% of total malignancies.
Among hematological malignancies, previously diagnosed lymphomas with a remitting interval accounted for the majority of cases (7 cases; 63.64% of hematological diseases; 0.98% of all cases). Details by anatomical site are summarized in Table II.

Risk assessment and second-opinion consultation

Among the 712 donors with malignant neoplasms, 23 (3.2%) were classified as standard risk, 298 (41.9%) as non-standard negligible risk, and 391 (54.9%) as non-standard acceptable risk. For the 13 donors with two malignancies, the risk classification was based on the more aggressive tumour regardless of the time between diagnosis and organ donation. A second-opinion consultation was requested in 611 cases (85.8%), most often resulting in an "acceptable non-standard risk" classification (345 cases, 56.5%). Table III displays the distribution of risk profiles and second-opinion consultations by tumour site.

Transplant procedures, recipient demographics, and follow-up

During the study period, 32,307 patients underwent transplants, with 1,284 (4%) receiving a total of 1,382 organs from donors with a history of or active malignancies. The most commonly transplanted organs were the liver (669, 51.7%) and the kidney (532, 41.1%), followed by the heart (61, 4.7%) and the lungs (27, 2.1%). Transplant procedures categorized by year and organ type are summarized in Table IV. Of the 1,284 recipients, 920 (71.7%) were male and 364 (28.3%) were female, with a median age of 56.8 years (range, 6-79 years). The age distribution was as follows: 0-17 years (7 recipients, 0.55%), 18-39 years (79, 6.2%), 40–59 years (631, 49.1%), and 60-79 years (567, 44.2%). Follow-up data were available for 1,143 patients (89.02%), with an average follow-up duration of 1,219.5 days (range, 0–3,364 days). Missing data in 150 cases resulted from incomplete SIT reporting or loss to follow-up.
Among those with available follow-up, 971 recipients (8%) were alive, and 172 (15.0%) had died. Graft function was known for 1,121 patients (98.08%): 1,020 (91%) had a functioning graft, while 101 (9%) experienced graft failure.
Among the 172 deaths, infections were the most common cause (75, 43.6%), followed by cardiovascular complications (27, 15.70%). The main causes of graft failure were hepatic complications (30, 29.7%), vascular events (14, 13.9%), and chronic rejection (9, 8.9%).

Development of post-transplant cancer

Out of 1,284 patients who received organs from donors with a history of or active malignancies, 57 (4.4%) developed cancers during follow-up after the transplant. Based on the clinical histories of donors and recipients, cancer transmission was excluded in 13 cases (1%), including 9 post-transplant recurrences, 2 Kaposi sarcomas, and 2 Epstein-Barr virus (EBV)-related lymphoproliferative diseases. The average time between transplantation and diagnosis of cancer was 656 days. No two recipients received grafts from the same donor, and none of the other recipients from these donors developed malignancies.
Donor-related transmission was suspected in 44 patients (3.4%), which included 19 cases of skin cancer (8 SCCs, 7 basal cell carcinomas, 2 melanomas, one Bowen disease, and one not otherwise specified); 8 cases of urogenital malignancies (4 bladder cancers, 3 renal, and one ureteral); 6 cases of gastrointestinal malignancies (hepatocarcinoma, biliary tract, colon, pancreatic adenocarcinoma, bowel, and not otherwise specified in one case each); 4 cases of respiratory malignancies (2 lung, one mesothelioma, and one not otherwise specified); 3 lymphoproliferative cases (2 lymphomas and one myeloma); 2 thymic malignancies, and one case each of sarcoma and malignancy of unspecified site. A total of 15 patients with malignancies (1.1%) died: 7 (0.5%) in the unsuspected donor-related transmission group (5 recurrences and 2 lymphoproliferative diseases) and 8 (0.6%) in the suspected group (2 SSCs, bladder, ureter, lung, mesothelioma, colon, and thymus in one patient each).
The average interval between transplantation and diagnosis was 876 days. In 8 cases, the tumour developed in the same anatomical system as the donor's malignancy: 5 cutaneous and 3 urinary (recipient bladder tumour with donor prostate, bladder, or kidney cancer in one case each).

Incidental cases and donors with occult cancers

In 34 donors, a malignancy was detected after procurement, usually once at least one organ had been transplanted. Only one donor with hidden cancer was reported because the recipients of one liver and two kidneys developed lymphoma in the transplanted organs, despite no evidence of malignancy in the donor. Histology and the timing of onset after transplantation confirmed the occult transmission. Of the 35 donors included in the serious adverse event/reaction registry, malignancies involved the hematopoietic system (8 lymphomas), endocrine system (1 adrenal, 3 thyroid), gastrointestinal tract (10: 1 hepatic, 6 biliary/extrahepatic ducts or gallbladder, 2 intestinal, 1 pancreatic), respiratory system (4, all pulmonary), male reproductive system (3, all prostatic), CNS (1 medulloblastoma, WHO grade IV), skin (2), and urinary tract (7: 5 renal, 1 bladder, 1 ureter).
From these donors, 77 organs were transplanted into 76 recipients (5 hearts, 3 lungs, 36 livers, 31 single kidneys, and 1 dual kidney). Follow-up was available for all recipients, and the data are summarized in Table V.

Table II. Site and type of neoplasia.

Site and type of neoplasia	No	% of system neoplasia	% of total neoplasia
Male reproductive system			
Prostate	122	94.6	17.1
Testis	7	5.4	1
Subtotal	129	100	**18.1**
Urinary system			
Bladder	65	51.2	9.1
Kidney	59	46.5	8.3
Ureter	1	0.8	0.1
Urethra	1	0.8	0.1
Urothelium	1	0.8	0.1
Subtotal	127	100	**17.8**
Integumentary system			
Skin	117	100	16.4
Subtotal	117	100	**16.4**
Central nervous system (CNS)			
CNS	106	100	14.9
Subtotal	106	100	**14.9**
Gastrointestinal system			
Colon	48	51.1	6.7
Stomach	19	20.2	2.7
Pancreas	11	11.7	1.5
Oral cavity	4	4.3	0.6
Anus	3	3.2	0.4
Oesophagus	3	3.2	0.4
Rectum	3	3.2	0.4
Small intestine	3	3.2	0.4
Subtotal	94	100	**13.2**
Female reproductive system			
Uterus	37	50.0	5.2
Breast	30	40.5	4.2
Ovary	7	9.5	1
Subtotal	74	100	**10.4**
Haematopoietic system			
Hodgkin lymphoma	4	36.4	0.6
Chronic myeloproliferative disorder	4	36.4	0.6
Lymphoma (histological subtype not specified)	2	18.2	0.3
Non-Hodgkin lymphoma	1	9.1	0.1
Subtotal	11	100	**1.5**
Endocrine system			
Thyroid	35	81.4	4.9
Adrenal gland	6	14	0.8
Thymus	2	4.7	0.3
	43	100	**6**
Respiratory system			
Larynx and epiglottis	4	44.4	0.6
Skin	2	22.2	0.3
Lung	2	22.2	0.3

Table II. *continues.*

Site and type of neoplasia	No	% of system neoplasia	% of total neoplasia
Nasopharynx	1	11.1	0.1
Subtotal	9	100	**1.3**
Musculoskeletal system			
Bone	2	100	0.3
Subtotal	2	100	**0.3**
Total	**712**		**100**

Table III. Risk profile and second opinion.

Site of neoplasia	Risk profile						Total, site (n, %)	Total, second opinion (n)
	Standard (n, %)	Including second opinion (n)	Non standard, negligible (n, %)	Including second opinion (n)	Non standard, acceptable (n, %)	Including second opinion (n)		
Male reproductive system	2 (0.3)	1	62 (8.7)	56	65 (9.1)	57	129 (18.1)	114
Female reproductive system	2 (0.3)	1	20 (2.8)	19	52 (7.3)	51	74 (10.4)	71
Haematopoietic system	0 (0)		3 (0.4)	3	8 (1.1)	1	11 (1.5)	4
Endocrine system	2 (0.3)	1	13 (1.8)	12	28 (3.9)	25	43 (6)	38
Gastrointestinal system	3 (0.4)	3	24 (3.4)	23	67 (9.4)	62	94 (13.2)	88
Musculoskeletal system	1 (0.1)		0 (0)		1 (0.1)	1	2 (0.3)	1
Respiratory system	0 (0)		3 (0.4)	3	6 (0.8)	6	9 (1.3)	9
Central nervous system (CNS)	4 (0.6)	2	43 (6)	30	59 (8.3)	52	106 (14.9)	84
Tegumentary system	2 (0.3)		78 (11)	57	37 (5.2)	29	117 (16.4)	86
Urinary system	7 (1)	6	52 (7.3)	49	68 (9.6)	61	127 (17.8)	116
Total, risk (N, %)	**23 (3.2)**	**14**	**298 (41.9)**	**252**	**391 (54.9)**	**345**	**712 (100.0)**	**611**

Two liver recipients died from donor-transmitted malignancies: one from a donor with cholangiocarcinoma and another from a donor with occult lymphoma. Five other liver recipients, who received organs from donors with prostatic adenocarcinoma, hepatocellular carcinoma, pulmonary carcinoma with nodal metastases, or gallbladder carcinoma, underwent re-transplantation within days and have not developed malignancies so far. Four kidney recipients (from donors with urothelial carcinoma, lymphoma, or ureteral carcinoma) had graft explantation; two were subsequently retransplanted, and none have experienced neoplastic recurrence. One kidney recipient with papillary carcinoma diagnosed three months post-transplant underwent resection and remains disease-free at the latest follow-up. No additional evidence of donor-derived tumour transmission was observed among other recipients of organs from these donors. The results are summarized in Table VI.

Overall

Among the 32,307 recipients overall, 4 developed malignancies of donor origin. The risk of cancer transmission per transplant was 0.012% in the entire group, and 0.29% (4 out of 1,360) among recipients who received grafts from donors with malignancies. The fatality rate of donor-transmitted cancers was 0.006% in the overall cohort (4 out of 32,307) and 0.14% among recipients of grafts from donors with malignancies (2 out of 1,360).

Table IV. Transplants from donors with malignant neoplasms.

Year	Heart	Liver	Liver–pancreas–double lung	Double lung	Kidney	Kidney-liver	Kidney-pancreas	Double kidney	Total
2016	4	58		4	52		1	11	130
2017	4	79		2	75	1	1	7	169
2018	7	67		5	48			6	133
2019	10	68		4	46			4	132
2020	7	64			50	1		2	124
2021	9	80	1	2	40			10	142
2022	4	86		2	54			11	157
2023	6	86		4	45	1		5	147
2024	10	76		3	53	1	1	6	150
Total	**61**	**664**	**1**	**26**	**463**	**4**	**3**	**62**	**1,284**

DISCUSSION

Using older donors is linked to a higher chance of undetected cancers and, therefore, an increased risk of transmitting neoplastic disease from the donor. This finding aligns with previous reports on donor-transmitted cancers and supports the broader idea of immunosenescence, which connects aging to decreased immune surveillance and the development of tumours [13,14].

Compared to 2015, the average age of potential donors in Italy – at the time of death determination, procurement, effective donors, and utilized donors – has gradually increased from 59.5, 59.9, 59.2, and 58.5 years to 62, 62.9, 62.8, and 62.6 years, respectively. The distribution and median/mean ages for DBD and DCD donors in 2024 are shown in Table VII. In 2024, 51.3% of death determinations and 53.2% of utilized donors were aged 65 or older, a demographic shift that naturally increases the likelihood of latent malignancy. In our cohort, the overall incidence of malignancy among utilized donors was 5.49%. Notably, 81.46% of donors diagnosed with malignancies were aged 65 or older. These figures are like those reported in other European countries, supporting the idea that malignancy prevalence in donors is related to demographic aging and the increasing inclusion of extended-criteria donors. Although direct comparison is limited by variations in donor selection criteria and registry definitions, the overall trend parallels that observed across other European programmes.

The advanced age of donors warrants a comprehensive, time-sensitive, multidisciplinary assessment strategy that encompasses the entire donation process. This demographic evolution underscores the need for early multidisciplinary involvement to contextualise age-related oncological risk rather than to exclude elderly donors outright. Semiotically, donor assessment mirrors a comprehensive clinical work-up: structured history taking, physical examination, imaging, intraoperative inspection and palpation at the procurement table, and, when indicated, histopathological evaluation. History should investigate any past or current neoplastic disease using all available sources (primary care physician, family members, caregivers, medical records). When a hematological disorder is reported in the medical history or when laboratory findings suggest such a condition, morphological and/or immunophenotypic analyses of bone marrow and/or peripheral blood should be performed. In cases where a remote solid-organ malignancy is reported, critical factors to assess include the completeness of previous surgical treatment, pathological staging, documented and regular follow-up, and any clinical or biochemical evidence of recurrence.

A minimum disease-free interval of five years after curative surgery is recommended for most malignancies; exceptions include breast cancer and melanoma, for which more than 15-20 years should be considered, along with factors such as histotype, stage, and predictive markers for breast cancer.

Physical examination should include inspection for signs of transmissible disease, with particular attention to skin scars or lesions (especially pigmented lesions). Palpation should focus on the abdomen, thyroid, breasts, testes, and superficial lymph node stations, with digital rectal examination advised for donors over 50 years old. Imaging typically involves chest X-ray and abdominal ultrasonography, although contrast-enhanced CT is now performed in about 90% of donors.

During surgery, the surgeon must carefully examine and palpate any previously identified masses using intraoperative imaging techniques such as Doppler ultrasound or X-ray, as well as frozen-section analysis when needed. Two main points in the donation process typically require a second opinion at the national level: (i) during procurement planning when there is a history of malignancy; and (ii) at organ retrieval when a suspicious lesion is

Table V. Incidents and transplanted organs.

Site		No. of donors	No. of transplanted patients	
System/apparatus	Organ			
Haematopoietic				
Lymphoma		8	Liver	8
			Kidney	5
Endocrine				
Adrenal gland		1	Liver	1
Thyroid		3	Heart	1
			Lung	2
			Liver	2
			Kidney	4
Gastrointestinal				
Liver/Intrahepatic bile ducts		1	Liver	1
Extrahepatic bile ducts/gallbladder		6	Liver	6
			Kidney	3
Intestine		2	Heart	1
			Kidney	2
Pancreas		1	Liver	1
			Kidney	2
Respiratory				
Lung		4	Liver	4
			Kidney	2
Male reproductive system				
Prostate		3	Liver	3
			Kidney	6
CNS				
Brain (medulloblastoma, grade IV WHO)		1	Liver	1
Tegumentary				
Skin (Melanoma in situ)		2	Liver	2
			Kidney	2
Urinary				
Kidney		5	Heart	3
			Lung	1
			Liver	5
			Kidney	4
Ureter		1	Liver	1
			Kidney	1
Bladder		1	Liver	1
			Kidney	1
Total		**39**		**76**

newly discovered and a frozen-section diagnosis is considered. Whenever possible, these situations should be handled separately, following European guidance, which clearly differentiates between malignancy diagnosed at

Table VI. Incidents and transmissions.

Case n°	Year	Donor neoplasia	Organ transplanted	Corrective actions	Outcome and year last-FUP
1	2017	Prostate adenocarcinoma (Gleason 9)	Liver	Re-OLT	No neoplasia - 2021
2	2017	Cholangiocarcinoma	Liver	Monitoring	Exitus/transmission - 2018
3	2017	Hepatocellular carcinoma	Liver	Re-OLT	No neoplasia - 2023
4	2019	Infiltrating urothelial carcinoma	Right kidney	Explant - ReTx 2019	No neoplasia - 2025
5	2019	Renal carcinoma (Papillary type II)	Right kidney	Resection	No neoplasia - 2020
6	2020	Pulmonary carcinoma with lymph node metastasis	Liver	Re-OLT 2020	No neoplasia - 2025
7	2020	Lymphoma detected in recipients	Liver	Monitoring	Exitus/transmission - 2021
			Left kidney	Explant - ReTx 2023	No neoplasia 2024
			Right kidney	Explant	No neoplasia 2025
8	2022	Gallbladder carcinoma	Liver	Re-OLT 2022	No neoplasia - 2025
9	2024	Gallbladder adenocarcinoma	Liver	Re-OLT	No neoplasia - 2025
10	2024	Ureteral carcinoma	Right kidney	Explant	No neoplasia - 2025

Table VII. Distribution, mean, and median age of donors after brain death (DBD) and donors fater cardiocirculatory death (DCD) in Italy in 2024.

Age range (years)	AM	Oppositions	Procured	Real	Effective	Utilized
0-17	75 (2.4%)	21 (2.3%)	45 (2.3%)	41 (2.2%)	42 (2.3%)	42 (2.4%)
18-49	582 (18.4%)	200 (22.1%)	322 (16.6%)	312 (16.7%)	305 (17%)	300 (17.3%)
50-64	883 (27.9%)	252 (27.8%)	540 (27.8%)	509 (27.2%)	484 (27%)	468 (27.1%)
65-79	1,165 (36.8%)	311 (34.3%)	743 (38.3%)	725 (38.8%)	701 (39.1%)	670 (38.7%)
⩾ 80	460 (14.5%)	123 (13.6%)	289 (14.9%)	283 (15.1%)	263 (14.7%)	250 (14.5%)
Total	**3,165**	**907**	**1,939**	**1,870**	**1,795**	**1,730**
Median	65	63	66	66	66	66
Mean	62	60.2	62,9	63,1	62,8	62,6
Range	0-124	0-94	0-98	0-98	0-98	0-98
p25	53	50	54	54	54	54
p75	76	75	76	76	76	76

procurement and a remote history of malignancy. In the first case, thorough examination of any lesion suspected of malignancy based on clinical or imaging findings is crucial, and histological confirmation should be sought during the procedure as logistics permit.

In our previous national analysis [15], 415 out of 11,271 (3.68%) donors had malignancy, compared to 712 out of 12,962 (5.49%) in the current series – an increase that likely reflects not only a higher background incidence but also improved diagnostic detection and a broader, evidence-based use of donors with selected malignant neoplasms [16]. This trend likely reflects both demographic ageing and the intentional expansion of donor eligibility under controlled risk frameworks, illustrating the progressive acceptance of "acceptable risk" donors within the Italian system. Importantly, more than 85% of donors underwent a formal second opinion process, underscoring the systematic adherence to national governance policies.

The predominance of prostate, bladder, and skin cancers reflects national oncological patterns and the age profile of the donor population. This distribution mirrors the epidemiological landscape of the general population and highlights the importance of tailored assessment for these tumour types, which now account for most neoplastic findings in donors over 65. Donor age and malignancy

prevalence mirror European patterns, reflecting demographic ageing and broader donor acceptance. The Italian experience demonstrates that, through multidisciplinary evaluation and strict histopathological validation, it is possible to safely use organs from selected donors previously considered ineligible [17].

The national data align with findings reported by Greenhall et al., who described minimal transmission risk in donors with central nervous system tumours, if metastases are excluded and craniotomy has not breached the tumour capsule [18]. Similarly, Turra et al. and Barreiros et al. emphasized that donors with treated or localized malignancies may be accepted when rigorous screening protocols are applied, resulting in negligible risk to recipients [19,20].

Despite thorough screening, 35 out of 12,962 (0.27%) donors had malignancies discovered late, meaning after at least one organ had already been transplanted. This remaining miss rate probably shows the limits of current diagnostic methods. This residual miss rate likely represents the inherent limitation of imaging-based screening rather than procedural oversight, underscoring the balance between diagnostic sensitivity and operational feasibility. While universal whole-body CT could improve the detection of small lesions, imaging often cannot fully assess biological behavior, necessitating frozen section for tissue diagnosis. However, frozen section may be inconclusive for certain lesions (e.g., small or poorly represented lesions, biliary strictures, low-cellularity tumours), which could lead to excluding otherwise transplantable donors. Performing early back-table examination immediately after retrieval can reduce the number of malignancies first identified at the hepatic hilum/bile ducts during vascular preparation or within the kidney after removing perinephric fat.

Even if detected late, prompt recognition enables corrective actions, including graft explantation (in nine recipients of our cohort) and increased surveillance of co-recipients, to facilitate earlier diagnosis and treatment of donor-transmitted malignancies. In our series, two liver recipients died from transmitted tumours originating from donors with incidentally discovered malignancies, representing 0.006% of all 32,307 transplants during the study period. These two cases of confirmed DTC represent a transmission rate of 0.016%, consistent with the international range reported in large multicentre analyses and registry-based studies, where donor-transmitted cancer occurs in approximately 0.01-0.03% of transplant recipients. [21,22]. Finally, even long after transplantation, the development of *de novo* recipient malignancy should trigger a national-level case review to identify potential donor-derived events and institute targeted follow-up for co-recipients from the same donor.

This analysis is limited by incomplete or sparsely filled follow-up fields within the SIT for some recipients – except for cases linked to incidentally discovered donor malignancies, where the CNT, through transplant centers, performs enhanced monitoring beyond routine SIT reporting. Another limitation is the imprecise classification of certain recipient tumours. Additionally, confirming donor origin for late-onset de novo neoplasms can be challenging without specific investigative techniques (e.g., chimerism studies, donor–recipient HLA or sex-chromosome mismatch analysis, or molecular profiling) that require access to donor tissue.

Taken together, these findings delineate a framework where oncological vigilance and ethical pragmatism coexist, paving the way for a broader yet safe donor inclusion.

CONCLUSIONS

In conclusion, a growing body of evidence has focused on the oncological safety of organ transplantation from donors with a history of current or previous malignancies. Recent studies, particularly from European and international registries, have demonstrated that when donor selection is guided by rigorous histopathological assessment and multidisciplinary evaluation, the actual rate of donor-transmitted cancers remains exceedingly low, often below 0.02%. Moreover, emerging data support the potential reclassification of selected neoplasms, previously considered high-risk, into acceptable categories for donation under controlled conditions. This evolving evidence base underscores the need for harmonized risk stratification protocols and for continuous post-transplant surveillance, ensuring both graft safety and optimal organ utilization.

This study represents one of the largest national analyses of organ donation from donors with a history of neoplasia, providing a comprehensive overview of donor characteristics, tumour types, and post-transplant outcomes over a nine-year period. The findings confirm that, when supported by rigorous risk stratification and adherence to national guidelines, organs from donors with selected malignancies can be used safely, thereby expanding the donor pool without significantly increasing the risk of tumour transmission [23].

This national analysis confirms that organs from donors with selected malignancies can be safely used when managed within a structured governance framework and supported by rigorous histopathological validation. The findings demonstrate that donor malignancy, in isolation, should not be considered an absolute contraindication to donation. Instead, it should be evaluated through a transparent, multidisciplinary process that ensures both clinical safety and optimal organ utilisation.

The Italian experience illustrates the effectiveness of a centralised assessment model led by the Centro Nazionale Trapianti, which standardises second-opinion procedures

and guarantees consistency across transplant centres. This approach validates the principle of acceptable risk, now recognised as a cornerstone of modern transplant ethics — balancing oncological caution with the ethical imperative to expand organ availability for patients in need. As emphasised by Desai et al. [24], the residual risk of cancer transmission is unavoidable but can be responsibly managed within structured governance frameworks.

Future perspectives point towards deeper European harmonisation of donor evaluation frameworks and enhanced data sharing across registries such as Eurotransplant, Scandiatransplant, and NHSBT. Integrating molecular tumour profiling, donor-derived cell-free DNA, and AI-based predictive models into donor assessment workflows will refine risk stratification and further reduce the already minimal likelihood of transmission.

In summary, transplantation from donors with selected malignancies represents an ethical and scientific evolution in the field: from categorical exclusion to informed acceptance. By combining rigorous pathology, transparent governance, and continuous international collaboration, the transplant community is redefining the boundaries of safety and broadening the horizon of therapeutic opportunity.

Acknowledgements

The authors thank the national second-opinion panel for their contribution to donor malignancy assessment, in particular the pathologists Antonia D'Errico (Anatomical Pathology Unit, Sant'Orsola-Malpighi University Hospital, Bologna), Albino Eccher (Department of Pathology and Diagnostics, University Hospital of Verona), Claudia Mescoli (Surgical Pathology Unit, University-Hospital of Padua), Luca Novelli (Pathology Unit, Careggi University Hospital, Florence), Debora Malvi (Pathology Unit, Sant'Orsola-Malpighi University Hospital, Bologna) and the haematologists Corrado Girmenia (Department of Hematology, Policlinico Umberto I, Sapienza University of Rome), Anna Paola Iori (Department of Hematology, Policlinico Umberto I, Sapienza University of Rome), and Luigi Rigacci (Hematology and Stem Cell Transplant Unit, Campus Bio-Medico University Hospital, Rome). Their expertise supported the uniform application of national risk evaluation criteria.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

All authors contributed equally to the work.

Ethical consideration

Data are presented in anonymized form as required by current national regulations. Approval from the local ethics committee (LEC) was waived due to the monitoring role of the CNT. This study was conducted fully in accordance with the ethical principles outlined in the Declaration of Helsinki.

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