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Transplant quality in Italy: analysis of the 1995–2000 period

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Abstract Evaluation of outcomes is a major step in quality assessment of any health process. In the transplant field, the evaluation of outcome is extremely important for both patients' growing demand for health and for the joint commitment the transplant process requires. In this study, the outcome of 12,647 transplants, carried out between 1995 and 2000 were analysed. Graft survival at 5 years was 79% for kidney, 67% for liver, 72% for heart and 38% for lung. Patient survival was 92% for kidney, 76% for liver, 72% for heart and 38% for lung. In comparison to other international case records [Collaborative Transplant Study (CTS) and The United Network for Organ Sharing (UNOS)], results are similar or even better for all transplant programmes. As a whole, survival after solid organ transplant in Italy ranks among the best for both donations and transplantation. The quality of transplants carried out is above European standards. Nevertheless, the growing health needs of patients require improvement in both the procurement process and in the use of available organs.

Keywords Organ transplantation · National registry · Transplant co-ordination · Graft survival

Introduction

Regulations issued on the basis of Italian law (April 1st 1999) fix both the number of transplants and the minimum quality values which are prerequisites for centres, in order to maintain authorisation to perform organ transplants. However, such indications cannot be considered comprehensive, as neither different recipient risk factors (case mix), nor various donor selection criteria in different transplant centres have been taken into account. Data collection records from various centres can differ greatly, therefore making results incompatible and difficult to compare, this means that addressing the transplant quality issue at national level was difficult. It was possible because a central system of pooling data from the individual centres has been in place in Italy since 1995 [1], this allowed us to evaluate the achievements of the Italian transplant systems in terms of quality. The quality project is extremely important for the Italian transplant system, as detailed legal guidelines were issued by the Minister of Health on the outcome of transplants as a consequence of the work presented in this article. Moreover, guidelines issued by the National Transplant Centre (NTC) on different items are to be acknowledged at a national level in the future on: transplant programmes, waiting lists, management of patients who have difficulties in being transplanted, funding conditions for co-ordination centres and safety level in donor management. In order to get this project going, the energetic participation of the nine working groups of experts has been crucial. They were set up by the NTC, with the aim of achieving a joint and shared method and results interpretation, as well

as effective collaboration between local, regional and interregional co-ordinating centres that collected and transmitted the data.

In this article we describe the number of transplants carried out at the 90 transplant centres that were accredited to perform this procedure between 1995 and 2000, clinical and demographic data of both donors and recipients, and graft and patient survival at 5 years.

Materials and methods

In January 1995, the Laboratory of Immunology and the Laboratory of Medical Engineering of the Italian National Institute of Health started collecting and assembling data concerning each transplant carried out in the national territory, through a form similar to the one used by the Heidelberg Collaborative Transplant Study (CTS) [2]. This made it possible to monitor national transplant activities, including both donor and recipient features. The Italian organisational retrieval and transplant system is articulated on four levels: local, regional, inter-regional and national.

Local co-ordination

Experienced physicians in potential donor detection and maintenance were appointed in each hospital where retrievals are carried out. The experts transmit data on potential donors to the regional centre, keep contact with donors' families, co-operate with regional or inter-regional centres, in order to set up all organisational procedures for organ and tissue retrieval.

Regional co-ordination

Regional co-ordination includes 19 regional reference centres, one for each region. In the regional area, the Regional Transplant Centre manages waiting lists and contacts with outlying centres, organ donations and connections with ICUs, retrievals, transplants, transplant centres and the inter-regional centre.

Inter-regional co-ordination

At present, three inter-regional organisations (Organizzazione Centro Sud Trapianti, Nord-Italia Transplant, Associazione InterRegionale Trapianti) cover the whole national territory (Fig. 1). These organisations are in close contact with the National Centre, and they manage contact with regional centres for reporting of potential donors and allocation of surplus organs, emergencies, return of organs, connections with other inter-regional Centres, relations with the NTC for the paediatric national program. Furthermore, they are responsible for the registries of retrievals carried out over the national territory, for grafts, follow-up data and organ exchanges with other co-ordination organisations.

National co-ordination

The National Transplant Centre (NTC) is composed of: the President of the National Institute of Health (ISS); the Director-General (nominated and appointed by the Health Minister); representatives of the Inter-regional or Regional Centre (nominated by the State-Regions Conference and appointed by decree of the Minister).

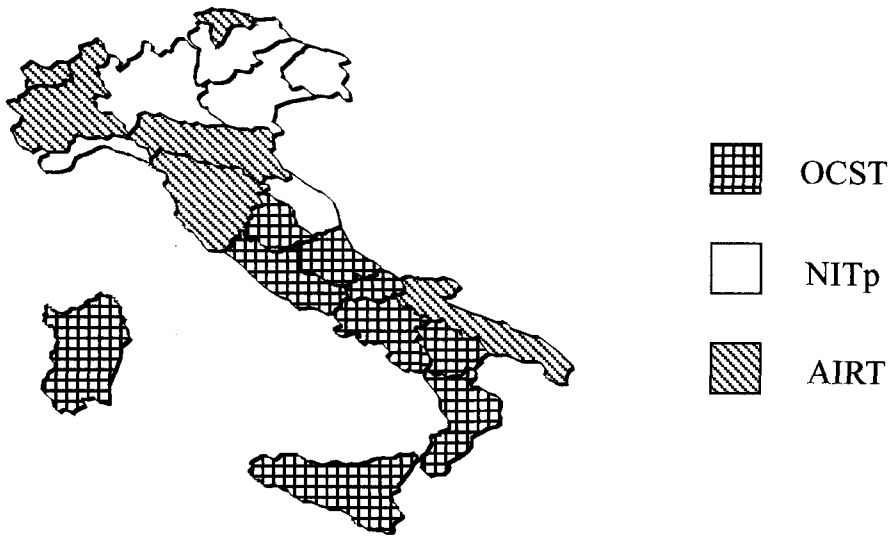


Fig. 1 Geographical distribution of transplant organisations in Italy (*OCST* Organizzazione Centro Sud Trapianti, *NITp* Nord-Italia Transplant, *AIRT* Associazione InterRegionale Trapianti)

Table 1 Number of transplanted organs in Italy between 1995 and 2000

Organ	1995	1996	1997	1998	1999	2000	Total
Kidney	1,042	1,121	1,190	1,160	1,274	1,261	7,048
Liver	404	426	473	548	680	724	3,255
Heart	390	345	366	333	332	293	1,959
Lung	32	55	79	65	98	56	385
Total	1,868	1,947	2,108	2,106	2,384	2,334	12,647

Through the Transplant Information System (TIS), the NTC monitors the number of organ extractions and transplants carried out in the national territory, manages the lists of patients waiting for a transplant and calculates survival rates. It also fixes criteria and procedures for organ allocation, lays down guidelines for regional centres and transplant programmes, collaborates with the Transplant Standing Technical Council that fixes technical and operational directives for donation and transplant activities, keeps contact with some institutional bodies, e.g. the Health Ministry and the Higher Health Council. This complex organisation has allowed retrievals to increase considerably over the last few years, so much so that in 1992 our country had 329 utilised donors (5.8 p.m.p.) whereas in 2001 the number raised to 913 (15.8 p.m.p.) which is an increase of 177.5% over 10 years.

Data collection on graft follow up during the reference period started in February 2001 and has been just completed. At present, available results cover 97.3% of total cases, they refer to kidney, liver, heart and lung transplants and are presented here as national data.

After performing each transplant, peripheral centres send a data form divided into three sections to the National Centre within 30 days. This form included the following details: a section on donor characteristics, a section on recipient characteristics and a section on the type and the methodology of the transplant. A total of more than 100 correlated records were collected.

While donor data for all transplant programmes are similar, data concerning recipients can differ. For this reason, data were classified and analysed for each single type of transplant. In short, required donor parameters

Table 2 Primary disease in transplanted recipients between 1995 and 2000

Original pathology	1995		1996		1997		1998		1999		2000		**Total**	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	***n***	**%**
Kidney														
Glomerulonephritis	348	33.4	435	38.8	533	44.8	453	39.1	472	37	290	23	**2,531**	**35.9**
Congenital cystic disease	93	8.9	157	14	158	13.3	178	15.3	173	13.6	144	11.4	**903**	**12.8**
Systemic disease + diabetes	62	5.9	93	8.3	95	7.9	98	8.5	94	7.4	61	4.9	**503**	**7.1**
Tubulointerstitial pyelonephritis	88	8.4	126	11.2	122	10.3	84	7.2	92	7.2	69	5.5	**581**	**8.2**
Vascular pathologies	8	0.8	4	0.4	13	1.1	21	1.8	20	1.6	12	1	**78**	**1.1**
Other, not specified	443	42.5	306	27.3	269	22.6	326	28.1	423	33.3	685	54.3	**2,452**	**34.8**
Liver														
Biliary atresia	7	1.7	12	2.8	16	3.4	29	5.3	15	2.2	11	1.5	**90**	**2.8**
Fulminant hepatitis	14	3.5	27	6.3	25	5.3	22	4.0	26	3.8	19	2.6	**133**	**4.1**
Post-B cirrhosis	10	2.5	10	2.3	31	6.6	48	8.8	41	6.0	84	11.6	**224**	**6.9**
Post-C cirrhosis	37	9.2	39	9.2	65	13.7	92	16.8	102	15.0	92	12.7	**427**	**13.1**
Metabolic disease	9	2.2	14	3.3	19	4.0	20	3.6	32	4.7	17	2.3	**111**	**3.4**
Post-alcoholic cirrhosis	20	5.0	69	16.2	21	4.4	18	3.3	12	1.8	24	3.3	**164**	**5.0**
Non-A non-B cirrhosis	44	10.9	41	9.6	27	5.7	7	1.3	1	0.1	–	–	**120**	**3.7**
Not specified cirrhosis	113	28.0	123	28.9	171	36.2	156	28.5	166	24.4	109	15.1	**838**	**25.7**
Retransplant	4	1.0	1	0.2	–	–	2	0.4	3	0.4	–	–	**10**	**0.3**
Tumour	–	–	1	0.2	11	2.3	24	4.4	34	5.0	32	4.4	**102**	**3.1**
Other, not specified	146	36.1	89	20.9	87	18.4	130	23.7	248	36.5	336	7.5	**139**	**4.3**
Heart														
Cardiomyopathies	125	32.1	137	39.7	184	50.3	212	63.7	234	70.5	108	36.9	**1,000**	**48.6**
Congenital disease	–		–		12	3.3	4	1.2	6	1.8	4	1.4	**26**	**1.3**
Coronary disease	84	21.5	134	38.8	85	23.2	29	8.7	27	8.1	14	4.8	**373**	**18.1**
Valvular disease	–	–	–	–	–	–	1	0.3	1	0.3	–	–	**2**	**0.1**
Other, not specified	181	46.4	74	21.5	85	23.3	87	26,1	64	19.3	167	56.9.	**658**	**32**
Lung														
Emphysema	0	0	9	16.4	19	24.1	15	23.1	23	23.5	7	12.5	**73**	**19.0**
Cystic fibrosis	0	0	9	16.4	14	17.7	10	15.4	26	26.5	2	3.6	**61**	**15.8**
Lung fibrosis	3	9.4	15	27.3	20	25.3	13	20.0	26	26.5	15	26.8	**92**	**23.9**
Other, not specified	29	90.7	22	40	25	31.7	25	38.5	20	20.4	32	57.2	**57.2**	**39.8**

Table 3 Age groups and recipient gender in organ transplantation between 1995 and 2000. Results are expressed as percentages

Age groups	1995		1996		1997		1998		1999		2000		Total	
	M	F	M	F	M	F	M	F	M	F	M.	F	M	F
Kidney														
0–18	4.2	2.6	3.7	3.6	3.8	2.4	3.3	3.1	2.4	1.0	2.6	1.3	3.4	2.4
19–50	41.1	23.5	41.8	22	41.7	21.9	40.3	20.9	36.1	22.3	36.2	17.8	39.8	21.8
> 50	19.7	8.9	19.9	9.0	20.3	9.9	20.7	11.7	22.5	15.7	25.4	16.7	21.0	11.5
Partial incidence	65.0	35.0	65.4	34.6	65.9	34.1	64.3	35.7	61.0	39.0	64.2	35.8	64.3	35.7
Liver														
0–18	3.9	2.3	3.4	3.9	3.2	3.9	3.3	4.8	3.7	2.3	5.6	5.0	3.7	3.5
19–50	34.0	14.3	35.7	11.8	33.7	9.3	30.6	12.9	30.1	13.0	33.8	5.6	32.6	11.9
> 50	33.2	12.2	33.3	11.8	36.7	13.2	34.1	14.3	35.3	15.5	33.8	16.3	34.6	13.8
Partial incidence	71.2	28.8	72.5	27.5	73.6	26.4	68.0	32.0	69.2	30.8	73.1	26.9	70.8	29.2
Heart														
0–18	3.6	2.5	1.9	2.5	5.4	2.1	3.7	3.0	2.6	3.0	3.6	3.6	3.5	2.6
19–50	23.1	5.8	25.4	5.0	24.8	6.0	26.6	7.0	21.3	8.6	20.2	10.7	24.0	6.6
> 50	55.0	10.0	54.5	10.8	52.6	9.1	52.8	7.0	52.6	11.9	47.6	14.3	53.3	10.0
Partial incidence	81.7	18.3	81.7	18.3	82.8	17.2	83.0	17.0	76.5	23.5	71.4	28.6	80.8	19.2
Lung														
0–18	0	0	0	1.9	1.4	4.1	5.7	1.9	3.1	2.0	0	5.0	2.3	2.6
19–50	40.0	60.0	30.2	24.5	29.7	33.8	34.0	20.8	35.7	16.3	15.0	20.0	31.7	23.8
> 50	0	0	32.1	11.3	24.3	6.8	32.1	5.7	34.7	8.2	50.0	10.0	31.7	7.9
Partial incidence	40.0	60.0	62.3	37.7	55.4	44.6	71.7	28.3	73.5	26.5	65.0	35.0	65.7	34.3
Total incidence	**64.4**	**35.6**	**70.5**	**29.5**	**69.4**	**30.6**	**71.8**	**28.2**	**70.0**	**30.0**	**68.4**	**31.6**	**70.4**	**29.6**

were as follows: personal data; clinical assessment data; immunological and serological data; cause of death; time of ischemia (first hot, second hot, cold); method and maintenance solution.

Recipient parameters were: personal data; time spent on the waiting list; time on dialysis and type of treatment (for kidney alone); clinical data; immunological and serological data; original disease and pre-transplant therapeutic treatments; type of immunosuppressive therapy.

Collected transplant parameters were: date; kind of transplant; number of transplants and length of function of the previous transplant; the highest reactive serum value and the last serum value (total lymphocytes, T-cells, B-cells, B-cells at 5°C); the highest autologous serum value and the last serum value to the recipient (B-cells, B-cells at 5°C, X-match DTT).

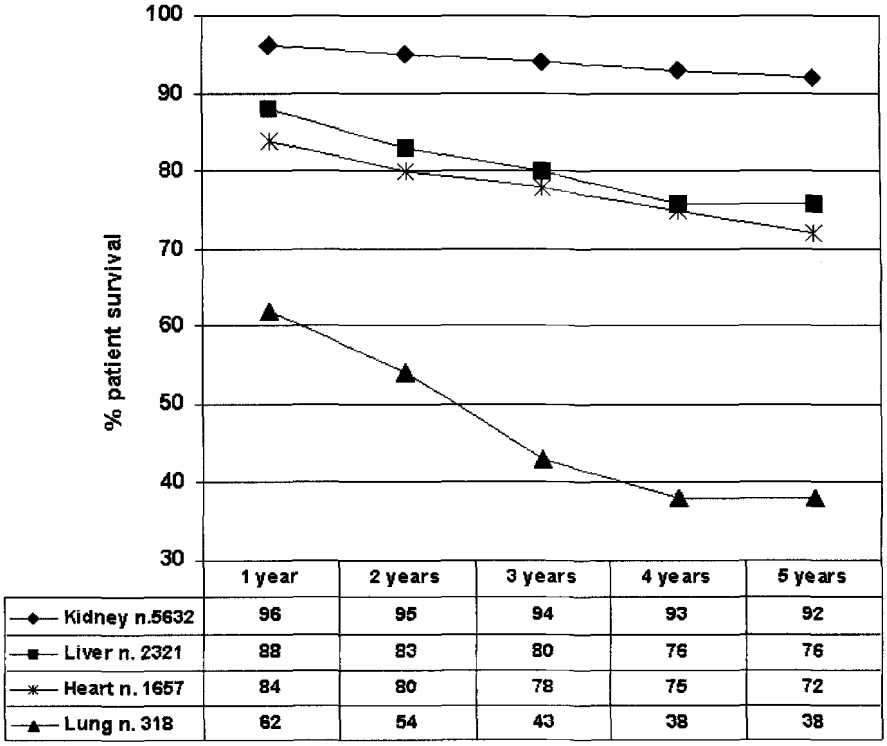
All data were put in an electronic register, the National Transplant Register, using a filing and analysis software based on Access and specifically designed for such data

Table 4 Causes of death of utilised donors between 1995 and 2000

Causes of death	1995		1996		1997		1998		1999		2000		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Trauma	278	52.5	318	51.8	292	46.4	308	44.0	319	44.2	286	42.1	1,801	47.1
Vascular	238	45.0	286	46.6	316	50.3	361	51.6	378	52.3	376	55.3	1,955	49.9
Other	13	2.5	10	1.6	21	3.3	31	4.4	25	3.5	18	2.6	118	2.9
Donor registry	529		614		629		700		722		680		3,874	
Effective donors	576		629		667		707		788		821		4,188	

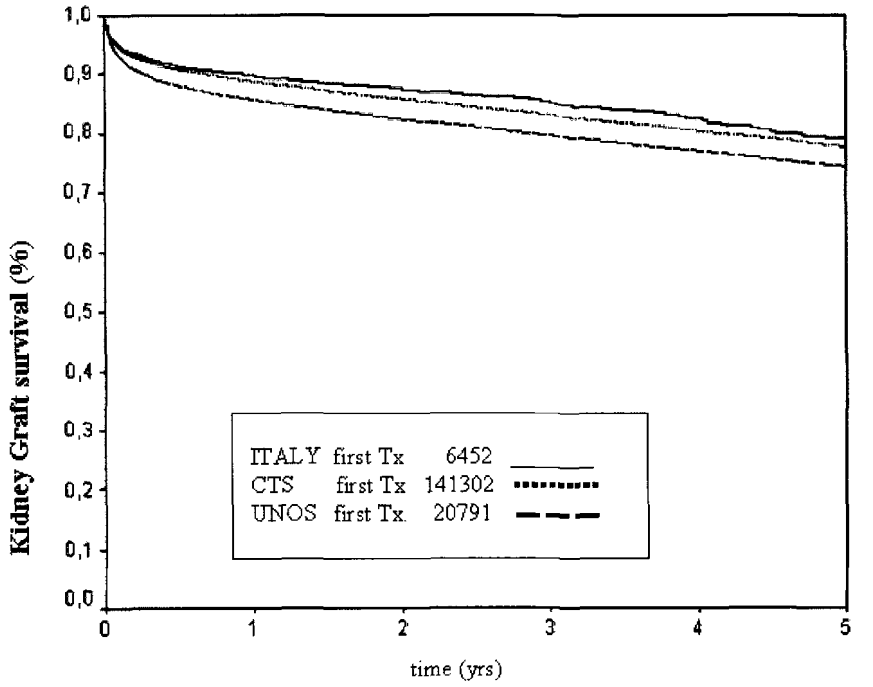
Table 5 Age groups and donor gender between 1995 and 2000. Results are expressed as percentage

Age groups (years)	1995		1996		1997		1998		1999		2000		**Total**	
	M	F	M	F	M	F	M	F	M	F	M	F	**M**	**F**
0–15	2.8	5.3	1.7	5.5	2.5	5.6	1.7	7.1	0.9	5.2	0.7	5.2	**1.7**	**5.6**
16–60	35.8	50.7	37.5	48.0	29.3	51.5	27.8	47.4	31.2	46.9	33.9	45.1	**32.6**	**48.3**
> 60	2.3	3.1	4.1	3.2	5.3	5.7	7.7	8.3	6.9	8.8	6.7	8.4	**5.5**	**6.2**
Total incidence	40.9	59.1	43.3	56.7	37.1	62.8	37.2	62.8	39.0	60.9	41.3	58.7	**39.8**	**60.1**



	1 year	2 years	3 years	4 years	5 years
Kidney n.5632	96	95	94	93	92
Liver n. 2321	88	83	80	76	76
Heart n. 1657	84	80	78	75	72
Lung n. 318	62	54	43	38	38

Fig. 2 Patient survival after organ transplantation (1995–2000)



Graft Survival (% per year)					
ITALY	1	2	3	4	5
	90%	87%	85%	83%	79%

Fig. 3 Kidney graft survival in Italy (1995–2000): comparison with the CTS and UNOS. Annual percentage of graft survival is also shown

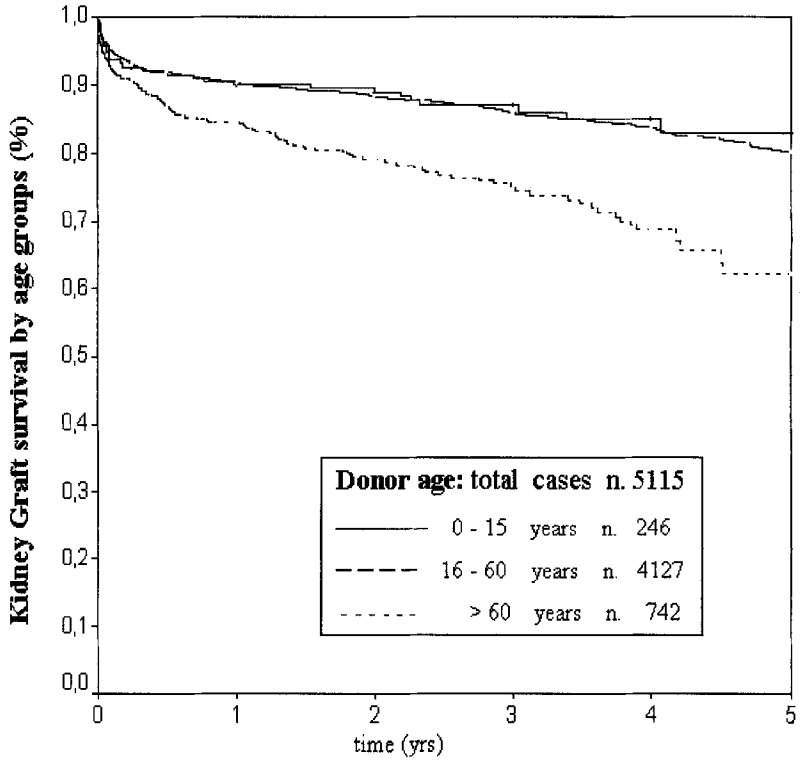


Fig. 4 Graft survival per donor age in kidney transplants (1995–2000). Annual percentage of graft survival is also shown

Graft Survival (% per year)					
	1	*2*	*3*	*4*	*5*
0-15 years[a]	90%	89%	87%	85%	84%
0-60 years	90%	88%	86%	84%	82%
> 60 years	84%	79%	75%	69%	62%

a: Reffered to pediatric recipients (<18 years old)

processing (a database was implemented using MS Access) [3]. The data format has been conceived as required by Heidelberg CTS. Particular attention was paid to security systems using authentication protocols and encrypted data transmission and Virtual Private Networks. The different database copies used by authorised users are updated through synchronisation mechanisms.

The analysis presented in this paper takes into account the subset of variables relevant for transplant quality. For each transplant we have considered: first-transplant graft survival 5 years after surgery, and comparison with international data; patient survival 5 years after surgery and comparison with international data; first-transplant graft survival as a function of recipient primary pathology; first-transplant graft survival as a function of donor age; first-transplant graft survival as a function of recipient age.

For each organ the following variables or covariants have been taken into account: age of donors and recipients; original disease; gender of recipients. Since follow-up data did not include donor age and primary disease of the recipient, this information was obtained by matching our data with those contained in the Transplant Registry. This explains why the number of cases may vary depending on the variable considered in the analysis. Patients lost during follow-up were considered as "right censored", i.e. the patient was included in the sample as long as data could be collected.

Statistical analysis

The analysis of follow-up data was performed using the method of "censoring", since it is not possible to follow the whole clinical history of each patient (lost during follow-up) and since neither transplant failure nor recipient death timings are normally distributed as a function of time.

The Kaplan–Meier method allows estimation of transplant or patient cumulative survival, giving a first indication of how a factor may influence the possibility of transplant failure or patient death. In order to analyse independent and concurrent variables in more detail,

Table 6 Time-independent Cox regression analysis applied to graft failure in kidney transplantation. Number of cases 2,947

Variable	Adjusted relative risk (RR) [a]	95% Confidence interval	
		Lower	Higher
Time (per year increase)	0.858	0.796	0.925
Disease			
Glomerulonephritis	1		
Cystic disease	1.065	0.805	1.409
Other	0.989	0.757	1.290
Systemic	1.082	0.759	1.543
Tubulointerstitial	0.862	0.597	1.243
Vascular	0.884	0.363	2.154
Donor age			
> 60 years	1		
16–60 years	0.531	0.413	0.682
0–15 years	0.401	0.197	0.817
Recipient age			
> 50 years	1		
19–50 years	0.748	0.604	0.926
0–18 years	0.970	0.485	1.938
Gender (male vs female)	1.064	0.870	1.302

[a]Adjusted for all the variables in the table

follow-up data was analysed by a multivariate semi-parameter regression analysis (Cox regression or Mantel–Haenszel method), that evaluated risk function for transplant failure.

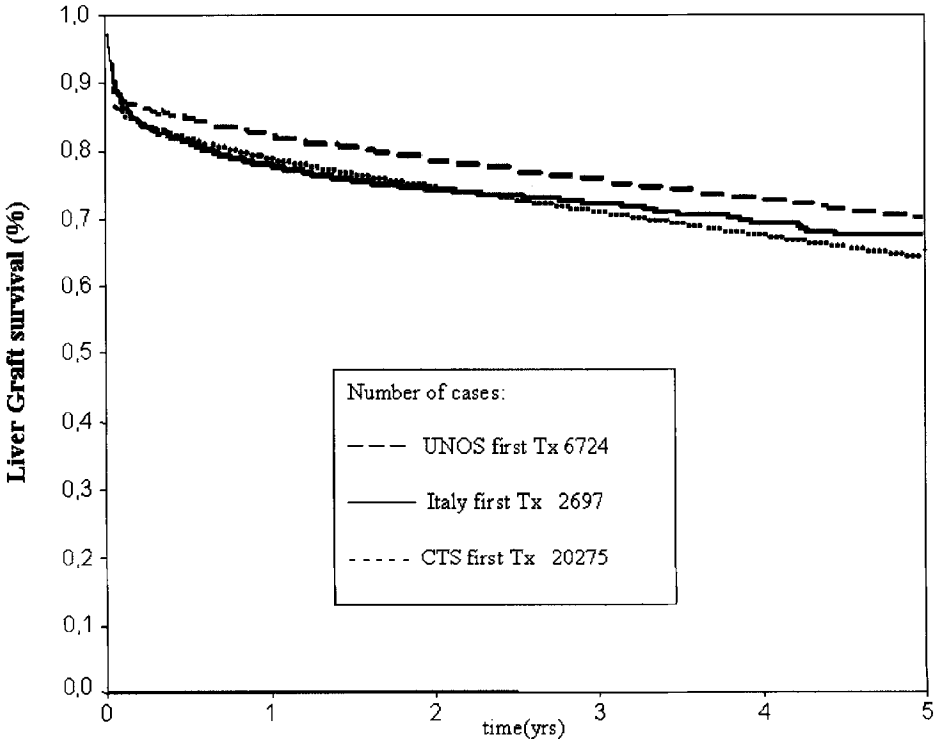
The analysis of patient survival was carried out by taking into account the date of the first transplant as the starting date, and the outcome of the last surgery as the end-point . Patient death was considered as a failure event. Statistical analysis was conducted using SPSS (Statistical Package for the Social Sciences).

Results

The number of transplants carried out in Italy between 1995 and 2000 is shown in Table 1, such activity only refers to consolidated transplant programs. The total number of transplants carried out was 12,647:7048 kidney transplants, 3255 liver transplants, 1959 heart transplants and 385 lung transplants. Pancreas transplants have not been taken into account, due to the low number ($n = 14$); combined transplants (liver plus pancreas) corresponded to 1.74% of total cases (227 out of 12,988) over the reference period. The primary disease of recipients, for each transplant program, in shown in Table 2.

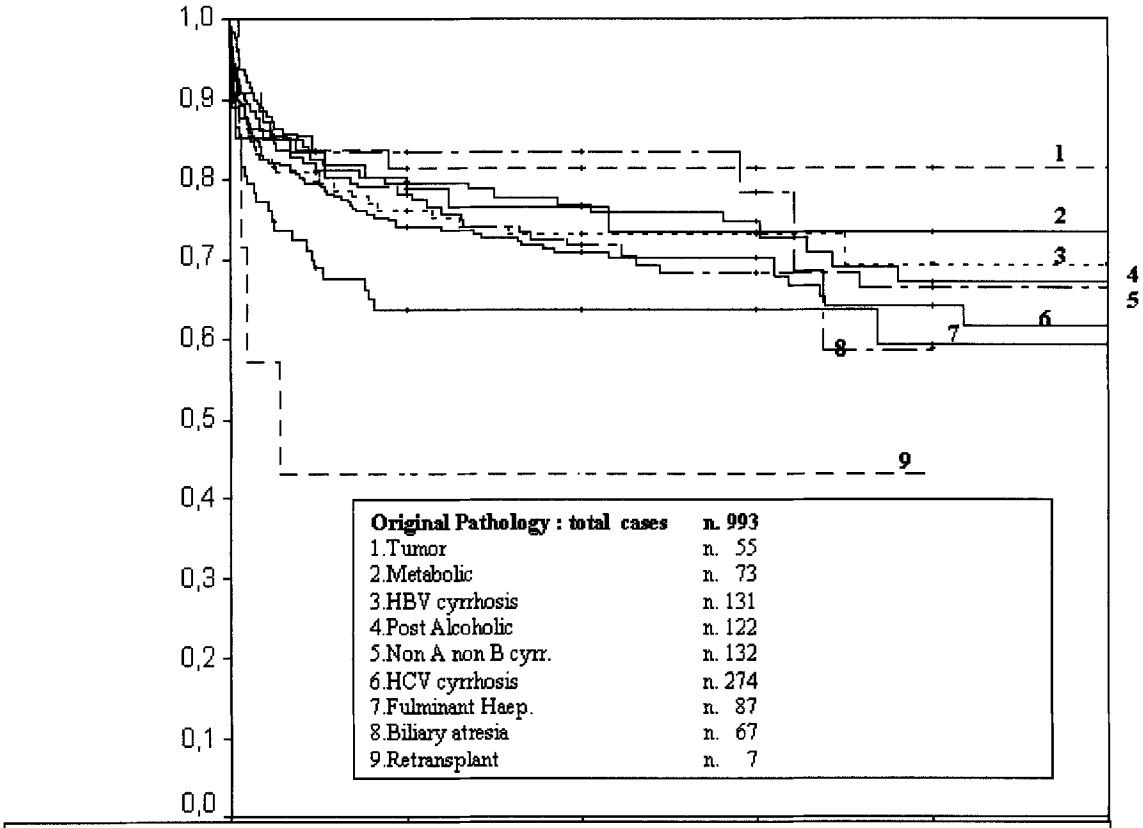
Kidney

The most frequent primary disease was glomerular disease (35.9%), followed by cystic–congenital disease



Graft Survival (% per year)					
ITALY	1	2	3	4	5
	79%	75%	73%	69%	67%

Fig. 5 Liver graft survival in Italy (1995–2000). Comparison with the CTS and UNOS. Annual percentage of graft survival is also shown



Diagnosis	Graft Survival (% per year)				
	1	*2*	*3*	*4*	*5*
Tumor	81%	81%	81%	81%	81%
Retranspl.	43%	43%	43%	43%	
Non A Non B Cyrrhosis	78%	73%	69%	66%	66%
Post alcol. Cyrr.	80%	77%	75%	68%	68%
Metabolic dis.	80%	77%	73%	73%	73%
HCV cyrr.	74%	72%	71%	65%	62%
HBV cyrr.	76%	74%	72%	69%	69%
Fulminant haep.	64%	64%	64%	63%	63%
Biliary atr.	83%	83%	79%	59%	

Fig. 6 Graft survival per recipient disease in liver transplants (1995–2000). Annual percentage of graft survival is also shown

(12.8%); systemic illnesses (7.1%) (among which diabetes was included); tubular-interstitial disease and pyelonephritis (8.2%); vascular pathologies (1.1%); other pathologies (8.5%). For 26.3% of transplants the pathology of recipients was not diagnosed or reported, these patients were not included in the statistical analysis. The average number of all kidney transplants was roughly 1000 per year, with a stable trend over the examined period.

Liver

The number of transplants steadily increased over the period, with a 79.2% total increase (Table 1). The most frequent reason for transplant was non-specified cirrhosis (25.7%), followed by: biliary atresia (2.8%); fulminant hepatitis (4.1%); post-B cirrhosis (6.9%); post-C cirrhosis (13.1%); metabolic disease (3.4%); post-alcoholic cirrhosis (5%); non-A non-B cirrhosis (3.7%); retransplant (0.3%); tumours (3.1%); other pathologies (4.3%). Several primary pathologies were not-specified (27.6%) (Table 2). The national Italian database did not collect more detailed information on liver diseases dur-

Table 7 Time-independent Cox regression analysis applied to graft failure in liver transplantation. Number of cases 1,431

Variable	Adjusted relative risk (RR) [a]	95% Confidence interval	
		Lower	Higher
Time (per year increase)	0.939	0.866	1.019
Disease			
Cirrhosis HCV	1		
Biliary	0.995	0.391	2.533
Fulminant hepatitis	1.566	0.979	2.505
HBV cirrhosis	0.925	0.595	1.438
Metabolic	1.069	0.622	1.839
Other	0.845	0.630	1.134
Post-alcoholic hepatitis	0.902	0.588	1.382
Not specified cirrhosis	0.779	0.511	1.187
Retransplant	2.347	0.730	7.545
Tumour	0.727	0.349	1.515
Donor age			
> 60 years	1		
16–60 years	0.509	0.390	0.663
0–15 years	0.378	0.197	0.726
Recipient age			
> 50 years	1		
19–50 years	0.896	0.713	1.127
0–18 years	0.686	0.330	1.424
Gender (male vs female)	1.065	0.848	1.338

[a]Adjusted for all the variables in the table

ing the period analysed, however the new Italian transplant information system will allow us to perform more specific analysis.

Heart

Transplant activity had a swinging trend, with a steady decrease (−24.9%) (Table 1) probably due to progressive improvement in pharmacological treatment of cardiopathic patients, which led to a reduction of indication to transplant. The most frequent pathology of the recipient was dilated cardiomyopathy (48.6%) followed by: coronary diseases (18.1%); congenital diseases (1.3%); valvular diseases (0.1%); other pathologies (7.9%) . In 24.1% of the cases, the recipient pathology was not specified (Table 2).

Lung

The activity had a changing trend, until 1997 (79 transplants) an upward trend was observed, then a fall during the following year (65 cases), an increase in 1999, and a new decrease in 2000 (56 transplants) (Table 1). This pattern may be due to the small number of subjects transplanted. The most frequent pathology of the recipients was: pulmonary fibrosis (23.9%), cystic fibrosis (15.8%), emphysema (19.0%), other pathologies (14.3%). In 25.5% of the cases the pathology was not specified. The age groups and gender of patients undergoing transplant is shown in Table 3. The overall distribution of transplanted patients was as follows: 6.1% belonged to the 0 to 18-year-old group, 48.5% to the 19 to 50-year-old group and the remaining 45.9% to the older than 50-year-old group.

Table 4 shows data referring to the 3,874 subjects who had a known cause of death reported in the registry (92.5% of total donors), of these, 47.1% died due to trauma, 49.9% vascular injuries and 2.9% other causes. There has been a substantial change in the incidence of the two main causes of death: vascular pathologies have been growing, while traumas decreased from 52.5% in 1995 to 42.1% in 2000. The number of "real donors" (Table 4) refers to both the donors reported to the registry and those which were not reported because reporting was not statutory until 2000. Donor age distribution was: 0–15 years (7.3%); 16–60 years (80.9%); > 60 years (11.7%) (Table 5). It should be stressed that the percentage of utilised donors whose age was less than 60 years old has been growing steadily, from 5.4% in 1995 to 15.1% in 2000. Females have always been more numerous in the three age groups (60% vs. 40%), at variance from what has been shown in recipients, where males represent 70.4% and females only 29.6% (Table 3).

Survival

Kidney

Patient survival was 92% after 5 years (Fig. 2). Five-year graft survival after first transplants was 79% in Italy as a whole (Fig. 3), this result is comparable to major international registries (The United Network for Organ Sharing [4] and the CTS [5]). Graft survival as a function of recipient's pathology does not show significant differences. Better results have been found in transplants carried out on patients affected by vascular pathologies (at 5 years 87% of the organs are still functioning). Five-year graft survival for other pathologies ranged between 76% and 80%, with the lowest survival in transplants carried out on patients affected by systemic disease, including diabetes (graft survival, 76%).

Substantial differences were observed in graft survival according to the donor age (Fig. 4). For kidneys removed from more than 60-year-old donors, 5 year survival was 62%. Kidneys removed from donors younger than 15 years, transplanted in recipients < 18 years old

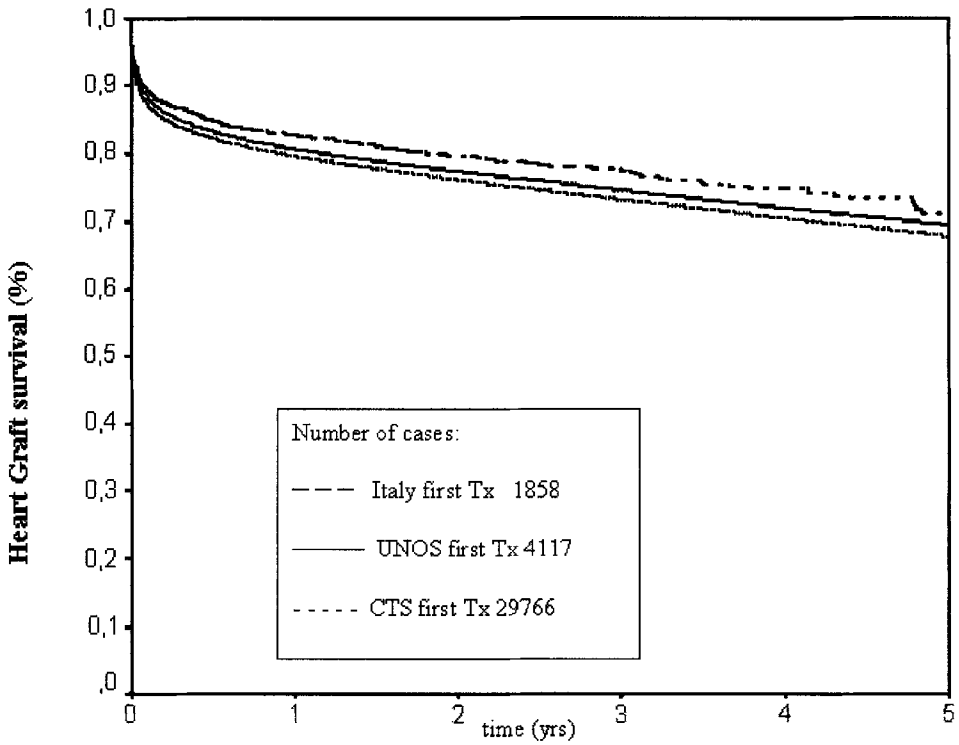


Fig. 7 Heart graft survival in Italy (1995–2000). Comparison with the CTS and UNOS. Annual percentage of graft survival is also shown

Graft Survival (% per year)					
	1	*2*	*3*	*4*	*5*
ITALY	**84%**	**82%**	**78%**	**74%**	**72%**

(paediatric programme) showed a better survival rate (84%). Kidneys removed from donors younger than 60 years, irrespective of recipient disease, also showed a good graft survival (82%).

Multivariate analysis confirmed these data and showed better survival of organs removed from donors younger than 15 years (Table 6). Another variable independently associated with graft survival was recipient age between 19 and 50 years.

Liver

Patient survival was 76% (Fig. 2) and graft survival after the first transplants was 67%, this is similar to major international case records (UNOS and CTS, Fig. 5). Graft survival as a function of recipient pathology showed relevant differences in the first post-transplant year (Fig. 6), this difference remained 5 years later, except for transplants carried out on recipients affected by biliary atresia. The graft survival for this group was very good in the first 3 years (79%), but fell to 59% afterwards. Graft survival was low for patients undergoing retransplant (43% from the first year).

Transplants on cancer-affected patients showed very good results (81% survival at 5 years). Such data are different from those reported in the European registry, where transplant in tumour-affected patients has a 47% graft survival after 5 years. However, in order to compare these two databases, it is necessary to know the criteria for selection of cancer-affected patients, and their disease staging.

Graft survival according to donor age showed an inverse relationship. Livers removed from paediatric donors (0–15 years) had a good performance (73% graft survival after 5 years), while graft survival was lower for organs removed from 16 to 60-year-old donors (69%), and was even lower for organs from donors older than 60 years (55% after 5 years). In contrast, graft survivals did not differ greatly as a function of recipient age. Multivariate analysis confirmed that retransplanted patients have a higher risk of graft failure (OR = 2.3, CI: 0.7–7.5), and that donor age is an independent risk factor for graft failure (Table 7).

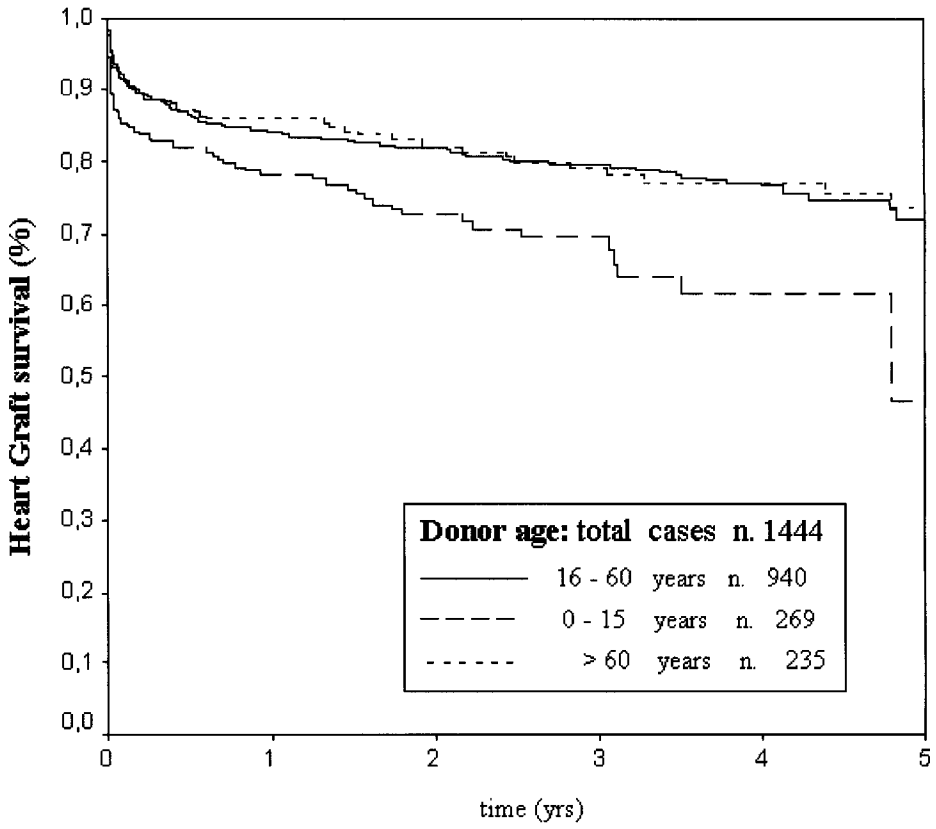


Fig. 8 Graft survival per donor age in heart transplants (1995–2000). Annual percentage of graft survival is also shown

Graft Survival (% per year)					
Age groups	*1*	*2*	*3*	*4*	*5*
16-60 years	86%	82%	80%63%	78%	77%
0-15 years	84%	82%	79%	78%	75%
> 60 years	78%	72%	70%		45%

Heart

Patient survival was 72% after 5 years (Fig. 2) and graft survival in first transplants was comparable to that observed in major international case records (UNOS and CTS) (Fig. 7). Graft survival was the same for both coronary disease and dilated cardiomyopathies (71%). For transplants carried out for congenital pathologies, only 2 years of follow-up data are available. The 2 year graft survival rate was 77% and graft survival varied significantly with donor age. Graft survival hearts removed from patients older than 60 years was 45%, whereas this value was 75% in donors younger than 60 years, and was 77% in paediatric donors (Fig. 8).

Graft survival with recipient age showed values that were higher in recipients between 19 and 50 years (80%) than in paediatric recipients (71%) and in recipients older than 50 years (70%). Multivariate analysis (Table 8) confirmed that both donor and recipient age are independent risk factors for graft failure.

Lung

Graft survival in first transplants was similar to patient survival (Figs. 2 and 9), whereas it was lower than in the European data set after 5 years (38 vs 47%). UNOS data were not available for this condition. A distinction between single and double transplants would have been interesting, but collected data does not allow such division. Graft survival at 4 years was higher in patients affected by cystic fibrosis (64%) than in patients affected by emphysema (53%) and pulmonary fibrosis (23%)

Table 8 Time-independent Cox regression analysis applied to graft failure in heart transplantation. Number of cases 1,431

Variable	Adjusted relative risk (RR) [a]	95% Confidence Interval	
		Lower	Higher
Time (per year increase)	0.902	0.783	1.036
Disease			
Cardiomyopathy	1		
Other	1.469	0.977	2.209
Congenital	1.968	0.702	5.515
Coronary	1.316	0.961	1.802
Donor age			
>60 years	1		
16–60 years	0.705	0.511	0.972
0–15 years	0.709	0.444	1.132
Recipient age (years)			
>50	1		
19–50	0.539	0.379	0.766
0–18	0.820	0.442	1.521
Gender (male vs female)	0.977	0.691	1.383

[a]Adjusted for all the variables in the table

Graft survival was better in grafts deriving from donors between 16 and 60 years (44% after 5 years), but survival of organs removed from paediatric donors was low (32%). Survival of organs from donors older than 60 years was 41% at 2 years (data at 5 years were not available). Data on graft survival as a function of recipients age were also available only at 2 years. Transplants carried out on recipients older than 19 years gave significantly better results (around 60% survival) compared with transplants on paediatric recipients (22%).

Discussion

Our results suggest that the overall quality of transplants in Italy seems to be excellent. Transplant outcome is comparable to that observed in other international registries. On the basis of analysed data, some preliminary observations can be made. The total number of transplants increased steadily until 2000. For kidney, the average transplant rate has been 21.9 transplants per million population. This places Italy within the first five European countries carrying out the most transplants, however the number of patients on the waiting list (almost 7000 patients) indicates the need for a further increase in the number of yearly surgeries. The liver transplantation program benefited from a progressive

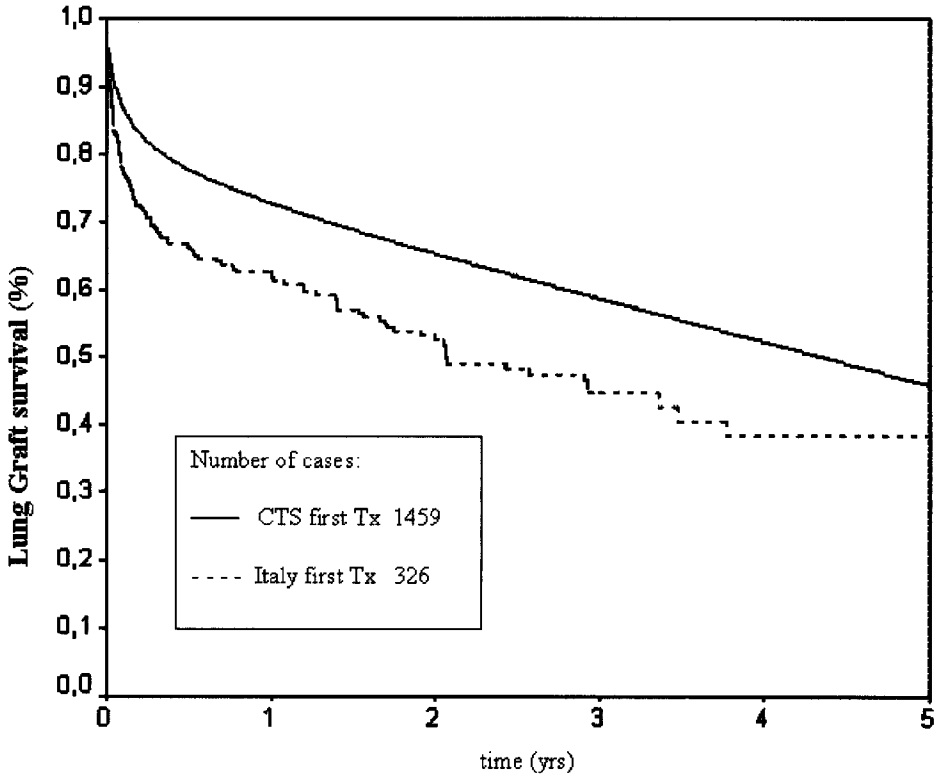


Fig. 9 Lung graft survival in Italy (1995–2000). Comparison with the CTS. Annual percentage of graft survival is also shown

Graft Survival (% per year)					
	1	*2*	*3*	*4*	*5*
ITALY	**61%**	**53%**	**42%**	**38%**	**38%**

broadening of selection criteria to donors older than 60 years, and better use of available grafts. Transplant activity increased considerably over the analysed period (+79.2% in 2000 vs 1995).

Graft survival in liver retransplanted patients was low (43% at 1 year). However, two variables should be taken into account, severe health conditions of retransplanted subjects, and graft quality (probably not the best). At present, no data are available for these two variables; a further analysis including risk factors in retransplanted recipients (case-mix) and evaluation and selection criteria for donors is required. After some years of steady results, heart transplants again reached the 1995 levels. Data in 2001 and 2002 indicated a further upward trend.

Lung transplants achieved good results, considering that such transplants are still rare. The program results explain some of the delays in other countries, both for its recent clinical application in Italy (1991), and for the risk associated with organs coming from intensive care units. Lung and heart transplant programs have also benefited less from the increasing use of donors older than 60 years (5.4% in 1995, 15.1% in 2000), in comparison with kidney and liver programs.

We were able to assess the factors that are independently associated with graft survival in a large population of transplanted subjects, through multivariate analysis. For heart, kidney and liver we had sufficient data to perform such a sophisticated analysis, and we observed that both donor and recipient age are significant, independent risk factors for the success of the transplant. In contrast, this analysis allowed us to assess graft survival adjusted for underlying risk factors, such as primary disease or age (case mix). This is the first time that a risk-adjusted analysis of graft survival was performed on such large numbers. The information obtained is useful in order to review or accept the existing national programs for organ allocation and/or waiting lists.

Quality of performance and quantity seem to be pivotal elements in order to meet patients' needs. Organ procurement programmes should carry out several activities, among which the management of waiting lists and the criteria for organ allocation. These essential components of the quality system should be measured continuously, identifying a method that would allow calibration and improvement of the system itself in order to ensure prompt correspondence between the delivered healthcare and national objectives [6].

In conclusion, the results of this study show that, in Italy, transplant outcomes are very positive. Therefore, the focus of our activity should now move from the quality of performance to increasing the number of available organs, in order to bridge the gap between offer and demand. Every year, this gap causes the loss of hundreds of patients waiting for heart or liver transplant. Present quality standards should therefore be at least maintained, but the whole organisation has to concentrate on satisfying the needs and requirements of patients on the waiting list. It is necessary to implement ad hoc measures to improve organisational aspects of the whole process, but also increase the participation of regional and local authorities in supplying high-level professional and social healthcare.

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References

1. Ghirardini A, Pugliese O, Quintieri F. Organ donation, retrieval, and transplantation in Italy, in 1994–1998. Ann Ist Super Sanita 2000; 36:141.
2. Opelz G. Transfusion and cadaver kidney transplants. The CTS data. Clin Transpl 1987; 2:239.
3. Chistolini P, Frustagli G, Macellari V, Mattucci DA, Pini C, Pugliese O, Quintieri F, Sargentini A. Rete nazionale trapianti di organo: requisiti, caratteristiche generali e specifiche di progetto. Istituto Superiore di Sanità, Roma. Rapporti ISTISAN 1999; 99/2
4. The United Network for Organ Sharing (UNOS).http://www.unos.org
5. Collaborative transplant study (CTS).http://cts.med.uni-heidelberg.de/
6. Vecchiato T. Nuovi contenuti e metodi della programmazione sanitaria. Ministero della Salute, Servizio Studi e documentazione. Annali della Sanità pubblica 1999, vol IV, p 53.