Short term and long term survival rate and risk factors of graft rejection after deceased donor kidney transplantation: a systematic review and meta-analysis

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Abstract

The purpose of the current meta-analysis is to determine the short-term and long-term graft and patient survival after deceased donor (DD) transplantation, as well as to determine prognostic factors.

Method : Articles published until March 2019 in PubMed, Scopus, and Google Scholar databases, reporting short-term and/or long term graft and patient survival were searched. In addition to this, we included articles that analyzed the hazard ratio (HR) of graft rejection and/or patient death caused by DD related risk factors. The summary measures of this study included the survival rate, the HR of graft rejection, and patient death in response to DD related risk factors.

This study, which is the first comprehensive meta-analysis of graft and patient survival rates after transplantation from the deceased donor, showed that overall short and long-term survival of graft and patient is desirable. In addition to this, it confirms that ECD and DCD recipients have a lower graft survival rate than standard donors.

Background

Among renal replacement therapies for patients with End-Stage Renal Disease (ESRD), kidney transplantation is the preferred treatment, due to improved quality of life, increased survival, and reduced financial costs (1, 2). The most critical risk factors that cause kidney transplant rejection have been reported in various studies. Among them are poor early graft function (3, 4), delayed graft function (5, 6), mismatch HLA (7, 8), blood group incompatibility (9), cold ischemia time (10), acute rejection (6, 11), age (12, 13), donor-recipient sex mismatch (14, 15), BMI of donor and recipient (16, 17), and immunosuppressive regime (18, 19). Increasing the incidence of ESRD in developed and developing countries on the one hand and a long waiting list for transplantation, on the other hand, has led to the revision and development of organ transplantation from the deceased donor (DD) (20, 21). Therefore, the type of donor (living or deceased) has been investigated in many studies individually as an essential factor affecting transplantation survival (22–24). The adequacy of kidney transplantation from a DD is controversial according to the findings of various studies. While some studies have shown that the kidney donated from the DD is less likely to survive due to immunological and hormonal changes compared to living donors (25, 26), other studies have reported desirable results from the function of the DD renal transplantation (27, 28). Even though various studies have been carried out in order to determine the effect of cadaveric donors on renal transplantation rejection, these estimations vary from one study to another, and some cases have rejected the results of other studies. The current meta-analysis was performed to determine the short and long-term survival rate of kidney transplantation from the deceased donor, as well as to determine the factors influencing it, using all of the observational and registry-based studies.

Method

In this systematic review and meta-analysis, all prospective, retrospective, and registry-based studies that examined the survival rate of kidney transplantation from DDs all around the world were included without any restriction.

Inclusion criteria for studies

All of the stages of this study were performed under PRISMA guidelines. The criteria for including studies were: study design (prospective, retrospective or registry-based studies), report of patient or graft survival rate, or report of hazard ratio (HR) for determination of the effect of DD related factors on graft rejection. Articles that did meet at least two of these inclusion criteria were included. The outcome measures included the one-year, five-year or ten-year patient or kidney transplantation survival rates from DD and risk factors of rejection related to characteristics of DD such as age, sex, weight, history of chronic disease, and type of DD which includes donation after brain death (DBD), donation after circulatory death (DCD), expanded-criteria donors (ECDs) or standard-criteria donors (SCDs).

Search strategy

In this study, using the search strategy shown in Table 1, we searched PubMed and Scopus databases to obtain relevant studies until March 2019. In order to obtain more articles and to ensure proper search of databases, references of selected articles were reviewed.

Table 1. Search strategy in Scopus and PubMed until 4/2019

SCOPUS
(TITLE-ABS ("Survival Rate") OR TITLE-ABS ("Survival Rates") OR TITLE-ABS ("Mean Survival Time") OR TITLE-ABS ("Mean Survival Times") OR TITLE-ABS ("Cumulative Survival Rate") OR TITLE-ABS ("Cumulative Survival Rates") OR TITLE-ABS ("Graft Rejection") OR TITLE-ABS ("Graft Rejections") OR TITLE-ABS ("Transplant Rejection") OR TITLE-ABS ("Transplantation Rejection") OR TITLE-ABS ("Transplant Rejections") OR TITLE-ABS ("transplantation") OR TITLE-ABS ("rejection")) AND (TITLE-ABS ("Kidney Transplantation") OR TITLE-ABS ("Renal Transplantation") OR TITLE-ABS ("Renal Transplantations") OR TITLE-ABS ("Transplantations, Renal") OR TITLE-ABS ("Transplantation, Renal") OR TITLE-ABS ("Grafting, Kidney ") OR TITLE-ABS ("Kidney Grafting") OR TITLE-ABS ("Transplantation, Kidney") OR TITLE-ABS ("Kidney Transplantations") OR TITLE-ABS ("Kidney Transplantation") OR TITLE-ABS ("Renal Transplantation") OR TITLE-ABS ("Renal Transplantations") OR TITLE-ABS ("Transplantations, Renal") OR TITLE-ABS ("Transplantation, Renal ") OR TITLE-ABS ("Grafting, Kidney") OR TITLE-ABS ("Kidney Grafting") OR TITLE-ABS ("Kidney Transplantations") OR TITLE-ABS ("Transplantations, Kidney")) AND (TITLE-ABS (cadaveric OR cadaver OR cadavers OR corpse OR corpses OR deceased))
PUBMED
Search (((((((((((((((Survival Rate[MeSH Terms]) OR Survival Rates[Title/Abstract]) OR Survival Rate[Title/Abstract]) OR Mean Survival Time[Title/Abstract]) OR Mean Survival Times[Title/Abstract]) OR Cumulative Survival Rate[Title/Abstract]) OR Cumulative Survival Rates[Title/Abstract]) OR Rate, Cumulative Survival[Title/Abstract]) OR Graft Rejection[MeSH Terms]) OR Graft Rejection[Title/Abstract]) OR Graft Rejections[Title/Abstract]) OR Rejection, Graft[Title/Abstract]) OR Transplant Rejection[Title/Abstract]) OR Transplantation Rejection[Title/Abstract]) OR Transplantation Rejections[Title/Abstract]) OR Transplant Rejections[Title/Abstract]) OR Rejection, Transplant[Title/Abstract]) OR transplantation[Title/Abstract]) OR rejection[Title/Abstract])) AND (((((((((((Kidney Transplantation[MeSH Terms]) OR Kidney Transplantation[Title/Abstract]) OR Renal Transplantation[Title/Abstract]) OR Renal Transplantations[Title/Abstract]) OR Transplantations, Renal[Title/Abstract]) OR Transplantation, Renal[Title/Abstract]) OR Grafting, Kidney[Title/Abstract]) OR Kidney Grafting[Title/Abstract]) OR Transplantation, Kidney[Title/Abstract]) OR Kidney Transplantations[Title/Abstract]) OR Transplantations, Kidney[Title/Abstract])) AND (((((((cadaveric[Title/Abstract]) OR Cadaver[MeSH Terms]) OR Cadavers[Title/Abstract]) OR Corpse[Title/Abstract]) OR Corpses[Title/Abstract]) OR Deceased[Title/Abstract]))

Data extraction and statistical methods

To ensure the correct selection of articles in terms of their pertinence to the research topic and accordance with the inclusion criteria, two researchers (K.A. and M.S.) independently reviewed the articles. The names of the authors, the journals, and their results were not hidden from the reviewers. The Kappa percentage of the inter reviewer agreement was 85%. The variables taken in consideration in this review included the name of the first author, year of publication, country of the study, the mean age of the DD, gender, study design, weight of DD, type of DD (DBD or DCD), criteria (ECD or SCD), and history of chronic disease. STROBE checklist for cohort studies was used to assess the quality in terms of methodology and reporting. To determine the heterogeneity of the studies, Cochran's Q-test of heterogeneity was used at a 5% confidence level. Survival rates vary between zero and one and have no negative values; for this reason, all of the studies are located at the right side of the vertical line, and publication bias cannot be determined. The summary measures of this study, including the survival rate, the HR of graft rejection, and patient death in the presence of DD related risk factors, were calculated along with 95% confidence intervals (CIs) to perform a two-tailed test.

Data analysis was done using the Stata (version 11, StataCorp, College Station, Texas) and applying the random effects model at a 95% confidence level.

Results

In the first step, we identified 16968 articles, after removing duplicate papers, and reviewed the title and abstract of 10786 them. Secondly, considering the exclusion criteria, we excluded 9986 articles and studied 923 full-text articles. According to our objectives and quality assessment of selected articles, 845 papers were withdrawn, and finally, 75 articles were included in the final analysis (Fig 1). Table 2 represents article information including author, country, research design, donor sex, male donor (%), donor mean age (year) $\pm$ SE, type of the deceased donor (DBD or DCD), criteria (ECD or SCD), donor BMI, sample size, patient survival rate, and graft survival rate.

Table 2. Characteristics of the studies included in this meta-analysis

Author/ year	country	design	Sex	Male donor (%)	Donor Mean age ± SE (years)	Type of deceased donor	Criteria (%)	Donor BMI	SS	Survival %				
										patient		graft		
										One year	Three years	Five years	One year	Three year
Kute et al. 2014 (29)	India	R.cohort	both	61.5	45.9	DBD	-	-	294	81.6	-	-	92.5	-
Auglene et al. 2017 (30)	Lithuania	R.cohort	both	61.1	44.1±15.8	DBD & DCD	ECD & SCD	-	186	-	-	-	93.5	90.0
Cardinal et al. 2005 (31)	Canada	R.cohort	both	-	42.0	DBD & DCD	-	-	256	93.0	-	74.0	88.0	-
Centellas- Perez et al. 2019 (32)	Spain	R.cohort	both	62.8	60.5±13.6	DBD:92.9,DCD:7.1	ECD & SCD	-	183	-	-	-	86.9	-
Cho et al. 2014(33)	Korea	R.cohort	both	-	42.0±14.0	DBD & DCD	-	-	136	-	-	-	99.2	97.3
Terasaki et al. 1998 (34)	United states	R.cohort	both	-	-	DBD & DCD	-	-	DBD:22680,DCD:276	-	-	-	DBD:85.7,DCD:82.8	-
Czerwinski et al. 2016 (35)	Poland	Registry	both	-	-	DBD & DCD	-	-	15009	95.0	91.0	87.0	88.0	82.0
Kyllonen et al. 2000 (36)	Finland	R.cohort	both	62.8	38.8	DBD	-	-	1407	95.9	91.9	86.0	91.3	84.1
Laging et al. 2012 (37)	Netherlands	R.cohort	both	55.0	45.7±16.1	DBD & DCD	-	-	513	-	-	-	-	-
Lionaki et al. 2014 (38)	Greece	R.cohort	both	64.4	52.9±15.7	DBD & DCD	ECD:42.5, SCD: 57.5	-	334	-	-	ECD:93.7,SCD:96.4	-	-
McDonald et al. 2002 (39)	Australia	Registry	both	63.0	43.8	DBD & DCD	-	-	2362	-	-	-	91.0	85.0
Moers et al. 2009 (40)	Netherlands	Registry	both	45.0	67	DBD & DCD	-	-	1011	-	-	-	-	-
Mok et al. 2012 (41)	Singapore	R.cohort	both	63.3	44.7±11.7	DBD & DCD	ECD:72.6, SCD:14.2	-	332	96.7	94.8	91.5	89.8	85.9
Mukherjee et al. 2018 (42)	India	R.cohort	both	65.2	43.9±17.0	DBD & DCD	-	-	92	98.9	83.3	70.8	98.9	91.6
Nagaraja et al. 2012 (43)	United Kingdom	R.cohort	both	-	DBD: 52, DCD:46	DBD & DCD	-	-	DBD:52, DCD:46	DBD:95.0, DCD:96.0	-	-	DBD:88.0, DCD:96.0	-
Newstead et al. 1992 (44)	England	R.cohort	both	-	-	DBD & DCD	-	-	397	-	-	-	87.0	79.0
Noppakun et al. 2015 (45)	Thailand	Registry	both	73.1	34.7±13.3	DBD	-	-	1745	96.3	-	93.1	95.6	-
OKelly et al. 2001 (46)	Ireland	R.cohort	both	58.8	34.7	DBD & DCD	-	-	436	95.0	90.7	85.7	85.2	77.6
Pessione et al. 2003 (47)	France	R.cohort	both	65.7	41±13.7	DBD & DCD	-	-	7209	-	-	-	91.1	85.6
Salmela et al. 2001 (48)	Finland	R.cohort	both	-	-	DBD & DCD	-	-	1008	96.3	-	-	92.9	-
Saunders et al. 1984 (49)	USA	R.cohort	both	68.2	32.1±15.4	DBD & DCD	-	-	104	-	-	-	91.5	85.6
Savoye et al. 2007 (50)	France	Registry	both	58.7	54.8±14.9	DBD & DCD	ECD	-	2845	96.2	88.9	82.8	88.1	80.8
Sener et al. 2009 (51)	England	R.cohort	both	-	55	DBD & DCD	-	-	468	-	-	-	86.5	77.4
Stratta et al. 2016 (52)	USA	R.cohort	both	ECD:58.5,SCD:61.6	ECD:61.1±6.4, SCD: 37.0±13.8	DBD & DCD	ECD & SCD	ECD:28.1±6.1,SCD:26.7±7.8	ECD:354, SCD:589	ECD:93.7,SCD:96.3	-	-	ECD:83.3, SCD:91.7	-
Kandas et al. 2016 (53)	Slovenia	R.cohort	both	-	-	DBD & DCD	ECD	-	793	98.1	-	93.8	94.3	-
Jacobi et al. 2014 (54)	Germany	R.cohort	both	-	-	DBD & DCD	ECD & SCD	-	ECD:174, SCD:208	96.8	-	-	90.4	-
Heylen et al. 2017 (55)	Belgium	Registry	both	DBD:52.0,DCD:60.0	DBD:54,DCD:51	DBD & DCD	-	-	DBD:17006,DCD:1059	-	-	-	-	-
Heilman et al. 2015 (56)	USA	R.cohort	both	ECD:74.0,SCD:78.0	ECD:56.6±9.1,SCD:32.3±13.2	DBD	ECD & SCD	-	ECD:23,SCD:139	-	-	-	ECD:95.6,SCD:97.1	-
Hamed et al. 2015 (57)	UK	Registry	both	-	-	DBD & DCD	ECD & SCD	-	DBD:366,DCD:435	-	-	-	DBD:89.8,DCD:86.4	-
Gondos et al. 2013 (58)	Germany (Europe, white American, African American, Hispanic American)	Registry	both	-	-	DBD & DCD	-	-	Europe:23530, white American:15772, African American:11148, Hispanic American:5338	-	-	-	Europe:90.6, white American:91.1, African American:88.7, Hispanic American:91.5	-
Fujita et al. 2014 (59)	Japan	R.cohort	both	63.4	45.7±16.7	DBD & DCD	-	-	350	-	-	-	97.0	-
Ferreira et al. 2017 (60)	Portugal	R.cohort	both	67.3	46.3±16.5	DBD & DCD	ECD & SCD	-	ECD:150,SCD:467	95.8	91.3	88.2	93.9	90.5
Ergün et al. 2019 (61)	Netherlands	R.cohort	both	-	54.0	DBD	ECD & SCD	24.5	ECD:696, SCD:1173	-	-	-	90.9	-

Emiroglu et al. 2005 (62)	Turkey	R.cohort	both	-	45.0	DBD & DCD	-	-	58	94.8	-	-	92.6	-
Aceto et al. 2019 (63)	Italy	R.cohort	both	62.0	46.7±17.0	DBD & DCD	-	-	87	95.4	-	-	96.5	-
ALI et al. 2015 (64)	Saudi Arabia	R.cohort	both	87.7	35.7±12.3	DBD & DCD	-	-	284	98.8	-	94.8	94.1	-
Butala et al. 2013 (65)	United States	Registry	both	59	-	DBD & DCD	-	-	73714	94.7	-	80.0	94.0	-
Chen et al. 2013 (66)	China	R.cohort	both	76.0	26.7±11.9	DCD	-	20.5±3.1	71	100	-	-	95.7	92.4
Farrugia et al. 2013 (67)	England	R.cohort	both	-	-	DBD & DCD	-	-	19688	96.2	-	-	-	-
Harada et al. 2009 (68)	Brazil	R.cohort	both	57.5	42.2	DBD & DCD	ECD & SCD	-	ECD:135,SCD:641	ECD:71.1,SCD:80.2	-	-	ECD:82.2,SCD:88.2	-
Hassanian et al. 2009 (5)	Canada	R.cohort	both	-	-	DBD & DCD	ECD & SCD	-	335	86.3	-	7.4	-	-
Hwang et al. 2014 (69)	Korea	R.cohort	both	ECD:67.7, SCD:65.2	ECD:56.8±6.3,SCD:37.5±13.5	DBD & DCD	ECD & SCD	ECD:23.1±3.1,SCD:22.7±3.4	ECD:31,SCD:164	ECD:96.8,SCD:98.1	-	ECD:89.3,SCD:89.0	ECD:93.5,SCD:93.8	-
Kang et al. 2018 (70)	Korea	R.cohort	both	45.0	37.2	DBD & DCD	-	-	127	98.4	96.8	95.9	96.8	91.2
Kim et al. 2014 (71)	Korea	R.cohort	both	ECD:12.6,SCD:24.1	ECD:62.5±10.5,SCD:42.7±11.7	DBD & DCD	ECD & SCD	-	ECD:14,SCD:31	ECD:92.9,SCD:87.1	-	-	ECD:92.8,SCD:87.1	-
Lee et al. 2010 (26)	Korea	R.cohort	both	57.4	31.3	DBD & DCD	-	-	216	-	-	-	-	-
Lewandowska et al. 2016 (72)	Poland	R.cohort	both	-	42.1±14.5	DBD	-	-	8206	-	-	87.5	-	-
Papalia et al. 2010 (73)	Italy	R.cohort	both	-	-	-	-	24.4±2.6	194	-	-	-	-	-
Papachristou et al. 2014 (74)	Greece	R.cohort	both	ECD:54.7,SCD:63.6	ECD:56.0,SCD:27.0	DBD & DCD	ECD & SCD	ECD:27.3±4.3,SCD:25.1±6.4	ECD:53,SCD:162	ECD:93.6,SCD:96.8	ECD:93.6,SCD:93.9	ECD:85.3,SCD:92.2	ECD:88.4,SCD:90.7	ECD:81.8,SCD:81.8
Noseworthy et al. 2004 (75)	Canada	R.cohort	both	-	-	DBD & DCD	-	-	-	-	-	-	-	-
Nakamura et al. 2018 (76)	Japan	R.cohort	both	-	DBD: 37.3±19.8,CDC:49.8±13.0	DBD & DCD	ECD & SCD	-	DBD:9,DCD:19	-	-	-	DBD:100,DCD:100	DBD:100,DCD:100
Molina et al. 2015 (77)	Spain	R.cohort	both	81.0	45.0±16.0	DBD & DCD	-	-	59	97.0	-	-	92.0	-
Malek-Hosseini et al. 2006 (78)	Iran	R.cohort	both	67.3	33.6±12.5	DBD & DCD	-	-	97	93.0	90.5	-	-	-
Tasaki et al. 2014 (79)	Japan	R.cohort	both	-	45.7	DBD & DCD	-	-	56	98.2	-	96.2	89.0	-
Saghan et al. 2014 (80)	Germany	R.cohort	both	-	52.0±16.2	DBD & DCD	-	-	1134	-	-	-	-	-
Sirivongs et al. 2004 (81)	Thailand	R.cohort	both	76.4	30.18±11.4	DBD & DCD	-	-	89	-	-	-	90.6	-
Tomita et al. 2017 (82)	Japan	R.cohort	both	ECD:62.0,SCD:55.3	ECD:60.4±8.2,SCD:38.8±15.0	DBD & DCD	ECD & SCD	-	ECD:50,SCD:47	100.0	-	92.9	100.0	-
WOO et al. 1998 (83)	United Kingdom	R.cohort	both	-	-	DBD & DCD	-	-	589	95.0	-	82.0	84.0	-
Zhang et al. 2018 (84)	China	R.cohort	both	-	-	DBD & DCD	-	-	524	-	-	-	94.9	91.3
Zhu et al. 2018 (85)	China	Registry	both	DBD:59.5,DCD:72.1	DBD:40.3±16.7,DCD:42.2±15.8	DBD & DCD	ECD & SCD	-	DBD:415,DCD:133	DBD:98.9,DCD:98.4	-	-	DBD:98.4,DCD:92.4	-
Ko et al. 2018 (86)	Korea	R.cohort	both	ECD:68.9,SCD:67.0	ECD:58.2±5.4,SCD:41.7±10.9	DBD & DCD	ECD & SCD	-	ECD:90,SCD:200	-	-	-	-	-
Nakamura et al. 2017 (87)	Japan	Registry	both	-	49.6±15.0	DCD	-	-	589	95.5	92.9	90.9	85.6	80.4
Boer et al. 2002 (88)	Belgium	R.cohort	both	-	-	DBD & DCD	-	-	16	93.0	-	-	44.0	-
Davidson et al. 2019 (89)	South Africa	R.cohort	both	DBD:86.0,DCD:67.0	DBD:31.0,DCD:34.0	DBD & DCD	-	-	DBD:123,DCD:7	89.1	-	84.5	88.8	-
Gallinat et al. 2016 (90)	Germany	Registry	both	73.0	51.0	DBD & DCD	-	-	78	96.0	93.0	89.0	92.0	89.0
Lai et al. 2014 (91)	China	R.cohort	both	-	-	DBD & DCD	-	-	166	84.8	82.1	77.1	93.6	89.4
McLarena et al. 1999 (92)	UK	R.cohort	both	62.0	35	DBD & DCD	-	-	681	-	-	-	84.7	77.5
Nemati et al. 2014 (93)	Iran	R.cohort	both	-	-	DBD & DCD	-	-	103	95.1	95.4	-	97.0	67.4
Rezapour et al. 2017 (94)	Iran	R.cohort	both	67.0	-	DBD & DCD	-	-	120	-	-	-	90.8	-
Savdie et al. 1982 (95)	Australia	R.cohort	both	-	-	DBD & DCD	-	-	404	79.0	-	60.9	63.0	-

Seo et al. 2015 (96)	Korea	R.cohort	both	65.6	40.9±14.5	DBD & DCD	-	22.7±1.3	191	98.1	96.3	96.3	97.3	92.2
Dalinkeviciene et al. 2010 (97)	Lithuania	R.cohort	both	-	-	DBD & DCD	-	-	159	97.0	9.0	94.0	85.0	82.0
Molmenti et al. 2016 (98)	Greece	Registry	both	60.6	50.1±13.0	DBD & DCD	-	-	61167	-	-	-	-	-
Simforoosh et al. 2011 (99)	Iran	R.cohort	both	60.8	28.9	DBD & DCD	-	-	138	96.0	-	-	93.0	-
Yoshida et al. 2002 (100)	Japan	R.cohort	both	-	40.2	DCD	-	-	107	85.7	-	77.0	-	-
Vergoulas et al. 2008 (101)	Greece	R.cohort	both	-	51.5±16.9	DBD & DCD	-	-	29	100.0	-	100.0	100.0	-

DBD: donor after brain death, DCD: donor after cardiac death, ECD: expanded-criteria donor, SCD: Standard-criteria donor, SS: sample size, R.cohort: retrospective cohort

Descriptive of included articles

In this meta-analysis, data of 249369 patients from 29 countries were analyzed. The largest sample size was from the Gondos et al. (58) study in Germany in 2013. They used the registry data to report the graft survival of 55778 patients of different ethnicities, such as European, African, African- American, and Hispanic. The smallest sample size belonged to the Nakamura et al. (87) study in Japan, which had examined 16 kidney transplants survival from cadaver donors. Thirteen studies were registry-based (35, 39, 40, 45, 50, 55, 58, 65, 76, 85, 90, 98, 102) and others were retrospective case studies. Table 3 shows the most important causes of deaths in the deceased donor reported by twenty-six articles. Trauma and cerebrovascular were the most common causes of death.

Table 3. Cause of donor death in the studies included in this meta-analysis

1 Author (Year)	Intracranial Bleeding	Trauma	Cerebrovascular	Judicial Death	Traffic Accident	Anoxia	Suicide	Brain Hemorrhage	Ischemic Brain Injury	Cardiovascular Disease	Respiratory Disease	Brain Tumor	Other
Ali et al. 2015(64)	-	15.7	32.6	-	34.1	-	-	-	-	-	-	-	17.6
Augliene et al. 2017(30)	-	35.6	63.3	-	-	-	-	-	-	-	-	-	1.1
Boer et al. 2002(88)	-	55.3	-	-	-	-	-	-	-	-	-	-	43.0
Butala et al. 2013(65)	-	40.0	41.0	-	-	15.0	-	-	-	-	-	-	3.0
Centellas-Perez et al. 2019(32)	-	16.4	65.6	-	-	13.1	-	-	-	-	-	1.1	3.8
Chen et al. 2013(66)	-	52.0	36.0	-	-	12.0	-	-	-	-	-	-	-
Ferreira et al. 2017(60)	-	15.5	31.4	-	-	-	-	-	-	-	-	-	53.1
Fujita et al. 2014(59)	-	36.0	55.4	-	-	-	6.5	-	-	-	-	-	2.1
Heylen et al. 2017(55)	-	23.1	68.4	-	-	5.9	-	-	-	-	-	-	2.4
Hwang et al. 2014(69)	-	30.7	56.9	-	-	-	7.1	-	-	-	-	-	4.6
Kim et al. 2014(71)	-	-	53.3	-	-	-	-	-	-	-	-	-	46.7
Ko et al. 2018(86)	-	26.3	57.5	-	-	-	3.8	-	-	-	-	-	12.5
Kute et al. 2014(29)	59.4	21.6	-	-	-	-	-	-	-	-	-	-	19.0
Kyllonen et al. 2000(36)	60.0	31.6	-	-	-	-	-	-	-	-	-	-	8.4
Lionaki et al. 2014(38)	-	-	56.7	-	-	-	-	-	-	-	-	-	43.3
Moers et al. 2009(40)	-	14.0	-	-	-	-	-	-	-	-	-	-	86.0
Mok et al. 2012(41)	-	16.3	67.8	13.3	-	-	-	-	-	-	-	-	2.7
Molina et al. 2015(77)	-	-	39.0	-	-	-	-	-	-	-	-	-	61.0
Nakamura et al. 2017(87)	-	16.4	54.3	-	-	5.9	-	-	-	1.9	2.6	1.6	17.1
Noppakun et al. 2015(45)	-	-	11.2	-	49.7	-	-	-	-	-	-	-	13.9
Papachristou et al. 2014(74)	-	37.2	-	-	-	-	-	48.4	7.4	0.9	-	-	6.1
Pessione et al. 2003(47)	-	-	44.5	-	-	-	-	-	-	-	-	-	55.5
Savoye et al. 2007(50)	-	-	62.5	-	-	-	-	-	-	-	-	-	37.5
Tasaki et al. 2014(79)	-	-	48.7	-	-	-	-	-	-	-	-	-	51.3
Tomita et al. 2017(82)	-	-	55.6	-	-	-	-	-	-	-	-	-	44.4
Seo et al. 2015(96)	-	31.4	56.0	-	-	-	7.3	-	-	-	-	-	4.7

Graft and patient survival rate

The one-year graft survival rate was 90% (95% CI: 89% to 92%). Two, three, five and ten-year graft survival rates were 80% (95% CI: 90% -70%), 82% (95% CI: 75% -88%), 76% (95% CI: 73% -79%) and 52% (48% -60%), respectively (Fig 2). One-year patient survival rate was 95% (95% CI: 94% -96%). This rate decreased to 83% (95% CI: 91% -74%), 85% (95% CI: 80% -89%), and 73% (95% CI: 57% -89%)

after three, five, and ten years, respectively (Fig 3). Regardless of Savdia et al. (103) 10-year patient survival rate increased to 84%, but there were no significant changes in short-term patient and graft survival.

In figures 4, 5 and 6 the graft and patients survival based on the type of deceased donor (DCD and DBD) is shown. The rate of one-year graft and patient survival in DCD recipients were 87% (95% CI: 83%- 92%) and 95% (95% CI: 95%- 99%), respectively. One, five and fifteen-year graft survival rates in transplant recipients from DBD donor were 92% (95% CI: 88%- 96%), 79% (95% CI: 76%- 83%), and 65% (95% CI: 56%- 73%), respectively. One-year patient survival rate of transplant recipients from DBD was 94% (95% CI: 97%- 91%) and five-year survival rate was 90% (95% CI: 85%- 95%). One, three and five-year graft survival rates in ECD recipients were 88% (95% CI: 85%- 91%), 78% (95% CI: 70%- 87%), and 68% (95% CI: 61), respectively (Fig 7). In the case of SCDs recipients one-year and three-year patient survival rate were respectively 93% (95% CI: 91%- 94%) and 80% (95% CI: 78%- 83%) (Fig 8). Also one-year patient survival rate in SCD kidneys was 96% (95% CI: 94%- 97%). In the same category, three and five-year survival rates were 86% (95% CI: 79%- 92%) and 87% (95% CI: 79%- 95%), respectively (Fig 9). The one and five-year patients survival in SCDs were 96% (95% CI: 93%- 98%) and 92% (95% CI: 86%- 98%), respectively (Fig 10).

Hazard Ratio

Although most of the studies have found that the HR of graft rejection and patient death risk factors are attributed to the recipient, few studies have been performed to determine the HR of risk factors associated with the deceased donor. Therefore, only three factors, including the age of the donor, ECD kidney and male sex, were included for analysis. HR of age of deceased donor was 1.01 (95% CI: 0.99 to 1.04) for graft rejection and patient death (Fig 11). ECD kidney was a risk factor for graft rejection (HR: 1.14, 95% CI: 1.00, 1.27) (Fig 12). Male sex was a significant protective factor in patient survival rate. According to the results shown in graph 13, the risk of death in men had an HR of 0.86 (95% CI: 75, 97). However, the male sex does not affect the survival of the kidney transplant (HR=0.95, 95% CI: 0.83, 1.06) (Fig 13).

Discussion

In this systematic review and meta-analysis, we estimated the graft and patient survival after kidney transplantation from DD for the first time. Currently, the demand for kidney transplantation is much higher than the number of kidney donors. While in response to this need, kidney donation from DDs has been developed around the world, concerns and inconsistencies about the graft and patient survival after transplantation from these donors have also increased. Our findings showed that one-year kidney transplant and patient survival rates were respectively 90% and 95%. According to Fig. 1, Boer et al. (88) in 2002 and Savdie et al. (95) in 1982 reported the lowest rate of one-year graft survival (56%) and patient survival (79%). On the other hand, Mukherjee et al. (42) in 2018 reported the highest rate of one-year graft survival from 92 deceased donor transplantation in India. Also, Kang et al. (70) and Taski et al. (79) in respectively 2018 and 2014, reported the highest one-year patient survival rate. As mentioned earlier, no-meta-analysis has been performed to quantify kidney transplant and patient survival rate from the deceased donor. Thus the comparison of our results is limited. Noordzij et al. (104) reported that from 2005 to 2009, one-year kidney transplant and patient survival rate from DD in 12 European countries were 90.4% and 95.9%, respectively. Additionally, five-year kidney transplant and patient survival rate between 2002 and 2006 were 77.2% and 86.7%, respectively. As shown in Figs. 1 and 2, one-year graft survival is more variable compared to one-year patient survival. This issue has also been seen in long-term graft survival. It is crucial to consider the potential factors that might generate these differences and wide range of the reported one-year graft survival in the included study:

1. Immunosuppressive regime: Recent advances in the immunosuppressive protocols significantly reduced the rate of acute rejection from 60–35% (105, 106). With the use of Imuran and Prednisolone since 1960, the one-year survival rate of living donors has increased from 75–90% (107). In 1995, Cellcept was added to the treatment protocol. This immunosuppressive drug not only increased long-term kidney transplant survival rate from 15–20% but also reduced the rate of acute transplant rejection (108). Therefore, included articles from the 1980s and 1990s will increase the variability of short- and long-term graft survival and patient survival.

2: Deceased donor expanded criteria: Although some of the studies have reported kidney transplant survival by ECD or SCD, pooled reporting of graft survival in many other studies can be a source of heterogeneity in survival reports. Our findings showed that the one-year survival rate of a kidney transplant from SCD was three percent greater than ECD. This difference in the five-year patient survival rate increased to five percent. A systematic review study by Pascual et al. (109), which examined transplant outcomes from ECDs, reported no difference in graft and patient survival rates in comparison with SCDs according to single-center observational studies. In contrast, multicenter and registry-based studies found lower one-year to fifteen-year graft and patient survival in ECD recipients. Shortage of organ transplantation from living-related and living-unrelated donors led to the development of accepted standards for cadaveric transplantation and increased kidney transplant resources. In all of the articles that determined kidney transplant survival and patient's survival based on ECD and SCD included in this meta-analysis, ECD donors were: DDs older than 60 years and DDs 50 to 59 years old who met two of the following criteria: (1) history of hypertension, (2) cerebrovascular accident as a cause of brain death, and (3) final pre-procurement serum creatinine (SCr) level > 1.5 mg/dL. Also, a kidney that has a relative risk of rejection higher than 1.7 compared to the age group of 10 to 39 without hypertension and high creatine is considered an ECD

kidney. One of our inclusion criteria was the HR report for ECD compared to SCD. As shown in graph 12, only four studies, using Cox regression, measured the HR of graft loss for ECD. Our findings showed that HR of graft rejection for ECD donors was 14% higher than the standard group. OPTN/SRTR 2017 Annual Data Report (110) showed a dramatic increase in the number of deceased donation, and this increase in the age group of 18 to 34 years is more than other groups. Their report shows that despite a deceased donor increase, 18% have been discarded due to older age and diabetes. In summary, although ECD is associated with an increased risk of graft rejection in comparison with SCDs, the five-year increase in life expectancy of ECDs compared to dialysis patients makes the ECD kidney a better choice for ESRD treatment (111).

DBD vs. DCD

Although in 2009, only 10% of kidney transplants in the USA were DCD, this number increased to 15.8% in 2011 and about 20% in 2017 (112, 113). Even though the development of DCD transplantation policy and the importance of awareness of the outcomes of DCD recipients, one of the limitations of some of the articles in our study was that they did not report graft and patient survival according to the type of deceased donor and cause of death. We showed that one-year graft survival in DCD recipients was 5% lower than DBD recipients, whereas no differences were observed in one-year patient survival. Prolonged warm ischemia time, higher risk of ischemia-reperfusion injury,(114, 115), inferior quality of vessels, and/or endothelial activation (102) have been presented as the most important causes of lower graft survival in DCD recipients.

In one of the most extensive cohort studies in the UK, after adjusting the age of recipient and donor as well as cold ischemic time, the HLA mismatch level, number of HLA mismatches, HLA-DR mismatches, machine perfusion, and warm ischemic time showed no influence on graft rejection from DCD. According to the findings of this cohort, the age of the recipient and donor were the only factors affecting DCD graft rejection (116).

Although the incidence of DFG after DCD has been reported 27–73% in different studies (116–118), the practical factors such as donor and recipient age, cold ischemic time, and HLA-matching, make the result of kidney transplants from DCD acceptable compared to dialysis.

Conclusion

The findings of our study, which is the first comprehensive meta-analysis of graft and patient survival of the deceased donor, using all single-center, multicenter, and registry-based studies, show that overall, short-term and long-term graft and patient survival is desirable after kidney transplantation from DD. Our findings confirm that ECD recipients have lower graft survival rates than SCDs, and despite the shorter one-year survival rate in DCDs, the short-term patient survival rate is similar to DBDs. We also concluded that men had better survival than women but did not differ in graft survival.

Abbreviations

DD: deceased donor, DCD: donation after circulatory death, DBD: donation after brain death, EDCs: expanded-criteria donors, SCDs: standard-criteria donors, ESRD: End-Stage Renal Disease, HR: hazard ratio

Declarations

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Authors' contributions: MS conceived and designed the study. M-S MK-A were responsible for the collection of data and performing the statistical analysis and manuscript preparation. M-S and MK-A were responsible for checking the data. All authors were responsible for drafting the manuscript, and read and approved the final version.

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Figures

Figure 1

The flow of information through the different phases of the systematic review

Figure 2

1,2,3,5 and 10-year graft survival from deceased donor

Figure 3

1,3,5 and 10-year patient survival from deceased donor

Figure 4

1- year patient and graft survival year in DCD recipients

Figure 5

1, 5 and 15-year graft survival in DBD recipients

Figure 6

1 and 5-year patient survival in DBD recipients

Figure 7

1,3 and 5-year graft survival in ECD recipients

Figure 8

1,3 and 5-year patient survival in ECD recipients

Figure 9
1 and 3-year graft survival in SCD recipients

Figure 10
1 and 5-year patient survival in SCD recipients

Figure 11

Hazard ratio of graft rejection and patient death by age of donors

Figure 12

Hazard ratio of graft rejection and patient death by male sex of donors

Figure 13

Hazard ratio of graft rejection and patient death by ECD