

Deceased Organ Donor Characteristics and Organ Utilization in Israel, 2004–2013

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ABSTRACT: **Background:** The number of patients awaiting organ transplantation continues to exceed the number of available organs. **Objectives:** To document changes in the demographic characteristics of brain-dead, heart-beating organ donors over the past 10 years which may impact on organ utilization. **Methods:** Data were extracted from the Israel Transplant Registry and the Donor Action database for the 10 year period 2004–2013, inclusive. **Results:** The median age of the donors increased from 44 (range 3–73 years) to 53.5 years (range 1–79 years) ($P < 0.001$). There was a significant increase in the median age of donors of kidneys (33 to 51 years, $P < 0.001$), livers (41 to 53 years, $P < 0.001$) and lungs (40 to 49.5 years, $P < 0.001$). The number of donors dying from trauma decreased (34.5% to 20%, $P < 0.001$), while those with anoxic brain damage increased (14.5% to 25%, $P < 0.001$). The percent of male donors decreased over the study period, from 63% to 53%. An increase was noted in the mean number of organs transplanted per donor, from 3.29 to 3.82 per donor, due mainly to a significant increase in the utilization of lungs (31.5% to 51.3%, $P < 0.001$) and livers (76.3% to 82.4%, $P < 0.001$) while heart utilization decreased significantly since 2006 (40.9% to 17.5%, $P < 0.001$). **Conclusion:** Trends in the heart-beating, brain-dead organ donor pool in Israel over the past 10 years reveal significant changes in demographic characteristics which in the future will impact on the number of organs available for transplantation.

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KEY WORDS: organ donor, demographic data, organ transplantation

Organ transplantation is widely accepted as the best therapeutic and often life-saving option for many patients suffering from end-stage organ failure. However, in Israel as in many parts of the world, the number of patients awaiting transplantation continues to increase, far exceeding the number of organ donors. The result is that a significant number of patients die every year while on the waiting list.

In Israel, the largest source of organs for transplantation remains the brain-dead, heart-beating donor. Recent studies from around the world have documented significant shifts in the

demographic characteristics of organ donors, changes that may impact on the number of organs available for transplantation, i.e., organ utilization. Since no such study has been performed in Israel, we performed a retrospective, descriptive analysis to document organ donor demographic characteristics and organ utilization in Israel over the 10 year period 2004–2013.

PATIENTS AND METHODS

Data were extracted from the Israel Transplant registry and the Donor Action database for the 10 year period 2004–2013, inclusive. Donor data within the Israel Transplant registry were provided by transplant coordinators who serve all major hospitals in Israel. Donor Action is an international initiative that aims to alleviate organ shortage for transplantation through education and structured feedback of health professionals, allowing hospitals to improve donation rates through improved donation practices [1]. The program, which was adopted by Israel Transplant in 2004 as the national donor audit and quality control program, utilizes a standardized Medical Record Review that includes donor demographic data.

Permission to perform the study was obtained from the Israel Ministry of Health, which waived the need for Helsinki approval as this was a retrospective, observational study using data entered into central databanks.

Demographic data collected included age, gender and cause of death. Cause of death was defined as: i) anoxia, where the primary event was drowning, hanging, or following cardiac or respiratory arrest; ii) cerebrovascular accident (CVA), due to hemorrhage or infarction; and iii) trauma, due to motor vehicle/cycle crash, fall from a height, gunshot injury or other. The number and type of organ/s retrieved and transplanted from each donor as well as the number of donors who were treated in an intensive care unit were also noted.

For the purposes of the study, a donor was defined as a deceased person from whom at least one organ was retrieved and transplanted. Organ utilization was defined as all organs that were retrieved and subsequently transplanted (utilization = organ or organs transplanted/total number of donors). Organ counts were based on the number of organs retrieved to a maximum of seven (two kidneys, two lungs, heart, liver and

Table 1. Median age and gender of donors over the study period

Age	2004 (n=55)	2005 (n=53)	2006 (n=61)	2007 (n=47)	2008 (n=63)	2009 (n=61)	2010 (n=55)	2011 (n=80)	2012 (n=57)	2013 (n=74)
Median (years)	44	52	43	51.5	52	48.5	56	53.5	49.7	53.5*
Range (years)	3–73	3–83	1–74	5–79	1–73	2–75	2–78	1–80	1–83	3–79
< 18 (%)	20	15	14	5	19	8	9	13	12	8
18–29 (%)	20	13	14	7	15	9	7	11	14	13
30–39 (%)	3.6	5.6	10	8	4	14	10	11	9	10
40–49 (%)	18	13	25	22	8	19	5	8	16	8
50–59 (%)	12.7	22.6	11	22	29	23	31	24	12	13
60–69 (%)	20	26.4	17	18	18	20	22	21	21	33
> 70 (%)	5.4	4	8	18	6	8	16	12	14	14
Gender (% males)	63	60.3	62	68	55	50	62	51	54	53**

* $P < 0.001$ for 2004 vs. 2013** $P < 0.01$ for 2004 vs. 2013**Table 2.** Median donor ages for organs retrieved and transplanted

Year	Kidney	Liver	Lung	Heart	Pancreas
2004	33	41	40	26	27.5
2005	48.5	48	38	30	20
2006	43	43	42	33	27
2007	50	50	45	37	33
2008	49	40	52	21	22
2009	46	48.5	51	35	35
2010	48	57	57	43	32
2011	49.5	52.5	51	29	20.5
2012	47	49	45	29	27
2013	51*	53*	49.5*	28	26.5

* $P < 0.001$ for 2004 vs. 2013

pancreas). An extended-criteria donor was defined as a donor over 60 years old. A multi-organ donor was defined as a donor from whom ≥ 2 organs from different anatomical sites were retrieved and transplanted.

Data are presented as the mean with standard deviation or median with ranges, where appropriate. Changes in parameters studied over time were assessed using the chi-square test (IBM SPSS Statistics 19.0.1, 2010).

RESULTS

Donor age and gender are presented in Table 1. The median age increased from 44 (range 3–73) to 53.5 years (range 1–79) ($P < 0.001$). The percentage of donors under the age of 50 years decreased significantly from 61.6% in 2004 to 43% in 2013 ($P < 0.001$) while the percentage of extended-criteria donors (> 60 years) increased from 25.4% to 47% ($P < 0.001$). The percent of male donors over the study period decreased from 63% to 53% ($P < 0.01$). Regarding individual organs [Table 2], there has been a significant increase in the median age of kidney (33

Table 3. Cause of death over study period (%)

Year	CVA	Head injury	Anoxia	Other
2004	50.9	34.5	14.5	
2005	50.9	22.6	20.7	5.6
2006	34.4	34.4	19.6	11.4
2007	68	17	8.5	6.3
2008	50.7	22	25.3	1.6
2009	49.1	22.9	26.2	
2010	59	20	20	1
2011	44	28	28	1
2012	52	26	20	2
2013	53	20*	25*	2

* $P < 0.001$ for 2004 vs. 2013

CVA = cerebrovascular accident

Table 4. Organ utilization rates

Multi-organ donors* (%)	Organs/donor* (no.)	Pancreas (%)	Heart (%)	Liver (%)	Lung (%)	Kidney (%)	Year
33	3.29	14.5	30.9	76.3	31.5	71.5	2004
66	3.39	7.5	32	81	31	74.5	2005
83.6	3.9	21	40.9	75.4	46.5	78.5	2006
70.2	3.6	17	36	70.2	46.5	71	2007
84.1	3.9	20.6	33.3	79.3	51.5	78.5	2008
75.4	3.7	11.5	27.8	78.6	49.2	76.2	2009
69	3.1	5.7	21.1	75	40.3	62.5	2010
73.7	3.8	12.5	26	86	50	76.8	2011
80	3.74	12	28	86	52	72	2012
86.5**	3.82**	13.5	17.5**	82.4	51.3**	83.1	2013

*Organs retrieved and transplanted per donor

+ 2 or more organs from > 1 anatomical site

** $P < 0.001$ for 2004 vs. 2013** $P < 0.001$ for 2006 vs. 2013

to 51 years, $P < 0.001$), liver (41 to 53 years, $P < 0.001$) and lung donors (40 to 49.5 years, $P < 0.001$). There were no significant changes in age for heart or pancreas donors. Cause of death is presented in Table 3. The main cause of death over the entire study period was CVA (mean 51.2%) followed by trauma (mean 24.7%) and anoxia (mean 20.7%). There has been a significant change in cause of death over the study period, with a decrease in the number dying from trauma (34.5% to 20%, $P < 0.001$) and an increase in those with anoxic brain damage (14.5% to 25%, $P < 0.001$).

Organ utilization rates are shown in Table 4. Overall, the mean number of organs transplanted per donor increased from 3.29/donor in 2004 to 3.82/donor in 2013 ($P < 0.001$). There was a significant increase in the utilization of lungs (31.5% to 51.3%, $P < 0.001$) and livers (76.3% to 82.4%, $P < 0.001$), while kidney utilization has remained largely unchanged (71.5% to 72 %, $P = \text{NS}$). On the other hand, there was a significant decline in heart utilization since 2006 (40.9% to 17.5%, $P < 0.001$). The percentage of multi-organ donors increased from 33% in 2004 to 86.5% in 2013.

Over the study period the number of donors managed in intensive care units increased from 85% to 95.6%.

DISCUSSION

This first survey of its kind in Israel, summarizing trends in the demographic characteristics of deceased organ donors, revealed an aging donor pool with fewer male donors and fewer dying from head trauma. This resulted in changes in organ utilization, in particular increased utilization of organs from older liver and lung donors, flat utilization rates for kidneys, and a marked decrease in heart utilization.

The median age of organ donors increased significantly from 33 to 51 years ($P < 0.001$). In particular, the number of donors > 60 years, i.e., extended-criteria donors, has increased significantly, from 25.4% to 47%. Accepting older donors is the immediate result of an attempt to bridge the continuing gap between increasing transplant waiting lists in the absence of comparable increases in the number of transplants. This policy is, however, not universal. Thus, in Spain, 44.9% of donors are over the age of 60 compared to only 17.7% in the United States [2]. Increasing donor age may have important consequences for organ transplantation in both organ yield and organ quality. Regarding the former, donor age has been shown to affect organ retrieval in a concave manner, being highest at age 38 and declining as age either increases or decreases [3]. In our experience, organ yield was persistently and significantly higher in donors < 50 years old compared to those > 50 . However, while the number of organs retrieved from donors < 50 years remained largely static over the study period, it increased significantly for those > 50 years, largely due to increases in the number of transplanted kidneys, livers

and lungs in this age group. Regarding organ quality, this is known to be affected by advancing donor age. Thus, the utilization of older donor organs may lead to worse long-term survival following kidney transplantation [4], increase the relative risk of graft failure following liver transplantation [5], and result in a higher incidence of bronchiolitis obliterans syndrome following lung transplantation [6]. Donor age has also been associated with decreased patient survival after heart transplantation [7]. However, the reality of patients dying while awaiting transplantation has made it difficult for many centers to arbitrarily exclude organs from elderly donors. Instead, changes in retrieval strategies (e.g., shortening cold ischemic time as far as possible) and allocation policies (e.g., old-for-old kidney donation) [4,8] have resulted in more transplantations being performed from older donors with acceptable outcomes. In this regard, Ojo et al. [9] demonstrated that transplantation of a marginal kidney (the most common factor for being classified as a marginal donor was donor age > 55 years, which was present in 63.8% of the 7454 donors studied) was associated with a significant survival benefit when compared with maintenance dialysis. A recent paper from Italy, however, found significantly worse results when livers from donors > 70 years were transplanted (median age 74, range 70–86), and raises the question of an age limit [10].

Our survey also showed a decrease (63 to 53%) in the number of male as compared to female donors. This may have significance for organ utilization in view of reports of lower covariate-adjusted transplantation rates of organs from deceased males compared to females [11]. This mainly related to a greatly decreased transplantation rate of lung but also slightly lower liver and kidney rates. The reasons for these findings are not clear.

Significant changes in the cause of death have occurred over the study period. While most donors died following cerebrovascular accidents, there has been a significant decrease in those dying from head trauma. This may be explained at least in part by the consistent decrease in the number of fatal motor car crashes in Israel, from 427 in 2006–2007 to 289.5 in 2013–2014, a decrease of 48% [12]. This may also explain the decrease in male donors noted above, since more males than females were involved in fatal motor vehicle crashes. The number of donors dying following anoxic brain damage has increased. A possible reason is the increased access to early defibrillation following cardiac arrest, namely, increased defibrillators present in public and private facilities, increased competence of the public in performing cardiopulmonary resuscitation, and rapid arrival of emergency medical teams. Another explanation is the increased awareness by health care personnel of the possibility of organ donation, so that intensive therapy is applied and continued even in the presence of severe, persisting neurological deficits following cardiac arrest. Cause of death may influence both the number of organs retrieved and transplanted per donor

and the quality of the transplanted organs. Thus, organ yield per donor is higher when the cause of death is trauma relative to cerebrovascular accident (older subjects with associated comorbidities often associated with end-organ dysfunction) and anoxia (ischemic damage to organs, especially kidneys, liver and heart) [3]. Cause of death may also influence the quality of the transplanted organs, and CVA as cause of death has been associated with a higher incidence of graft failure following kidney transplantation [13] and decreased patient survival after heart transplantation [7].

Optimizing organ utilization in the face of changes in donor characteristics remains a prime focus for transplant agencies worldwide. We noted an increase in organs retrieved and transplanted per donor from 3.29 in 2004 to 3.82 in 2013. This was largely due to a significant increase in lung utilization rates, while lower increases were also noted for kidneys and livers. An increase in organ utilization may be due to one of two factors: improved donor management and/or broadened criteria for organ acceptance by transplant surgeons. Regarding the former, brain death is associated with widespread physiological and cellular abnormalities associated with ischemia/reperfusion injury [14]; it may also evoke an inflammatory response leading to endothelial dysfunction and cytokine release [15]. Despite these changes, it has been shown that optimizing cardiovascular performance in particular may result in significant increases in organ yield [16]. In this regard, donor management strategies have been protocolized and standardized throughout Israel and incorporate current internationally accepted practices [17,18]. These strategies, to optimize ventilatory and hemodynamic support and maintain volume status, normothermia and electrolyte balance, are aimed at achieving well-defined donor management goals. Achieving these goals has led to an increased number of organs transplanted per donor [19,20]. The management of these donors is work and technology intensive and the number of donors admitted to and managed in intensive care units in Israel has increased from 85% in 2004 to over 95% in 2013. The other potential reason for an increase in organ utilization relates to broadened criteria for organ acceptance, and specific interventions have been implemented in Israel to limit the possible negative impact of these so-called extended-criteria organs. These include shortening ischemic times (e.g., starting liver transplantation at the same time as the retrieval procedure) and increased use of machine perfusion of kidneys, which may improve their function while allowing functional assessment prior to transplantation. Finally, however, transplant surgeons assess suitability for transplantation according to the function of each organ, which is ultimately dependent on optimal donor management.

This study has some limitations. Firstly, we have not reported transplant outcomes, particularly in light of the increasing number of extended-criteria donors. Secondly, we did not discuss the reasons for non-utilization of those organs not transplanted.

While this was usually related to poor function of a particular organ, other reasons included lack of a suitable recipient (particularly organs from very young donors or those with hepatitis). Studies to further elucidate these two limitations are currently being planned.

In conclusion, trends in the heart-beating, brain-dead organ donor pool in Israel over the past 10 years revealed significant changes in demographic characteristics which may impact on the number of organs available for transplantation. While improved donor management and broadened organ acceptance criteria may result in increased organ utilization for some organs, the limit for these interventions may have been reached. Increasing use of additional sources for organ donation, including living donation, donation after the cardio-circulatory determination of death (DCD), and the use of artificial devices (left ventricular assist devices) need to be further explored and encouraged.

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