Trends in brain-dead organ donor characteristics: a 13-year analysis

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Background: Driven by disease trends, such as obesity and metabolic syndrome, that are increasingly prevalent in the general population, we aimed to evaluate the comorbidities and attributes of the brain-dead organ donor population over time in a longitudinal study.

Methods: We compared overall health and baseline attributes of organ donors between 2000–2005 and 2006–2012 using our prospective transplant database. Descriptive and comparative analyses of the 2 historical cohorts were performed.

Results: A total of 1040 brain-dead organ donors were included in our analysis: 496 from the 2000–2005 period and 544 from the 2006–2012 period. Our analysis revealed that donors from the recent (2006–2012) period were more likely to have increased body mass index (26.4 ± 6.0 v. 25.0 ± 4.8 , $p = 0.003$), smoking history (57.0% v. 27.2%, $p < 0.001$), coronary artery disease (14.3% v. 3.2%, $p = 0.015$) and dyslipidemia (19.1% v. 4.2%, $p < 0.001$), but less likely to have concurrent infection (1.1% v. 7.9%, $p < 0.001$) than those from the earlier period.

Conclusion: Our data suggest that the characteristics and comorbidities of brain-dead organ donors have somewhat deteriorated over the last decade. Further studies are needed to evaluate the impact of these health attributes on donated organ utilization and outcomes.

Contexte : Comme la prévalence de l'obésité et du syndrome métabolique est actuellement en hausse dans la population générale, nous avons voulu évaluer, dans une étude longitudinale, les comorbidités et les caractéristiques de la population de donneurs d'organes en état de mort cérébrale au fil du temps.

Méthodes : Nous avons comparé la santé globale et les caractéristiques de base des donneurs d'organes de 2000–2005 et de 2006–2012 au moyen de notre base de données prospective sur les greffes. Des analyses descriptives et comparatives des 2 cohortes ont été effectuées.

Résultats : Au total, 1040 donneurs d'organes en état de mort cérébrale ont été inclus dans notre analyse : 496 de la période de 2000–2005 et 544 de la période de 2006–2012. Notre analyse a révélé que les donneurs de la période récente (2006–2012) étaient plus susceptibles d'avoir un indice de masse corporelle élevé ($26,4 \pm 6,0$ c. $25,0 \pm 4,8$, $p = 0,003$), des antécédents de tabagisme (57,0 % contre 27,2 %, $p < 0,001$), une coronaropathie (14,3 % c. 3,2 %, $p = 0,015$) et une dyslipidémie (19,1 % c. 4,2 %, $p < 0,001$), mais moins susceptibles d'avoir une infection concomitante (1,1 % c. 7,9 %, $p < 0,001$) que ceux de la période antérieure.

Conclusion : Nos données semblent indiquer que les caractéristiques et les comorbidités des donneurs d'organes en état de mort cérébrale se sont quelque peu détériorées au cours de la dernière décennie. D'autres études sont nécessaires pour évaluer l'incidence de ces caractéristiques de santé sur l'utilisation des organes donnés et les résultats.

Despite the efforts of the transplant community to address the urgent need for donor organs, the disparity between the number of patients on the waiting list and available donor organs remains substantial.¹ It is now well recognized that solid organ transplantation is the most definitive and effective treatment for end-stage liver disease and kidney failure. Innovative measures, such as the use of split livers^{2–4} and living-related donation,^{5,6} have been

developed to try to reduce the gap between transplantable organ supply and demand. In fact, in 2001 in the United States, the use of living-related donor organs increased considerably to surpass the number of deceased organ donor procurements (52% v. 48%). Evidently the donation patterns of transplant centres are influenced by many factors, such as death and donation rates, allocation policy, listing regulations and usage of expanded criteria donors (ECD). Recently, Redelmeier and colleagues⁷ reported on the organ donation trends in Ontario, Canada. This population-based cohort study reported a small donation rate, yet noted a significant increase in deceased donors over a 16-year period.

On the other hand, population-based epidemiological studies from North American data suggest a persistent growth in the prevalence of certain disease states, such as metabolic syndrome.⁸ For instance, metabolic syndrome is defined by the presence of several risk factors, such as obesity, hyperlipidemia, diabetes and hypertension, all of which have their own negative impact on morbidity and mortality.^{9,10} Moreover, metabolic syndrome has been associated with fatty liver disease, steatosis and liver fibrosis^{11–13} as well as chronic kidney disease.^{14–16} Since deceased donors consist of a portion of the general population, such epidemiological changes and disease trends could potentially be reflected into the organ donor pool. Multiple clinical, biochemical, technical and ethical factors already play a role in organ donation discussions, but worse comorbidities and unfavourable metabolic profiles may potentially further challenge the decision to consider organ donation. Although multiple national reports on organ donation trends exist,^{17,18} data on specific characteristics and comorbidities of deceased donors are scarce.

We postulated that as some disease trends, such as metabolic syndrome, are increasingly prevalent in the general population, demographic characteristics of brain-dead organ donors might also be affected. We thus aimed to evaluate the changes in brain-dead organ donor characteristics in a longitudinal study over a period of 13 years, using the registry of deceased donors procured by our institution.

METHODS

Organ donor population

This study was approved by the McGill University Health Center (MUHC) and the Transplant Quebec Research Ethics Boards (REBs). All eligible brain-dead organ donors identified between January 2000 and December 2012 who donated 1 or more organs to a patient from the MUHC were included in the study. The donor inclusion criteria included only brain-dead donors who were 18 years of age or older. For the purpose of this study, living-related donors and donation after cardiac death (DCD) were excluded from the analysis. The extracted data from our prospective transplant database were limited to organ donor characteristics, such as donor age; sex; race; cause of death; ABO group; body mass

index (BMI); glomerular filtration rate (GFR) before procurement; history of smoking, coronary artery disease, hypertension, diabetes or dyslipidemia; history of malignancy or drug abuse; and presence of an active infection.

Brain death was declared as standard and defined as complete loss of motor or respiratory drive, absence of brainstem reflexes in the context of an irreversible injury and absence of metabolic or contributing reversible injuries.^{19–22} The donor GFR was calculated using the 4 variables in the Modification of Diet in Renal Disease (MDRD) Study:²³ serum creatinine, age, race and sex. For the causes of brain death, anoxic brain injury included brain death after events like respiratory or cardiac arrest, poisoning (e.g., carbon monoxide), drug overdose or drowning. Traumas causing brain death included motor vehicle accidents as well as penetrating and blunt traumatic head injuries. Although florid septicemia and severe infections were a contraindication to organ donation, presence of an infectious source (bacteremia, fungemia) did not preclude organ donation candidacy.²⁴ Expanded criteria donors are defined as those aged 60 years or older, or older than 50 years with at least 2 of the following conditions: hypertension history, serum creatinine > 1.5 mg/dL, or death due to stroke, which are the criteria used by the United Organ Sharing Network (UNOS).²⁵

Statistical analysis

Categorical and continuous variables are expressed as summary statistics (number, percentage, median, range, mean, standard deviation); all comparisons between groups were carried out using a 2-sided test. We used the Fisher exact test or the χ^2 test (for categorical variables) and the Wilcoxon rank-sum test (for continuous non-normally distributed variables) to assess differences between the groups. To identify variables independently associated with a time period (recent 2006–2012 v. remote 2000–2005), we performed multivariable logistic regression analyses. We considered results to be significant at $p < 0.05$. All analyses were performed using JMP statistics software version 11.0 (SAS).

RESULTS

Characteristics of organ donors

After excluding living-related donations and DCD donors, a total of 1040 brain-dead organ donors were included in this study (Fig. 1). A median of 84 (range 79–87) organ donor procurements were performed yearly during the study period. The median age of donors was 47 (range 31–58) years, and 586 (56.3%) were men. Donor BMI was greater than 30 in 133 (12.8%) cases. Among the 1040 donors, almost half (42.8%) had a smoking history, followed by hypertension (24%), dyslipidemia (12.0%), diabetes (6.8%) and coronary artery disease (4.8%; Fig. 2). The 3 most common causes of brain death were cerebrovascular events (586, 56.3%),

followed by trauma (241, 23.2%) and anoxic brain injury (133, 12.8%). The ratio of expanded criteria donors over standard criteria donors significantly increased over time, (Fig. 3).

Comparison of organ donor characteristics over time

The cohort was divided into 2 time periods — remote (2000–2005) and recent (2006–2012) — to evaluate changes over time in organ donor demographic profile and comorbidities. Baseline characteristics and comorbidities of the 2 groups are detailed and compared in Table 1. In fact, significant differences were noted between the 2 time periods in terms of donor age, BMI, history of smoking, hypertension, hyperlipidemia, diabetes and coronary artery disease (Table 1). Interestingly, there were fewer donors with documented infection at the time of procurement in the recent period (1.1% v. 7.9%, $p < 0.001$). The causes of death were also significantly different between the 2 time periods: in the recent period, fewer donors died as a result of trauma (19.7% v. 27.0%, $p < 0.001$), and more died from anoxic brain injury (17.3% v. 8.1%, $p < 0.001$), consistent with previously published North American data.¹⁷ Moreover, although the distribution of donors' average BMI did not demonstrate a steady slope year after year, there was increasing risk of BMI above 30 compared with the baseline period (Fig. 3A) and a significant increase in BMI above 30 over time (Fig. 3B).

Analysis of significant donor characteristics related to period of procurement

Since many of the variables analyzed were potentially related and concomitantly present as comorbidities, we wanted to ascertain independent predictors of the recent time period (2006–2012) compared with the remote period (2000–2005). The initial descriptive analysis demonstrated significantly greater associations of BMI, smoking history, coronary artery disease, hyperlipidemia and infection with procurements performed in the recent years. The multivariable logistic regression (Table 2) confirmed that several variables were independently predictive of the recent time period: BMI, smoking history, coronary artery disease, hyperlipidemia (more likely in the recent time period) and presence of infection (less likely in the recent time period). In addition, there were more women and better renal function among donors in the recent time period.

DISCUSSION

Organ transplantation is a life-saving treatment for many patients with acute or chronic solid organ failures. As a result of this ultimate and definitive therapy, more patients are considered eligible for organ transplantation, contributing to the persistent discrepancy between potential recipients and

Fig. 1. Organ donors included in the analysis.

available donated organs. The usage of ECD in kidney transplantation was an attempt to counterbalance the organ shortage crisis, and although initial studies reported lower survival after transplantation from ECD than from standard donors,^{26–28} some recent studies have reported more encouraging results.^{29,30} In parallel to these facts occurring in the transplant community, statistics resulting from public health surveillance institutes are all pointing toward a growing prevalence of chronic diseases, such as obesity, diabetes, hypertension, dyslipidemia and coronary artery disease; all of which contribute to an overall worsening health status among the general population, and hence the deceased standard criteria donor pool as well. Our aim was to characterize the trends in comorbidities and physical health attributes of organ donors over more than a decade. Our results indicate that there is a statistically significant increase in comorbidities, such as increased obesity, hyperlipidemia, smoking history and coronary artery disease, suggestive of an overall poorer health status. It may be argued that some of the significant variables probably reflect an increase in the use of ECD by the transplant centres and especially that the ratio of ECD increased over time. However, the situation in our centre may reflect that the increase in comorbidities among donors is associated with the increase in comorbidities in the general population, and this is evidenced by the stability of organs donated over time. There are 2 liver transplantation

centres in the province of Quebec, and ours is the only multiorgan site. We share the brain death donors under the management of Transplant Quebec. Our centre receives organs from about 75% of the donors, and our provincial donation rate has been stable over the last decade (around 120–130 donors each year); therefore, our data at least represent the situation of the whole province. We therefore are confident that there was no donor selection bias in our cohort and that the application of ECD worldwide did not affect our donor selections.

Also, because the rate of ECD use has been increasing^{29,31} and the total number of eligible donors increases at a slower rate,¹⁸ this suggests that the proportion of eligible donors with “bad” criteria has been rising at the expense of more healthy donors. Therefore, the worsening donor characteristics are most likely not related to surgeons’ willingness to procure organs from ECD, but rather to a donor pool of gradually poorer quality. Most of the variables we describe in the present study have been previously found to be associated with worse outcomes after transplantation.^{32,33} For instance, obesity has been reported to be associated with inflammation and modified immune responses,³² potentially impacting allorecognition and alloimmunity. Another argument may be that the difference in BMI between the remote and recent periods in our study was only 1.4 and that we may have overestimated the role

Fig. 2. Organ donors by period and donor category. 0 = standard criteria donors; 1 = expanded criteria donors.

of BMI. However, although such a difference might not be significant in general population, the higher BMI in the recent period of our study impacted the organ quality of the donors. Increasing obesity in the general population affects the BMI of organ donors, which causes problems for transplantation. Orman and colleagues³³ analyzed BMI over 15 years (1995–2010) and found that BMI increased

significantly in the past 15 years in the United States, which is consistent with our results. They also reported that obesity might not only affect the quality of the donated livers,^{11–13} but also of donated pancreas.³³ Declining health characteristics of the donor population may consequently have a negative impact on multiple potential solid organs.

Fig. 3. (A) Risk of body mass index (BMI) > 30 of organ donors procured by time period. **(B)** Percentage of organ donors by BMI category and time period. CI = confidence interval.

Limitations

We acknowledge that our study has some limitations. First, the data were derived from a single institution's transplant centre, which poses a limitation in terms of sam-

ple size and selection bias. Our centre's expertise lies in kidney, liver and pancreas transplantation, therefore the organ donation attributes will correspond to the recipients treated at our centre who required those donated organs. Although the number of organ procurements performed

Table 1. Baseline characteristics and comorbidities of organ donor population by time period (n = 1040)

Donor characteristic	Time period; no. (%) [*]		p value
	Remote cohort (2000–2005) n = 496	Recent cohort (2006–2012) n = 544	
Age, median (IQR), yr	46 (30–57)	49 (33–60)	0.006
Sex			0.29
Male	283 (57.1)	292 (53.7)	
Female	213 (42.9)	252 (46.3)	
Race			0.58
White	452 (91.1)	502 (92.3)	
Black	4 (0.8)	2 (0.4)	
Cause of death			< 0.001
Cerebrovascular/stroke	276 (55.6)	310 (57.0)	
Trauma†	134 (27.0)	107 (19.7)	
Anoxic brain injury‡	40 (8.1)	94 (17.3)	
Tumour	2 (0.4)	1 (0.2)	
Other/unknown	44 (8.9)	32 (5.9)	
ABO group§			0.76
A	202 (40.8)	223 (41.1)	
AB	22 (4.4)	18 (3.3)	
B	57 (11.5)	69 (12.7)	
O	214 (43.2)	233 (42.9)	
BMI, mean ± SD	25.0 ± 4.8	26.4 ± 6.0	0.003
GFR, median (IQR), mL/min/1.73 m ²	101.6 (76.7–128.3)	104.2 (78.2–138.2)	0.18
Smoking history	135 (27.2)	310 (57.0)	< 0.001
Hypertension history	83 (16.7)	140 (25.7)	< 0.001
Hyperlipidemia	21 (4.2)	104 (19.1)	< 0.001
Diabetes mellitus	21 (4.2)	50 (9.2)	0.002
CAD history	16 (3.2)	78 (14.3)	< 0.001
History of malignancy	0 (0)	12 (2.2)	< 0.001
Presence of infection	39 (7.9)	6 (1.1)	< 0.001

BMI = body mass index; CAD = coronary artery disease; GFR = glomerular filtration rate; IQR = interquartile range; SD = standard deviation.

^{*}Unless indicated otherwise.

†Includes motor vehicle accidents and other penetrating/blunt traumatic injury.

‡Includes drug intoxication and drowning.

§Based on n = 1038 (missing data for 1 donor per group).

Table 2. Forward stepwise multivariable logistic regression analyses depicting independent donor characteristics predicting their odds in the recent time period compared with the remote time period

Donor characteristic	OR	95% CI	SE	z	p value
Smoker	3.80	2.67–5.41	0.69	7.41	< 0.001
Hyperlipidemia	3.32	1.74–6.33	1.09	3.65	< 0.001
Infection	0.19	0.07–0.54	0.10	–3.17	0.002
BMI > 30	2.06	1.28–3.32	0.50	2.98	0.003
4th quartile (good) renal function	1.69	1.12–2.56	0.36	2.49	0.013
CAD	2.13	1.07–4.24	0.75	2.16	0.030
Female	1.43	1.01–2.03	0.25	2.03	0.042

BMI = body mass index; CAD = coronary artery disease; CI = confidence interval; OR = odds ratio; SE = standard error.

by our centre constitutes 75% of the total provincial donor pool,³⁴ our results can still not be generalized to a national level. Moreover, the impact of the deteriorating quality of deceased donors on the organ recovery and discard rate is still unclear. It has been previously shown that some donor attributes, notably older donor age, higher BMI, diabetes and DCD, are all independently associated with organ nonrecovery. Although these data could be extrapolated to our findings, further research would be required to correlate the physical attributes and comorbidities of deceased donors to organ utilization.

CONCLUSION

The present longitudinal analysis of 1040 brain-dead organ donors demonstrates overall worsening of general health attributes and comorbidities in this population. More research is required to evaluate the impact of these findings on organ utilization patterns and recipient outcomes.

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Contributors: P. Metrakos designed the study. M. Hassanain, M. Aljiffry, A. Aloraini and A. Madkhali acquired the data, which E. Simoneau and S. Doi analyzed. M. Hassanain, E. Simoneau, A. Aloraini and A. Madkhali wrote the article, which all authors reviewed and approved for publication.

References

1. Sheehy E, Conrad SL, Brigham LE, et al. Estimating the number of potential organ donors in the United States. *N Engl J Med* 2003; 349:667-74.
2. Busuttil RW, Goss JA. Split liver transplantation. *Ann Surg* 1999; 229:313-21.
3. Azoulay D, Castaing D, Adam R, et al. Split-liver transplantation for two adult recipients: feasibility and long-term outcomes. *Ann Surg* 2001;233:565-74.
4. Doyle MB, Maynard E, Lin Y, et al. Outcomes with split liver transplantation are equivalent to those with whole organ transplantation. *J Am Coll Surg* 2013;217:102-14.
5. Slooff MJ. Reduced size liver transplantation, split liver transplantation, and living related liver transplantation in relation to the donor organ shortage. *Transpl Int* 1995;8:65-8.
6. D'Alessandro AM, Sollinger HW, Knechtle SJ, et al. Living related and unrelated donors for kidney transplantation. A 28-year experience. *Ann Surg* 1995;222:353-64.
7. Redelmeier DA, Markel F, Scales DC. Organ donation after death in Ontario: a population-based cohort study. *CMAJ* 2013;185:E337-44.
8. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. *Diabetes Care* 2004;27:2444-9.
9. Eckel RH, Kahn R, Robertson RM, et al. Preventing cardiovascular disease and diabetes: a call to action from the American Diabetes Association and the American Heart Association. *Circulation* 2006;113:2943-6.
10. Grundy SM. Metabolic syndrome: a multiplex cardiovascular risk factor. *J Clin Endocrinol Metab* 2007;92:399-404.
11. Marceau P, Biron S, Hould FS, et al. Liver pathology and the metabolic syndrome X in severe obesity. *J Clin Endocrinol Metab* 1999;84:1513-7.
12. Hamaguchi M, Kojima T, Takeda N, et al. The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. *Ann Intern Med* 2005;143:722-8.
13. Hanley AJ, Williams K, Festa A, et al. Liver markers and development of the metabolic syndrome: the insulin resistance atherosclerosis study. *Diabetes* 2005;54:3140-7.
14. Chen J, Muntner P, Hamm LL, et al. The metabolic syndrome and chronic kidney disease in U.S. adults. *Ann Intern Med* 2004;140:167-74.
15. Vogt BP, Souza PL, Minicucci MF, et al. Metabolic syndrome criteria as predictors of insulin resistance, inflammation and mortality in chronic hemodialysis patients. *Metab Syndr Relat Disord* 2014;12:443-9.
16. Lin JH, Wu HC, Huang WH, et al. Association between management of metabolic syndrome and progression of early-stage chronic kidney disease: an observational cohort study. *Ren Fail* 2015;37:29-36.
17. Nathan HM, Conrad SL, Held PJ, et al. Organ donation in the United States. *Am J Transplant* 2003;3(Suppl 4):29-40.
18. Wolfe RA, Roys EC, Merion RM. Trends in organ donation and transplantation in the United States, 1999-2008. *Am J Transplant* 2010;10:961-72.
19. Wijdicks EF. The diagnosis of brain death. *N Engl J Med* 2001;344:1215-21.
20. Wijdicks EF. Brain death worldwide: accepted fact but no global consensus in diagnostic criteria. *Neurology* 2002;58:20-5.
21. Wijdicks EF, Varelas PN, Gronseth GS, et al. Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2010;74:1911-8.
22. Wood KE, Becker BN, McCartney JG, et al. Care of the potential organ donor. *N Engl J Med* 2004;351:2730-9.
23. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate. *Ann Intern Med* 2006;145:247-54.
24. Angelis M, Cooper JT, Freeman RB. Impact of donor infections on outcome of orthotopic liver transplantation. *Liver Transpl* 2003;9:451-62.
25. Metzger RA, Delmonico FL, Feng S, et al. Expanded criteria donors for kidney transplantation. *Am J Transplant* 2003;3(Suppl 4):114-25.
26. Pascual J, Zamora J, Pirsch JD. A systematic review of kidney transplantation from expanded criteria donors. *Am J Kidney Dis* 2008;52:553-86.
27. Schnitzler MA, Whiting JF, Brennan DC, et al. The expanded criteria donor dilemma in cadaveric renal transplantation. *Transplantation* 2003;75:1940-5.
28. Alexander JW, Zola JC. Expanding the donor pool: use of marginal donors for solid organ transplantation. *Clin Transplant* 1996;10:1-19.
29. Stratta RJ, Rohr MS, Sundberg AK, et al. Increased kidney transplantation utilizing expanded criteria deceased organ donors with results comparable to standard criteria donor transplant. *Ann Surg* 2004;239:688-97.
30. Matsuoka L, Shah T, Aswad S, et al. Pulsatile perfusion reduces the incidence of delayed graft function in expanded criteria donor kidney transplantation. *Am J Transplant* 2006;6:1473-8.
31. Sung RS, Guidinger MK, Lake CD, et al. Impact of the expanded criteria donor allocation system on the use of expanded criteria donor kidneys. *Transplantation* 2005;79:1257-61.
32. Heimbokel T, Floerchinger B, Schmider A, et al. Obesity and its impact on transplantation and alloimmunity. *Transplantation* 2013;96:10-6.
33. Orman ES, Barritt AS, Wheeler SB, et al. Declining liver utilization for transplantation in the United States and the impact of donation after cardiac death. *Liver Transpl* 2013;19:59-68.
34. *Annual report 2014-2015*. Transplant Québec. Available: http://transplantquebec.ca/sites/default/files/ra_1415_lowres.pdf (accessed 2016 Feb. 18).