R Open Source Programming Code for Calculation of the Kidney Donor Profile Index and Kidney Donor Risk Index

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Abstract

Background: The Kidney Donor Profile Index (KDPI) and Kidney Donor Risk Index (KDRI) were developed by the United States Organ Procurement and Transplantation Network (OPTN). They may influence the clinical decision whether to accept or discard a donor kidney, but still there are debates about KDPI/KDRI applicability and its consequences. To further evaluate these indexes in different populations, more data should be analyzed, and a universally applicable program code would facilitate it. Currently, KDPI/KDRI calculation could be readily done only on the OPTN website that is convenient for a single donor, but not suitable for processing data sets with many records. *Summary:* A universally applicable program algorithm in widely used R language for calculating KDPI and KDRI was developed according to donor factors and coefficients described in the OPTN guide. *Key Messages:* The open R code permits to calculate KDPI/KDRI either for a single donor or for an unlimited number of records in large data sets. The presented software code would save substantial time to research groups all over the world and help to clarify the KDPI/KDRI role in global settings.

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Introduction

The practice of science is changing rapidly, and open access is one of the principal drivers of these changes. In the field of clinical trials, a data-sharing statement is obligatory since July 2018 [1] and serves as an important step on the way to the all-round sharing of de-identified data. One of the most prominent open data repositories was established in 2000 by The National Heart, Lung, and Blood Institute of the National Institutes of Health and resulted in a substantial number of requests for data use and subsequent publications [2]. Since then, many other repositories were established by different stakeholders, from universities (http://dataverse.harvard.edu) to industry (https://clinicalstudydatarequest.com). Sharing primary data would flourish the analysis and provision of its results as a public good.

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Open access has also changed the world of analytical software, and the R project (https://www.r-project.org/) has become the most widely used software for analysis of biomedical data and has substantially outrun all commercial counterparts [3].

Thus, in medicine there are free data and free software for analysis. What is lacking in the field of different medical specialties is a repository of programming algorithms available to readily use and re-use by a wide research community. In case of R, diverse packages for sophisticated analysis have been independently designed by scientists across the globe, but for the specific nephrology needs there is only one package, "nephro" [4], containing functions for calculation of glomerular filtration rate by different equations. Due to this, every research group needs to write the code for the same scores and equations, spending substantial resources for performing work already done by others. The nephrology community needs to start to publish a universally applicable code of programming algorithms intended to use in nephrology, and this article introduces the open source R programming code for calculation of the Kidney Donor Profile Index (KDPI) and Kidney Donor Risk Index (KDRI). KDRI was developed by Rao et al. [5], and later the United States Organ Procurement and Transplantation Network (OPTN) adapted and modified it and introduced the KDPI to facilitate the interpretation [6]. Currently, only the web-based calculator for KDPI and KDRI is available on the OPTN website (https://optn.transplant.hrsa.gov/resources/allocation-calculators/kdpi-calculator/) that is useful for single-patient consideration, but not suitable for the processing of clinical trials or observational study data sets.

Materials and Methods

A universally applicable program algorithm in R language for calculating KDPI and KDRI was developed according to donor factors and coefficients described in the OPTN guide for calculating and interpreting KDPI/KDRI values for the years 2015–2017 (latest available) [6]. The structure of the presented R code lets easily adopt it to the subsequent OPTN revisions. The function uses the donor parameters (online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000492427), custom labels for parameters in the user's data set (online suppl. Table 2), and several general parameters (online suppl. Table 3). The appropriately documented R code of the algorithm is listed in the online supplementary material. The R code is presented as a function in the online supplementary material. It was incorporated in the R package *kidney.epi* which is available on the Comprehensive R Archive Network (CRAN) at https://cran.r-project.org/web/packages/kidney.epi/index.html, and could be installed by any R user with the *install.packages("kidney.epi")* instruction. Current implementation of the function includes mapping tables with the OPTN coefficients for the years 2015, 2016, and 2017, and could be updated upon the new OPTN revisions. The function was tested in the R version 3.4.3.

Results

The list of arguments for R function is defined by the OPTN guide and includes age, height, weight, ethnicity, history of hypertension and diabetes, cause of death, creatinine, hepatitis C virus (HCV) status, and circulatory death status for deceased donor (online suppl. Table 1). All these parameters are transferred as the named arguments to the R function, as is shown in the example below:

ktx.kdpi.optn (age = 30, height_cm = 176, weight_kg = 82, ethnicity = 'White',

hypertension = 'NA', diabetes = 'no', causeofdeath = 'roadinjury', creatinine = 150,

hcv = 'negative', dcdstatus = 'no', creatinineunits = 'micromol/l', return_output_type = 'KDPI', mapping_values_year = 2016)

The algorithm is maximally flexible to be easily adapted to application on any data set by modification of the function arguments values in the R code (see online supplementary material). Thus, in the provided function the positive history of hypertension by default is defined as "yes." In case a data set has a definition "1" or "HTN" for it, the following string of R code could be easily modified to fit any particular definition:

 # label for a positive history of hypertension
label_hypertension_positive = c ('yes', 1, 'HTN')

For some donors, the history of hypertension or diabetes could be unknown, and thus during the calculation of KDRI, the chance of having one of these conditions according to the OPTN guide should be assumed the same as for a randomly selected donor. The R function contains label definitions for the unknown statuses that also could be customized based on the "not available" values used in a particular data set in the following R code strings:

 # label for an unknown history of hypertension
label_hypertension_unknown = 'NA'

Noteworthy regarding these unknown values is that even if the data set has missing values, which are by default defined in R as *NA*, the definition in the aforementioned code has to include quotes (i.e., *'NA'*) due to the subsequent function algorithm.

In the presented R function, age has to be expressed in years, while height could be expressed either in cm (by us-

ing function argument *height_cm*) or in feet and inches (by using arguments *height_ft* and *height_inch*). Similarly, weight could be defined either in kg (by using function argument *weight_kg*), or in pounds (by argument *weight_lb*). Serum creatinine could be expressed either in mg/dL, micromol/L, or mmol/L – with the definition of dimension in the *creatinineunits* argument of the function (by default assuming that creatinine is measured in micromol/L).

By default, the parameter *mapping_values_year* is set to the *"latest,"* and the function takes the latest available OPTN mapping table and coefficients from the R function. However, a user could set parameter *mapping_values_year* to the exact year (for example, *mapping_values_year = 2016*) to perform mapping to OPTN coefficients for a given year. The list of available years with OPTN mapping values in the R function is available by the function *ktx.kdpi.optn.show.years()*.

The output of the R function depends on the argument *return_output_type*, which could be one of the three values. Depending on the chosen value, the code mentioned above will produce the following:

ktx.kdpi.optn (… , return_output_type = 'KDRI_Rao')
[1] 0.995
ktx.kdpi.optn (… , return_output_type = 'KDRI_median')
[1] 0.82
ktx.kdpi.optn (… , return_output_type = 'KDPI')
[1] 30

KDRI Rao (*kdri_rao*) could be interpreted as the relative risk of post-transplant graft failure for a given donor compared to a reference healthy 40-year-old donor defined by Rao et al. [5], and in the aforementioned example the value 0.99 refers to almost the same risk of graft failure in comparison with a reference donor.

The median KDRI (*kdri_median*) could be interpreted as the relative risk of post-transplant graft failure for a given donor compared to the median kidney donor recovered in the previous year. This value is scaled to the median KDRI that was 1.20659821120231 for the year 2016, and the value 0.82 in the example above indicates decreased by 18% risk of graft failure in comparison to a median deceased donor for the year 2016.

KDPI percent (*kdpi_percent*) is just a mapping of the KDRI from a relative risk scale to a cumulative percentage scale, specific to each year. Lower KDPI values are associated with increased donor quality and expected longevity. In the considered example, the value 30% means that the estimated risk of kidney graft failure from this donor is higher than in 30% and lower than in the other 70% of all kidney donors recovered in 2016.

In case of KDPI calculation for all data set, the function output should be assumed to a new variable(s):

dta$kdpi <- ktx.kdpi.optn (dtaage, dtaheight, dta$weight, dta$ethnicity, dta$hypertension, dta$diabetes, dta$causeofdeath, dta$creatinine, dtahcv, dtadcdstatus, creatinineunits = 'micromol/l', return_output_type = 'KDPI')

Discussion

This article presented the open source program code, written in widely used R language, for calculation of KDPI and KDRI according to the OPTN algorithm. KDPI was introduced in 2012 for supporting the new kidney allocation system in the USA, and has raised a lot of interest as a graft failure prediction tool. At least in the USA, KDPI has a potential to influence the clinical decision on whether to accept or discard a donor kidney, but there is no uniform view on its robustness since the graft outcomes depend also on other donor factors and recipient characteristics. Up to now, there have been a lot of debates about KDPI, and while some authors found its use increased the acceptance of donors and lead to rise in transplantation rate [7] and robustly predicted kidney graft survival [8], others doubted about its generalizability to non-US [9] and non-adult populations [10, 11], and caution about formal KDPI use as a criterion of organ discard [12, 13]. KDPI >85% is thought to be equivalent to an extended criteria donor (ECD) kidney (while the KDPI is based on 10 parameters, the historical ECD definition is based on only 4 parameters), but almost twice less donors were classified as ECD according to KDPI>85% in comparison with the historical ECD definition, and thus were accepted for transplantation [12]. However, the usage of kidneys with higher KDPI, and particularly >85%, has declined in the USA [12, 13], that leaves some potential recipients on dialysis. Of note, even the recipients of kidneys with KDPI >85% were at a much lower risk of death 2 years after transplant compared to those remaining on dialysis waiting for low-KDPI kidneys [13]. Moreover, such ECDs could be considered for the double kidney transplantation to a single recipient that provide better patient and graft survival in comparison to transplantation of such kidneys to 2 recipients [14, 15], and the use of the additional pre-transplant donor biopsy morphology score [16] secures the kidney transplantation from a high KDPI donor that otherwise may be discarded [17–20] and helps to allocate a donor organ to single or double transplantation. The results of the aforementioned stud-

ies highlight the important limitation of the current version of KDPI that could overestimate the prognostic weight of age based on the generalization from the total deceased donor population, and do not assume the specific constellation of parameters of a given donor. Indeed, the authors of the KDPI stated that the primary purpose of KDPI introduction was to give a priority for low-KDPI kidneys to be transplanted to recipients with longer estimated post-transplant longevity [6]. However, the donors with high KDPI should not be rejected by default, but with the additional personalized evaluation by the morphology score could serve for transplantation and improving the prognosis of life for potential recipients on the transplant waiting list.

To further evaluate the role of KDPI and KDRI, more data should be analyzed in different populations, and the availability of a universally applicable program algorithm in R language in public access would boost such an analysis. Moreover, the presented code could be translated to other program languages and incorporated in different software. I hope the use of this program code would save substantial time to other research groups and facilitate the evaluation of KDPI and KDRI on the already collected data and in prospective studies.

Statement of Ethics

Disclosure Statement

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