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ORIGINAL SCIENTIFIC REPORT

Medical Contraindications to Transplant Listing in the USA: A Survey of Adult and Pediatric Heart, Kidney, Liver, and Lung Programs

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Abstract

Introduction Listing practices for solid organ transplantation are variable across programs in the USA. To better characterize this variability, we performed a survey of psychosocial listing criteria for pediatric and adult heart, lung, liver, and kidney programs in the USA. In this manuscript, we report our results regarding listing practices with respect to obesity, advanced age, and HIV seropositivity.

Methods We performed an online, forced-choice survey of adult and pediatric heart, kidney, liver, and lung transplant programs in the USA.

Results Of 650 programs contacted, 343 submitted complete responses (response rate = 52.8%). Most programs have absolute contraindications to listing for BMI > 45 (adult: 67.5%; pediatric: 88.0%) and age > 80 (adult: 55.4%; pediatric: not relevant). Only 29.5% of adult programs and 25.7% of pediatric programs consider HIV seropositivity an absolute contraindication to listing. We found that there is variation in absolute contraindications to listing in adult programs among organ types for BMI > 45 (heart 89.8%, lung 92.3%, liver 49.1%, kidney 71.9%), age > 80 (heart 83.7%, lung 76.9%, liver 68.4%, kidney 29.2%), and HIV seropositivity (heart 30.6%, lung 59.0%, kidney 16.9%, liver 28.1%).

Conclusions We argue that variability in listing enhances access to transplantation for potential recipients who have the ability to pursue workup at different centers by allowing different programs to have different risk thresholds. Programs should remain independent in listing practices, but because these practices differ, we recommend transparency in listing policies and informing patients of reasons for listing denial and alternative opportunities to seek listing at another program.

Introduction

The allocation of scarce organs for transplantation starts with deciding which patients should be placed on the waiting list. This process requires evaluation by a multidisciplinary team of physicians, surgeons, psychiatrists, nurse coordinators, and social workers. Patient characteristics including psychiatric disease, social support, and demographics are often considered in making listing decisions [1].

Advanced age, obesity, and HIV seropositivity have been identified as potential contraindications to listing for

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transplantation [1–3]. A 1993 survey of heart, liver, and kidney programs found that "significant obesity" was an absolute or relative contraindication to listing in a majority of programs, regardless of organ type [1]. A more recent survey of liver transplant providers found that a majority of providers considered HIV seropositivity, age greater than 70 years old, and body mass index (BMI) greater than 40 either absolute or relative contraindications to transplant listing [2]. Another survey of Canadian and US liver transplant centers found that one-third of Canadian and one half of US transplant centers consider HIV seropositivity a contraindication to liver transplantation [3]. These studies suggest that there is variability regarding the influence of these characteristics on listing for transplantation.

Study design and population

We conducted an online forced-choice survey of adult and pediatric heart, kidney, liver, and lung transplant programs in the USA. In June 2016, we identified all eligible programs using databases and annual reports provided on the websites of the Organ Procurement and Transplant Network (OPTN) and the Scientific Registry of Transplant Recipients (SRTR). Six hundred and sixty-six programs that had transplanted at least one organ as recorded in the end-2015 SRTR report were initially included. Contact information for medical directors, surgical directors, social workers, nurse coordinators, and transplant physicians at each center was located on each program's website. After excluding twelve centers whose email addresses we could not find and four that had responded saying that they were no longer active programs, we distributed surveys to a final group of 468 adult and 182 pediatric programs (n = 650).

Survey instrument

The survey instrument was created using the online survey engine Qualtrics (Provo, Utah) and pilot-tested by medical directors and social workers at our institution using three rounds of iterative cognitive testing to ensure consistent interpretation of each question. The final survey instrument addressed 38 patient characteristics. For each characteristic, participants were asked three questions: (1) whether their program would consider the characteristic an absolute, relative, or irrelevant contraindication for transplant listing, (2) whether their program retains any formal, informal, or no guidelines for each characteristic, and (3) whether their program has encountered a patient with the characteristic (yes, no). This paper discusses the results related to age, BMI, and HIV seropositivity.

Data collection and analysis

The survey was distributed from August 2016 to March 2017. Responses were de-identified and analyzed in aggregate to protect the confidentiality of each participant. We used Microsoft Excel for the descriptive statistics required to identify characteristics of interest and statistical software R (version 3.3.3, Vienna, Austria) to conduct Pearson's Chi-squared test and Fisher's exact test for count data.

Human subjects protocol

The Institutional Review Board of Stanford University approved the study design and survey instrument as IRB exempt on May 26, 2016 (Protocol #37403).

Results

Response rate

Of 650 programs contacted, 343 submitted complete responses (response rate = 52.8%). After excluding 6 duplicate survey responses (a second response from the same program), responses from 234 adult programs and 101 pediatric programs were included for an analyzed sample size of 335. Participant profiles from the four organ types were similarly matched; most participants were physicians with an average of 15–19 years of experience as a transplant professional, evenly distributed across different regions of the country. Table 1 shows the characteristics of respondents and their programs.

Age

Adult transplant programs were asked questions regarding advanced age as a contraindication to transplant listing. Table 2 shows program responses by organ type to each age category as an absolute contraindication, relative contraindication or irrelevant to listing, and whether a formal guideline exists for this category. A majority of programs consider age $\geq$ 80 an absolute contraindication to transplant listing (58.1%, n = 136), but only half have formal guidelines for this variable (50.0%, n = 116). Heart and lung programs had more stringent absolute age contraindications to listing. A majority of heart (69.4%, n = 34) and lung (59.0%, n = 23) programs had an absolute contraindication to listing patients aged 75–79. A majority of heart (83.7%, n = 41), lung (76.9%, n = 30), and liver (68.4%, n = 39) programs had an absolute contraindication to listing patients aged $\geq$ 80. Kidney programs were the least likely to have absolute

Table 1 Respondent and program characteristics

Provider role	Adult		Pediatric	
	Respondents (*n*)	Percent of respondents (%)	Respondents (*n*)	Percent of respondents (%)
Physician	173	73.9	83	82.2
Surgeon	39	16.7	11	10.8
Social worker	8	3.4	2	2.0
Nurse coordinator	8	3.4	4	4.0
UNOS region	Respondents (*n*)	Percent of respondents (%)	Respondents (*n*)	Percent of respondents (%)
1	13	5.6	4	4.0
2	30	12.8	12	11.9
3	26	11.1	11	10.9
4	23	9.8	10	9.9
5	32	13.7	17	16.8
6	12	5.1	2	2.0
7	15	6.4	8	7.9
8	17	7.3	10	9.9
9	16	6.8	8	7.9
10	19	8.1	9	8.9
11	31	13.2	10	9.9
Time worked in transplant	Years	Years		
Minimum	1	1		
Maximum	47	42		
Mean	16.7	17.0		
SD	9.2	10.1		
Median	16	15		
Number of transplants per year	Number of transplants	Number of transplants		
Minimum	2	0		
Maximum	500	360		
Mean	85.6	32.4		
SD	95.3	62.1		
Median	60	12		

Respondent role, UNOS region, time worked in transplant, and program volume.

contraindications to listing based on advanced age. Only 29.2% ($n = 26$) of kidney programs had an absolute contraindication to listing patients aged ≥ 80.

Body mass index

Table 3 shows adult program responses by organ type to each BMI category as an absolute contraindication, relative contraindication or irrelevant to listing, and whether a formal guideline exists for this category. A majority of all adult programs consider BMI 40–45 kg/m^2 (56.4%, $n = 132$) and BMI ≥ 45 kg/m^2 (73.5%, $n = 172$) an absolute contraindication to listing. Formal guidelines existed across all BMI ranges for the majority of programs. Lung transplant programs had the most stringent absolute contraindications for listing based on BMI. A majority of lung transplant programs considered BMI ≥ 35 kg/m^2 an absolute contraindication to transplant listing (BMI 35–39 kg/m^2: 82.1%, $n = 32$; BMI 40–44 kg/m^2: 92.3%, $n = 36$; BMI ≥ 45 kg/m^2: 92.3%, $n = 36$). A majority of heart and kidney transplant programs considered BMI ≥ 40 kg/m^2 an absolute contraindication to listing (BMI 40–44 kg/m^2: heart 79.6%, $n = 39$; kidney 50.6%, $n = 45$; BMI ≥ 45 kg/m^2: heart 89.8%, $n = 44$; kidney 71.9%, $n = 64$). Only 49.1% ($n = 28$) of liver transplant programs considered BMI ≥ 45 kg/m^2 an absolute contraindication to transplant listing.

A total of 101 pediatric programs responded to questions regarding BMI. 88.0% ($n = 89$) of pediatric programs had encountered patients with BMI 30–34 kg/m^2, and 59.4%

Table 2 Advanced age

Age-group organ	Total respondents (*n*)	Absolute contraindication [*n* (%)]	Relative contraindication [*n* (%)]	Irrelevant [*n* (%)]	Formal guideline [*n* (%)]
65–69					
All	234	0 (0.0)	77 (32.9)	157 (67.1)	116 (50.0)
Heart	49	0 (0.0)	23 (46.9)	26 (53.1)	28 (57.1)
Lung	39	0 (0.0)	20 (51.3)	19 (48.7)	28 (71.8)
Kidney	89	0 (0.0)	24 (27.0)	65 (73.0)	43 (48.3)
Liver	57	0 (0.0)	10 (17.5)	47 (82.5)	17 (29.8)
70–75					
All	234	16 (6.8)	155 (66.2)	63 (26.9)	108 (46.2)
Heart	49	8 (16.3)	36 (73.5)	5 (10.2)	28 (57.1)
Lung	39	6 (15.4)	25 (64.1)	8 (20.5)	27 (69.2)
Kidney	89	2 (2.2)	51 (57.3)	36 (40.4)	45 (50.6)
Liver	57	0 (0.0)	43 (75.4)	14 (24.6)	8 (14.0)
75–79					
All	234	83 (35.5)	119 (50.9)	32 (13.7)	113 (48.3)
Heart	49	34 (69.4)	14 (28.6)	1 (2.0)	28 (57.1)
Lung	39	23 (59.0)	12 (30.8)	4 (10.3)	30 (76.9)
Kidney	89	7 (7.9)	59 (66.3)	23 (25.8)	45 (50.6)
Liver	57	19 (33.3)	34 (59.6)	4 (7.0)	10 (17.5)
≥ 80					
All	234	136 (58.1)	73 (31.2)	25 (10.7)	114 (48.7)
Heart	49	41 (83.7)	6 (12.2)	2 (4.1)	28 (57.1)
Lung	39	30 (76.9)	7 (17.9)	2 (5.1)	29 (74.4)
Kidney	89	26 (29.2)	46 (51.7)	17 (19.1)	45 (50.6)
Liver	57	39 (68.4)	14 (24.6)	4 (7.0)	12 (21.1)

Adult program responses regarding advanced age as a contraindication to transplant listing and formal guidelines for this characteristic

(n = 60) of pediatric programs had encountered patients with BMI ≥ 45 kg/m^2. A majority of pediatric programs consider BMI ≥ 45 kg/m^2 an absolute contraindication to transplant listing (53.5%, n = 54) but only 41.6% (n = 42) of programs consider the lower BMI ranges absolute contraindications to listing (BMI 30–34 kg/m^2: 2.0%, n = 2; BMI 35–39 kg/m^2: 10.9%, n = 11; BMI 40–44 kg/m^2: 37.6%, n = 38).

HIV status

Table 4 shows program responses by organ type and adult versus pediatric population to HIV seropositivity as an absolute contraindication, relative contraindication or irrelevant to listing, and whether a formal guideline exists for this category. 50.5% (n = 51) of pediatric programs and 91.0% (n = 213) of adult programs had encountered a patient with HIV seropositivity. A majority of programs had formal guidelines for listing HIV-positive patients (adult 76.9%, n = 180; pediatric 54.5%, n = 55). However, a minority of programs regard HIV seropositivity as an absolute contraindication to transplantation (adult 29.5%, n = 69; pediatric 25.7%, n = 25). Only a majority of adult lung transplant programs considered HIV seropositivity an absolute contraindication to listing (59.0%, n = 23).

Discussion

Advanced age

There are conflicting data regarding the effect of advanced age on outcomes in solid organ transplantation. One study of UNOS and European outcomes found no difference in liver transplant patient or graft survival in patients over 60 versus younger patients [4]. However, a study of liver transplant patients in Taiwan over a 14-year period found that patients over 60 had a significantly increased mortality rate within 3 years of transplant and that the impact of age was magnified in patients with associated comorbidities [5]. Contrary to this study, a single-center study in the USA found no difference in 10-year survival of liver transplant

Table 3 Body mass index

BMI range (kg/m^2) organ	Total respondents (*n*)	Absolute contraindication [*n* (%)]	Relative contraindication [*n* (%)]	Irrelevant [*n* (%)]	Formal guideline [*n* (%)]
30–34					
All	234	7 (3.0)	53 (22.6)	174 (74.4)	151 (64.5)
Heart	49	1 (2.0)	10 (20.4)	38 (77.6)	37 (75.5)
Lung	39	6 (15.4)	23 (59.0)	10 (25.6)	35 (89.7)
Kidney	89	0 (0.0)	13 (14.6)	76 (85.4)	53 (59.6)
Liver	57	0 (0.0)	7 (12.3)	50 (87.7)	26 (45.6)
35–39					
All	234	58 (24.8)	104 (44.4)	72 (30.8)	163 (69.7)
Heart	49	17 (34.7)	25 (51.0)	7 (14.3)	41 (83.7)
Lung	39	32 (82.1)	7 (17.9)	0 (0.0)	36 (92.3)
Kidney	89	7 (7.9)	52 (58.4)	30 (33.7)	62 (69.7)
Liver	57	2 (3.5)	20 (35.1)	35 (61.4)	24 (42.1)
40–44					
All	234	132 (56.4)	90 (38.5)	12 (5.1)	181 (77.4)
Heart	49	39 (79.6)	10 (20.4)	0 (0.0)	44 (89.8)
Lung	39	36 (92.3)	3 (7.7)	0 (0.0)	37 (94.9)
Kidney	89	45 (50.6)	42 (47.2)	2 (2.2)	71 (79.8)
Liver	57	12 (21.1)	35 (61.4)	10 (17.5)	29 (50.9)
≥ 45					
All	234	172 (73.5)	57 (24.4)	5 (2.1)	184 (78.6)
Heart	49	44 (89.8)	5 (10.2)	2 (0.0)	42 (85.7)
Lung	39	36 (92.3)	3 (7.7)	0 (0.0)	37 (94.9)
Kidney	89	64 (71.9)	23 (25.8)	2 (2.2)	74 (83.1)
Liver	57	28 (49.1)	26 (45.6)	3 (5.3)	31 (54.4)

Adult program responses regarding BMI as a contraindication to transplant listing and formal guidelines for this characteristic

Table 4 HIV seropositivity

HIV status organ	Total respondents (*n*)	Absolute contraindication [*n* (%)]	Relative contraindication [*n* (%)]	Irrelevant [*n* (%)]	Formal guideline [*n* (%)]
HIV-positive					
All adult	234	69 (29.5)	82 (35.0)	83 (35.5)	180 (76.9)
Heart	49	15 (30.6)	28 (57.1)	6 (12.2)	30 (61.2)
Lung	39	23 (59.0)	11 (28.2)	5 (12.8)	31 (79.5)
Kidney	89	15 (16.9)	25 (28.1)	49 (55.1)	72 (80.9)
Liver	57	16 (28.1)	18 (31.6)	23 (40.4)	47 (82.5)
All pediatric	101	26 (25.7)	52 (51.5)	23 (22.8)	55 (54.5)

Adult and pediatric program responses regarding HIV seropositivity as a contraindication to transplant listing and formal guidelines for this characteristic

patients over the age of 70 versus patients in their fifties [6]. In kidney transplantation, older patients have a four-year longer life expectancy with transplant than they would staying on dialysis. Kidney transplant patients older than 70 have a lower risk of dying within the first 18 months after transplant than patients who remain on the waiting list [7]. One study of heart transplant recipients found that patients older than 60 have a better reported quality of life post-transplant than younger cohorts. They report less stress, less depression, and better adherence to treatment

[8]. Another study of heart transplant patients over 70 found similar 1-, 3-, and 5-year survival compared with patients under the age of 70 [9]. A multicenter study from France found decreased 1-, 5-, and 10-year survival in heart transplant patients over the age of 60 and that the decreased survival was mainly attributed to non-skin solid tumors [10]. These studies suggest that older heart transplant patients can have similar outcomes to their younger counterparts. There are little data regarding lung transplantation in patients with advanced age. However, one single-center study of lung transplant patients older than 60 versus those younger than 60 found a similar 5-year survival [11].

Overall, studies of patients with advanced age who undergo liver, kidney, and heart transplantation suggest that appropriately selected older patients can benefit from transplantation. There are sparse data on older lung transplant patients, so more research is needed regarding advanced age and lung transplantation. We found that kidney transplant programs were the least likely to consider advanced age a contraindication to transplant listing as compared to other organs, which is appropriate given that transplantation has been shown to increase both quality and quantity of life in these patients. We also found that over 40% of programs will consider patients with advanced age for listing, so older patients can be evaluated and listed by selected centers.

Obesity

The effect of obesity on solid organ transplantation has been widely evaluated. Most obese end-stage renal disease patients gain a survival benefit from kidney transplantation, but this benefit is lower for patients with BMI $\geq$ 40 kg/m^2 and is not demonstrated in black patients with BMI $\geq$ 40 kg/m^2 [12]. Obesity in kidney transplantation increases the risk of delayed graft function, wound complications, longer hospital admissions, readmission, new onset diabetes, coronary events, and mortality post-transplant [13, 14]. Pediatric kidney transplant patients with a BMI $\geq$ 35 kg/m^2 have a substantially increased risk of graft loss at 10 years [15]. The data for obesity in liver transplantation are less clear than with kidney transplantation. A single-center retrospective review found obesity is associated with longer operative times, more transfusions, wound complications, and biliary complications. The data for obesity in liver transplantation are less clear than with kidney transplantation. A single-center retrospective review found obesity is associated with longer operative times, more transfusions, wound complications, and biliary complications [16]. However, it did not show obesity as an independent risk factor for patient death or graft loss. A retrospective review of UNOS data found that obesity was an independent predictor of 5 years post-transplant mortality but that these patients still benefitted from liver transplantation [17]. Another UNOS database review of liver transplant patients found that morbid obesity (BMI $>$ 40 kg/m^2) had a significantly higher 5-year mortality rate and that the major cause of increased mortality was cardiovascular events.

BMI $>$ 30 kg/m^2 in lung transplant patients has been associated with increased rates of primary graft dysfunction, surgical complications, and mortality [18–21]. For heart transplantation, data are less available with respect to the association between obesity and outcomes. One study of LVAD patients bridged to heart transplantation found that obese patients had worse post-transplant survival rates [22]. Another review of heart transplant patient data found that there is no significant evidence to suggest that obesity is associated with worse post-transplant outcomes [23].

We found that most kidney transplant programs consider a BMI $\geq$ 40 kg/m^2 a contraindication to transplant listing and most have formal BMI guidelines, which is appropriate given the decreased survival benefit from kidney transplantation in obese patients. However, this may change as advances in robotic kidney transplantation have shown promise in expanding kidney transplantation to obese patients with excellent early results [24]. We found that liver transplant programs were the least likely to consider obesity an absolute contraindication to listing, reflecting the fact that there is still a survival benefit with liver transplantation in obese patients despite increased risk of morbidity compared to non-obese patients. Our results show that most lung transplant programs consider a BMI $\geq$ 35 kg/m^2 to be a contraindication to transplant listing and most of these programs have formal BMI guidelines, which is appropriate given the significantly worse outcomes in obese lung transplant patients.

HIV seropositivity

HIV-positive patients have been a particular concern in transplantation because of their underlying immunocompromised status. There are several studies that show that properly selected HIV patients benefit from kidney transplantation as compared to remaining on dialysis [25, 26]. The most common cause of non-AIDS-related death in HIV patients is liver disease, and these patients have similar liver transplant outcomes as compared to HIV-negative patients [27, 28]. While there are less data regarding the effect of HIV seropositivity on heart and lung transplantation, case reports and case series suggest that these operations can be done safely with good outcomes [26, 29, 30]. Notably, HIV seropositivity is associated with higher rates of acute rejection in kidney and liver transplant

patients. However, there is no difference in opportunistic infections or malignancy rates [25, 26].

Despite strong data to support liver and kidney transplantation in HIV-positive patients, we found that 17.3% of kidney programs and 22.4% of liver programs consider HIV seropositivity an absolute contraindication to transplantation. Most of these programs do have formal guidelines regarding HIV status. Just over a third of heart transplant programs and nearly two-thirds of lung transplant programs consider HIV seropositivity an absolute contraindication to transplantation and most of these programs have formal guidelines.

Region and transplant center volume variation

Beyond organ type and pediatric versus adult programs, we assessed variation among regions and among high- versus low-volume transplant programs. We found that age 65–69 ($p = 0.047$) and BMI 30–34 ($p = 0.003$) were the only characteristics that were significantly different among regions. Because there is not variation at the more extreme age or BMI categories, we cannot make the claim that there are significant regional differences in listing practices based on our survey.

We also evaluated our results for variation between high- and low-volume transplant centers. For kidney and liver transplant, we defined the threshold for high volume as greater than 50 transplants per year. For heart and lung, we defined the threshold for high volume as greater than 35 transplants per year. Compared to low-volume programs, we found that high-volume programs are less likely to consider age 65–69 an RC versus an IC (RR 0.54, $p = 0.03$), less likely to consider age 70–74 an AC versus an IC (RR 0.16, $p = 0.008$), and less likely to consider age 75–79 an AC versus an IC (RR 0.27, $p = 0.003$). There is no significant difference between high- and low-volume programs in how they consider patients over the age of 80. Compared to low-volume programs, high-volume programs are less likely to consider BMI 35–39 an AC versus an IC (RR 0.28, $p < 0.001$). There is no significant difference for other BMI ranges. Compared to low-volume programs, high-volume programs are less likely to consider HIV seropositivity an AC versus an IC (RR 0.20, $p < 0.001$). Overall, respondents from high-volume centers were less likely to consider advanced age (65–80), BMI 35–39, and HIV seropositivity as absolute contraindications to listing for transplantation.

Limitations

There are several limitations to this study. First, a higher response rate would increase the generalizability of our findings. Although a rate of 52.8% allowed for robust data analysis, our results are still susceptible to reporter bias. Second, our unit of analysis was the individual participant, and we were unable to verify that the responses represented the exact practices at each program. However, this design protected our data from being skewed by multiple responses from larger programs because it ensured that we weighed each program equally. Finally, our survey design asked the participants to consider each patient characteristic separately, which does not accurately represent how listing decisions are often made using multiple characteristics. The alternative strategy of using vignettes would have made determining if particular characteristics are used independently as listing contraindications impossible.

Conclusions

Our study found that there is variability among programs regarding listing decisions based on advanced age, BMI, and HIV seropositivity even when evidence supports certain listing practices. For example, while there are good data to support liver and kidney transplantation in HIV-positive patients, one in five of these programs considers HIV seropositivity as an absolute contraindication to transplant listing. Moreover, we found that there was generally more willingness to consider older, obese, and HIV seropositive patients in higher-volume centers. While prior studies identifying variation in listing practices recommend decreasing this variation in order to create equity among programs, we disagree with this premise. Each transplant program has a risk threshold based on volume, expertise, and experience, among other factors. We believe that variability in listing practices creates more rather than less access to transplantation, in general, as centers can decide where they are willing to push boundaries. However, increased access may only be available to patients who have the means to pursue workup at different centers. Patients who do not have the means to access centers outside of their immediate geographic area may have a lower chance of being listed for transplantation if they only have access to a conservative center. With that being said, there may be some common ground to set baseline policies (e.g., BMI > 45, age > 85). We recommend transparency rather than uniformity in listing practices, meaning that centers should develop guidelines for internal consistency, inform patients of the reason or reasons why they are denied listing and at minimum, inform them that listing practices are variable with respect to these characteristics so patients have the opportunity to seek listing elsewhere. It is impractical to require programs to know the exact listing practices of all other programs, but if a patient is denied for a specific reason and there is knowledge that another program will likely list this patient, then we believe

that there is an obligation on the part of the denying center to inform the patient of the specific alternative. In addition, if there are a small number of centers that are outliers for a particular characteristic (e.g., high-BMI kidney transplants), there should be public awareness of these specific centers. While each program should remain independent in their listing parameters based on their risk adversity, transparency is important to allow patients with advanced age, HIV seropositivity, or obesity to seek evaluation at centers that do not automatically exclude them from listing.

Compliance with ethical standards

Conflicts of interest None of the authors have any conflict of interest to disclose.

Informed consent Informed consent was obtained from all individual participants included in this study.

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