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Effect of Recipient Body Mass Index on Kidney Transplantation Outcomes: A Systematic Review and Meta-analysis by the Transplant Committee from the French Association of Urology

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Abstract

Context: The impact of recipient obesity on kidney transplantation (KT) outcomes remains unclear.
Objective: The aim of this study was to perform a systematic review and meta-analysis to appraise all available evidence on the outcomes of KT in obese patients (body mass index [BMI] $\geq$30 kg/m^2) versus nonobese patients (BMI <30 kg/m^2).
Evidence acquisition: A systematic review and meta-analysis was performed. Search was conducted in the MEDLINE OvidSP, Web of Science, Google Scholar, Embase, and Cochrane databases to identify all studies reporting the outcomes of KT in obese versus nonobese recipients.
Evidence synthesis: Fifty-two articles met the inclusion criteria. Delayed graft function and surgical complications were significantly higher in obese recipients (delayed graft function: relative risk [RR]: 1.44, 95% confidence interval [CI]: 1.32–1.57, $p < 0.01$; surgical complications: RR: 1.74, 95% CI: 1.36–2.22, $p < 0.0001$). Five-year patient survival (RR: 0.96, 95% CI: 0.92–1.00, $p = 0.01$), 10-yr patient survival (RR: 0.90, 95% CI: 0.84–0.97, $p = 0.006$), and 10-yr graft survival (RR: 0.87, 95% CI: 0.79–0.96, $p = 0.01$) were significantly inferior in the obese group.
Conclusions: KT in obese recipients was associated with lower patient and graft survival, and higher delayed graft function, acute rejection, and medical and surgical complications than nonobese recipients. In the current situation of organ shortage and increasing prevalence of obesity, ways to optimize KT in this setting should be investigated.

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Patient summary: Compared with nonobese population, kidney transplantation in obese recipients has inferior patient and graft survival, and higher medical and surgical complications.

1. Introduction

The global epidemic of obesity is reflected in the end-stage renal disease (ESRD) population where the proportion of recipients with a body mass index (BMI) of ≥30 kg/m^2 is doubled every 15 yr [1,2]. According to the 2022 US epidemiological data [3], 16.5% of chronic kidney disease (CKD) patients were obese, and obesity increases the risk of progression to ESRD [4].

Kidney transplantation (KT) is the best renal replacement therapy and provides better quality of life than long-term dialysis [5,6]. Unfortunately, obesity may be an obstacle to transplantation access, due to a higher risk of surgical and medical complications, including wound healing, delayed graft function (DGF), hospital readmissions, or new-onset diabetes [7,8]. Obese recipients show shorter transplant survival than nonobese recipients after transplantation from a deceased donor [9]; together with the medical and surgical challenge, in the context of organ shortage, this may create some unconscious bias from transplant teams and discriminate obese patients by reducing their access to transplantation [10]. Therefore, KT in obese patients is still discussed controversially [11]. Obesity may be detrimental to recipient survival via its association with these early postoperative complications as well as with other medical conditions such as type 2 diabetes mellitus, cardiovascular disease, and chronic respiratory disorders [12–14]. Moreover, KT surgery presents several challenges in obese patients, related to the depth of the iliac vessels. However, compared with remaining on a waiting list, KT in obese recipients improves long-term survival [15] and enhances quality of life [16], even though morbid obesity is strongly associated with reduced long-term patient and graft survival [17,18]. Several meta-analyses investigated KT in obese recipients [19–22], with controversial outcomes, especially concerning patient and graft survival. These previous analyses, which are now >5 yr old, often included studies with abstracts only and lacked the incorporation of sensitivity analyses.

The aim of this study was to perform a systematic review and meta-analysis to appraise all available evidence about the outcomes of KT in obese (BMI ≥30 kg/m^2) versus nonobese (BMI <30 kg/m^2) patients.

2. Evidence acquisition

2.1. Data sources and search

This systematic review has been conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [23]. The systematic review protocol was registered with PROSPERO (CRD42023391884). Studies (January 1, 1995 to December 31, 2022) were identified by highly sensitive searches of electronic databases (Embase, Medline OvidSP, Cochrane Library databases, Web of Science, PubMed, and Google Scholar). The search was complimented by additional sources including the reference lists of included studies. The full strategy research and PICOTS (population, intervention, comparator, outcome, type of study, timing, and setting) table are provided in Supplementary Table 1.

2.2. Inclusion criteria and study selection

We included studies in which KT outcomes were stratified according to the patient's BMI. According to the World Health Organization [24], as a cutoff value, a BMI of 30 kg/m^2 was used to classify the included patients between "nonobese" (<30 kg/m^2) and "obese" (≥30 kg/m^2) groups. Underweight was defined by a BMI of <18.5 kg/m^2, normal weight by a BMI of 18.5–24.9 kg/m^2, and overweight by a BMI of 25.0–29.9 kg/m^2. Obesity was subdivided into three categories: class 1 (BMI 30.0–34.9 kg/m^2), class 2 (BMI 35.0–39.9 kg/m^2), and class 3 (≥40.0 kg/m^2). All study designs were eligible for inclusion, except reviews, editorials, letter to the editor, case reports, and studies published as conference abstracts only. Studies included were all comparative studies. All studies must have a minimum follow-up of 1 yr. Only studies published in 1995 and afterward were included to reflect current clinical practice. Language was restricted to English, French, and Spanish for pragmatic reasons.

All identified abstracts were placed in a bibliography management software program (Mendeley) and sorted according to inclusion and exclusion folders by drag and drop. Titles and abstracts of all identified studies were reviewed independently by two authors (T.P. and L.B.), and discrepancies were resolved by a third reviewer (R.B.). The detailed inclusion criteria are summarized in the Supplementary material (Research strategy).

2.3. Data collection and extraction

Data from eligible reports were extracted independently (by T.P. and L.B.) and discrepancies were resolved by a third reviewer (R.B.). A data-extraction sheet was created a priori, including authors' name; journal name; year of publication; study type; country; recruitment period; follow-up (months); total number of KTs performed in the period; number of patients according to BMI classification; donor mean age (years); donor sex; donor BMI (kg/m^2); donor type (deceased or living donor); cold ischemia time (hours); recipient mean age (years); recipient sex; recipient BMI (kg/m^2); recipient weight (kg); recipient medical history of hypertension, diabetes, and coronary disease; time on dialysis (months); pre-emptive KT rate; retransplantation rate; total operative time (minutes); rewarming ischemia time (minutes); postoperative complication and major postoperative complication rates (Clavien ≥3 [25]); urological and vascular complication rates; new-onset diabetes after transplantation (NODAT) rate; DGF; primary nonfunction (PNF) acute rejection; length of hospital stay (days); 6-mo, 1-yr, 2-yr, 3-yr, 5-yr, and 10-yr serum creatinine (mg/dl) and estimated glomerular filtration rate (eGFR; ml/min/1.73 m^2); 1-, 2-, 3-, 5-, and 10-yr non–death censored graft survival; death censored graft survival; and patient survival.

Non–death censored graft survival refers to the time from the date of transplantation to the date of irreversible graft failure signified by return to long-term dialysis (or retransplantation) or the date of the last follow-up during the period when the transplant was still functioning.

2.4. *Risk of bias assessment*

The risk of bias assessment was performed independently (L.B. and M.O.T.). An independent assessment of the risk of bias was conducted using the Newcastle-Ottawa Scale (NOS) to evaluate the quality of nonrandomized studies in meta-analyses [26]. The quality of the included studies was evaluated based on three factors:

1. Selection criteria, encompassing the representativeness of the exposed cohort, selection of the nonexposed cohort, ascertainment of exposure, and confirmation that the outcome of interest was absent at the beginning of the study
2. Comparability, which considered study design, analysis methods, and adjustment for confounding variables
3. Outcome evaluation, which accounted for the follow-up period, cohort retention, and the methods employed for independent blind assessment, record linkage, or self-reporting.

The quality rating of each study was determined by assigning stars to each domain following the guidelines of the NOS. The studies were categorized into three groups based on quality assessment: low quality (zero to four stars), medium quality (five to eight stars), and high quality (nine to 12 stars).

Since only nonrandomized studies were included, this tool was extended with a list of important potential confounders established a priori by the French Urology Association Kidney Transplantation Committee. The confounders were donor type, pre-emptive KT, time on dialysis, retransplantation, and BMI. For each study, it was assessed whether each confounder was considered and whether, if necessary, the confounder was controlled in the analysis.

2.5. *Data synthesis*

This review tabulates quantitative information and systematic descriptions of all the included studies. Frequencies and percentages were used to report categorical variables; mean and standard deviation were used to report continuous variables. Measures of association were assessed using the data reported in each study. Meta-analyses were conducted using studies with directly comparable groups, as determined by the existence of two categories (nonobese [BMI <30 kg/m^2] and obese [BMI $\geq$30 kg/m^2]). Random-effect models were used to account for possible clinical heterogeneity. Overall effects were determined using the Z tests. Statistical significance was defined as $p < 0.05$. Heterogeneity was evaluated using a tau-square test and chi- square, with $p < 0.1$ being considered statistically significant. In addition, I^2 statistics were used to assess clinical heterogeneity where I^2 thresholds of <25%, 25–49%, 50–75%, and >75% were considered to represent low, moderate, high, and very high heterogeneity, respectively. Where studies reported on two or more high or low BMI groups, pooled mean estimates and standard deviations were calculated. Group means were weighted by the number of recipients in each study group. The meta-analysis was conducted utilizing the "meta" and "metafor" software packages. Following the recommendations of Veroniki et al. [27], the Paule-Mandel tau-square estimator and the Q-Profile tau-square confidence interval (CI) estimator were used in this meta-analysis. The mean difference (MD) was estimated. Prior to pooling the point estimates, each study was assigned a weight based on the inverse variance approach, where studies with smaller variances were given higher precision and therefore assigned greater weight. In cases of high heterogeneity, the Knapp-Hartung–adjusted random-effect model was utilized. Conversely, in situations with low heterogeneity, the fixed-effect model was applied.

2.6. *Sensitivity analysis*

Various sensitivity analyses were conducted using the "dmetar" software package. Initially, the effect size was recalculated employing the leave-one-out technique. Subsequently, any basic outliers, that is, studies the CIs of which did not overlap with the pooled effect CI, were eliminated. Additionally, a diagnostic assessment was performed to identify influential cases, employing graphic display of study heterogeneity (GOSH) plots, and subsequently excluded from the meta-analysis.

3. Evidence synthesis

3.1. *Search results*

A total of 6768 studies were identified in the literature search. Two reviewers screened all study abstracts independently, and 6686 of these were excluded. Thus, a total of 82 full-text articles were assessed for eligibility. Of these, 30 were excluded.

In total, 52 studies were included in the meta-analysis, and pooled estimates were obtained for different outcomes: graft survival at 1, 3, 5, and 10 yr (respectively, 20, five, 14, and five studies); patient survival at 1, 3, 5, and 10 yr (respectively, 15, six, 11, and four studies); DGF (39 studies); PNF (seven studies); acute rejection (28 studies); serum creatinine and eGFR at 1, 3, and 5 yr (respectively, six, three, and two studies); operative time (six studies); warm ischemia time (six studies); and surgical complications (surgical site infection [11 studies], length of hospital stay [18 studies], and NODAT occurrence [nine studies]; Supplementary Fig. 1).

3.2. *Characteristics of studies, population, and interventions*

The 52 studies included a total of 250 297 patients. Table 1 summarizes the baseline characteristics of both groups, with a total of 69 990 obese (BMI $\geq$30 kg/m^2) and 180 266 nonobese (BMI <30 kg/m^2) recipients. Table 2 repre-

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Table 1 – Population's characteristics

	BMI <30	BMI ≥30
N = 250 297	180 266	69 990
Age (yr), SD	47.30 (15.71), *n* = 90 280	51.23 (12.58), *n* = 31 134
BMI (kg/m^2), SD	23.78 (3.24), *n* = 17 838	33.40 (3.10), *n* = 3070
Male, % (*n*)	61.38 (109 424/178 267)	59.34 (41 340/69 670)
Diabetes, % (*n*)	10.82 (16 778/155 088)	23.90 (15 325/64 126)
Hypertension, % (*n*)	75.47 (28 612/37 912)	80.12 (6610/8250)
Type of donor, % (*n*)		
LD	38 (66 111/173 326)	33 (22 697/68 644)
DD	62 (107 760/173 326)	68.7 (123 113/179 240)
Type of dialysis, % (*n*)		
Hemodialysis	83.21 (4167/5007)	75.49 (448/593)
Peritoneal dialysis	8.55 (765/5007)	10.48 (140/593)
Pre-emptive transplantation, % (*n*)	57.4 (58 886/93 881)	66.2 (18 484/27 910)
Number of KT, % (*n*)		
1st	97.15 (109 562/112 781)	98.69 (42 346/42 908)
Regraft	2.85 (3219/112 781)	1.31 (562/42 908)
Time on dialysis (mo), SD	47.29 (35.13), *n* = 37 085	49.19 (31.12), *n* = 17 843
Follow-up (mo), SD	61.59 (51.92), *n* = 2521	42.28 (36.16), *n* = 583

BMI = body mass index; DD = deceased donor; KT = kidney transplantation; LD = living donor; SD = standard deviation.

sents general features of the 52 retrospectives studies included.

Two studies by Chang et al. [28] and Johnson et al. [29]) drew upon the ANZDATA database. Similarly, two studies (by Aalten et al. [30] and Hoogeveen et al. [31]) were based on the NOTR database. Within the context of the USA-based investigations, six studies (by Cannon et al. [7], Gore et al. [18], Kamali et al. [32], Kwan et al. [33], Naik et al. [34], and Sureshkumar et al. [35]) harnessed data from the OPTN database, while two studies (by Ghahramani et al. [36] and Gill et al. [15]) relied on the USRDS database; these two databases may include common patients.

In the process of study selection, we prioritized the inclusion of the most recent and comprehensive data from each respective database to prevent redundancy in the results and potential bias that could arise from incorporating overlapping data. However, nuanced considerations arose with the US database studies. Here, we made a deliberate choice to prioritize the study conducted by Kwan et al. [33] due to its comparatively less restrictive inclusion criteria. This decision was made in contrast to the study led by Sureshkumar et al. [35], most recent but more restrictive, which exclusively enrolled patients subjected to perioperative antibody induction followed by maintenance therapy involving tacrolimus and mycophenolic acid. Our rationale was to ensure a broader representation of patient cases, thus enhancing the overall generalizability of the study findings. Excluded studies for each variable can be found in Supplementary Table 2.

Supplementary Figure 2 highlights the inclusion periods of the different studies, offering a visual representation of when each study was performed.

3.3. *Patient and graft survival*

A quantitative analysis, utilizing meta-analysis techniques, was conducted to pool and compare outcomes between the nonobese (BMI <30) and obese (BMI ≥30) groups. Figure 1 illustrates the forest plot representing the pooled relative risk (RR) for overall patient survival. The meta-analysis revealed significant difference in patient survival between the two groups, favoring nonobese patients at 10 yr. No significant difference was observed at 1, 3, and 5 yr.

There was significantly better graft survival at 1 and 10 yr in the nonobese group. No difference was shown at 3 and 5 yr (Fig. 2).

Fifteen studies incorporated BMI as a variable in their regression analyses, revealing a statistically significant association between BMI and graft survival (Supplementary Fig. 3).

3.4. *Kidney function outcomes*

Kidney function outcomes were assessed to evaluate the impact of obesity on post-transplant renal function (Fig. 3). An analysis of DGF revealed a significantly higher incidence in the obese group than in the nonobese group. The analysis of PNF revealed a significant difference between the two groups: the obese group had a higher risk of PNF than the nonobese group (common effect RR: 1.4962 [1.2191; 1.8361]; $p < 0.0001$). The occurrence of acute rejection was analyzed to assess its association with obesity. There was no significant difference between the obese and nonobese groups regarding the risk of acute rejection. There was no significant difference regarding eGFR between the two groups. (1-yr eGFR MD: 0.0482, 95% CI: –16.1363 to 16.2327, $p = 0.9942$; $I^2 = 88.9\%$, $p < 0.0001$, six studies; 3-yr eGFR MD: –3.8203, 95% CI: –16.6991 to 8.4676, $p = 0.3128$, three studies; 5-yr eGFR MD: –0.4789, 95% CI: –32.9420 to 31.9841, $p = 0.85$, two studies).

3.5. *Surgical complication outcomes*

The report of complication rates in the included studies of this systematic review was limited. Notably, only one study, conducted by Fellmann et al. [37], reported complications using the Clavien-Dindo classification system. Another study (by Scheuermann et al. [38]) reported only Clavien-Dindo ≥3b complications. Pooled results show increased risks for the obese group (RR: 1.7355, 95% CI: 1.3588–2.2166, $p < 0.0001$).

A comprehensive analysis of various complications, including urological, lymphatic, and infectious complica-

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Table 2 – Characteristics of the included studies

Year	Reference	Country	Database	Study duration	No. of recipients	<18.5	18.5–24.9	25–29.9	30–34.9	35–39.9	≥35	Groups
2006	Aalten et al. [30]	The Netherlands	NOTR	11 yr 11 mo	2067			1871	196			2 groups
2010	Abou-Jaoude et al. [55]	Bahrain	Single	9 yr	137	10	62	47	16			4 groups
2012	Bardonnaud et al. [56]	France	Single	4 yr 11 mo	200			179	21			2 groups
2014	Behzadi et al. [57]	Iran	Single	1 yr 9 mo	180			146	34			2 groups
2014	Bayoud et al. [58]	France	Single	10 yr 9 mo	402			354	48			2 groups
2020	Bellini et al. [59]	UK	Single	2 yr 2 mo	370	17	137	146	50	11	9	6 groups
2011	Bennett et al. [60]	USA	Single	8 yr 1 mo	642			439	109	94		3 groups
2013	Cannon et al. [7]	USA	OPTN	7 yr	74 983			52 668	15 010	5744	1561	4 groups
2007	Chang et al. [28]	Australia	ANZDATA	13 yr 8 mo	5684	218	2719	1880	867			4 groups
2014	Curran et al. [61]	Canada	Single	11 yr	1151	100	429	364	184	74		5 groups
2011	Ditonno et al. [62]	Italy	single	8 yr 11 mo	563	68	310	143	32	10		5 groups
2022	Dobrzycka et al. [63]	Poland	Single	4 yr	433		208	153	72			3 groups
2019	Erturk et al. [64]	Turkey	Single	7 yr 6 mo	561			373	148			2 groups
2003	Espejo et al. [65]	Spain	Single	11 yr 9 mo	80			40	40			2 groups
2020	Fellmann et al. [37]	France	Single	11 yr 11 mo	506			435	71			2 groups
2021	Foucher et al. [11]	France	DIVAT	11 yr 11 mo	4691			3944	747			2 groups
2011	Furriel et al. [66]	Portugal	Single	24 yr 4 mo	448		295	127	26			3 groups
2008	Ghahramani et al. [36]	USA	USRDS	9 yr 11 mo	56 988	2644	28 841	16 789	8279	435		5 groups
2013	Gill et al. [15]	Canada	USRDS	12 yr 5 mo	208 498	13 714	67 260	64 655	37 453	16 070	9346	6 groups
2006	Gore et al. [18]	USA	OPTN	2 yr 11 mo	27 377	1042	12 089	8765	3891	1590		5 groups
2012	Grosso et al. [67]	Italy	Single	10 yr 8 mo	376		122	190	64			3 groups
2014	Gusukuma et al. [68]	Brazil	Single	10 yr 4 mo	3054			2822	185	47		3 groups
2019	Heng et al. [69]	USA	Single	5 yr	893			513	380			2 groups
2011	Hoogeveen et al. [31]	The Netherlands	NOTR	14 yr	1810	305	972	432	101			4 groups
2001	Howard et al. [70]	USA	Single	9 yr 11 mo	833		457	278	98			3 groups
2002	Johnson et al. [29]	Australia	ANZDATA	5 yr 11 mo	493			434	59			2 groups
2010	Kamali et al. [32]	Iran	OPTN	1 yr 9 mo	180			146	34			2 groups
2011	Karabicak et al. [71]	USA	Single	9 yr	642	74	215	193	99	61		5 groups
2014	Kieszek et al. [72]	Poland	Single	16 yr 8 mo	859	57	565	198	39			4 groups
2020	Kostakis et al. [73]	UK	NHSBT	9 yr 11 mo	20 864	538	8167	7562	3790	807		5 groups
2016	Kwan et al. [33]	USA	OPTN	26 yr	191 091	5875	60 359	65 436	39 437	15 487	4497	6 groups
2007	Marcen et al. [74]	Spain	Single	NA	1000			935	65			2 groups
2019	Mehta et al. [75]	UK	Single	6 yr	610		294	224	92			3 groups
2007	Mehta et al. [76]	USA	Single	3 yr 10 mo	53			37	16			2 groups
1997	Modlin et al. [77]	USA	Single	25 yr	254			127	127			2 groups
2019	Montero et al. [78]	Spain	RMRC	22 yr	5607	194	2904	1900	609			4 groups
2013	Moreira et al. [79]	Brazil	Single	8 yr	447	31	248	120	48			4 groups
2014	Mos et al. [80]	Argentina	Single	2 yr 0 mo	110	8	55	30	17			4 groups
2016	Naik et al. [34]	USA	OPTN	8 yr 8 mo	108 654	2626	35 735	36 486	22 163	8356	3688	6 groups
2015	Orlic et al. [81]	Croatia	Single	24 yr 1 mo	521	75	265	140	41			4 groups
2011	Patel et al. [82]	USA	Single	8 yr 0 mo	475			315	160			2 groups
2020	Queruel et al. [83]	France	Single	5 yr 11 mo	694	51	360	218	65			4 groups
2005	Raiss-Jalali et al. [84]	Iran	Single	13 yr	182	56	86	28	12			4 groups
2022	Scheuermann et al. [38]	Germany	Single	24 yr 2 mo	578		304	205	69			3 groups
2005	Singh et al. [85]	Canada	Single	3 yr 9 mo	68			35	33			2 groups
2021	Sureshkumar et al. [35]	USA	OPTN	15 yr 11 mo	44 560		12 446	15 477	11 144	5493		4 groups
2016	Tremblay et al. [86]	USA	Two centers	11 yr	467	32	119	149	110	57		5 groups
2016	Wolyniec et al. [87]	Poland	Single	10 yr 0 mo	74			37	37			2 groups
2002	Yamamoto et al. [88]	USA	Single	7 yr 2 mo	56			28	28			2 groups
2022	Yemini et al. [9]	Israel	Single	14 yr 0 mo	1403			1089	314			2 groups
2010	Zaydfudim et al. [16]	USA	Single	10 yr 11 mo	464		154	192	80	38		4 groups
2012	Zrim et al. [89]	Australia	Single	8 yr	507	10	182	194	93	29		5 groups

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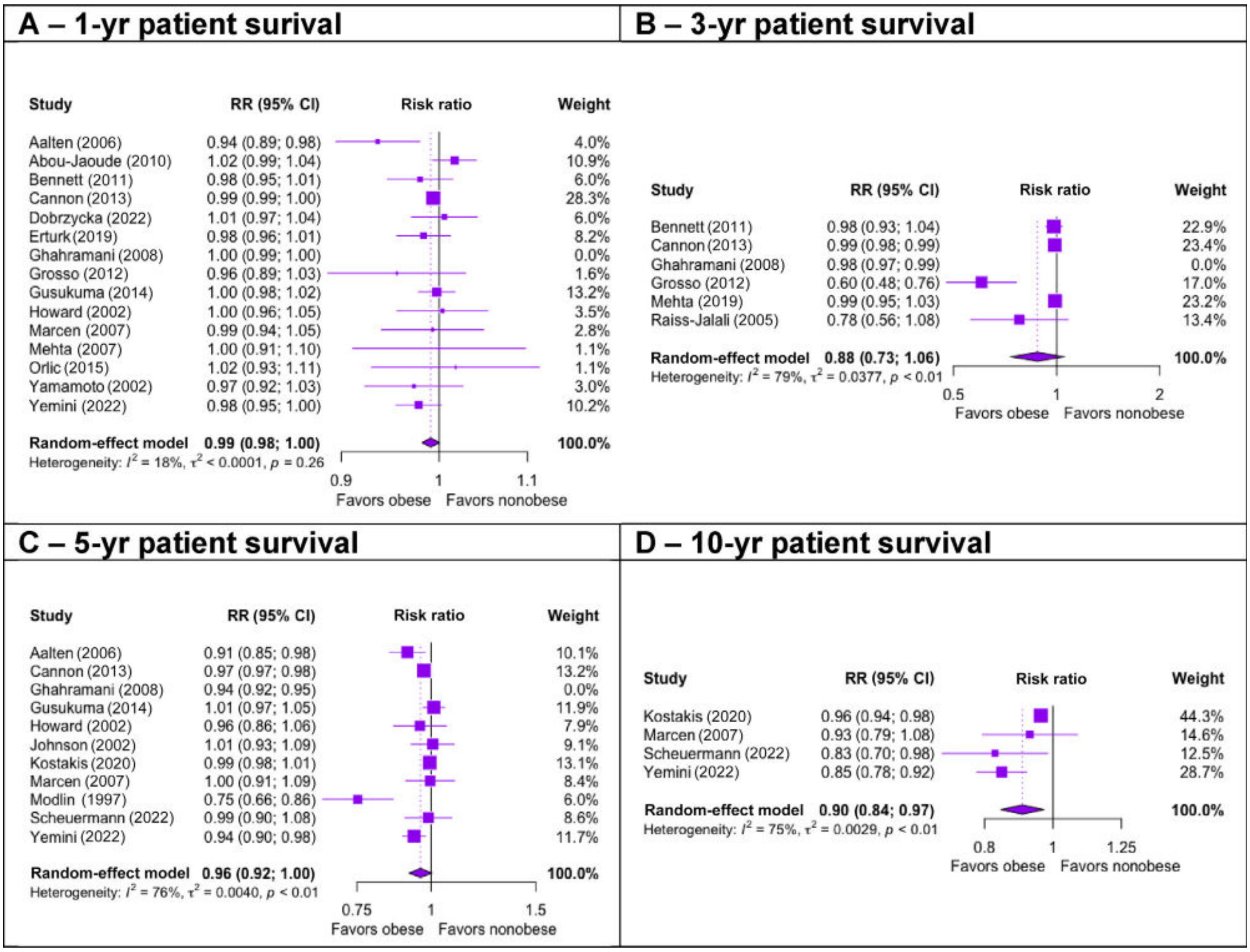

Fig. 1 – Forest plots of relative risk for patient survival at (A) 1 yr, (B) 3 yr, (C) 5 yr, and (C) 10 yr. CI = confidence interval; RR = relative risk.

tions, was conducted to evaluate the impact of obesity on post-transplant outcomes (Fig. 4).

1. The meta-analysis revealed an increased risk of urological complications, such as fistula (RR: 1.4357, 95% CI: 1.0919–1.8878, p = 0.0096, two studies), as well as a higher incidence of lymphocele in the obese group.
2. Postoperative complications such as hematoma, wound dehiscence, and wound complications (including wound infection and dehiscence) were consistently observed to be significantly higher in the obese group than in the nonobese group.
3. Additionally, infectious complications, including surgical site infections were significantly higher in the obese group than in the nonobese group.

3.6. *Surgical outcome parameters*

The duration of the surgical intervention was found to be significantly longer in obese individuals than in nonobese individuals. The meta-analysis revealed an MD of 24.19 min (95% CI: 2.3903–45.9847, p = 0.0357), indicating a substantial increase in surgical time for obese patients. The MD for warm ischemia time was 2.38 min, but it was not significantly different (95% CI: –0.3027 to 5.0600, p = 0.0715). The length of stay was significantly longer in the obese group. The MD was 2.40 d (95% CI: 1.1073–3.6899, p < 0.0011).

3.7. *Metabolic outcomes*

The risk of NODAT was more important in the obese group (Fig. 4).

3.8. *Risk of bias assessment of the included studies*

In our study, we assessed the methodological quality and potential biases of the included studies using the NOS. Out of the 52 studies reviewed, 50 (96%) were determined to have good quality according to the NOS criteria. These studies demonstrated robust methodologies, with careful consideration given to participant selection, comparability of groups, and ascertainment of outcomes. The remaining two studies (4%) were classified as having moderate quality, indicating some limitations in their design or execution. Despite these limitations, these studies still provided valuable insights into the research topic. The rigorous evaluation of biases using the NOS allowed us to ensure the overall reliability and validity of the findings in our study. All the results are shown in Supplementary Table 3.

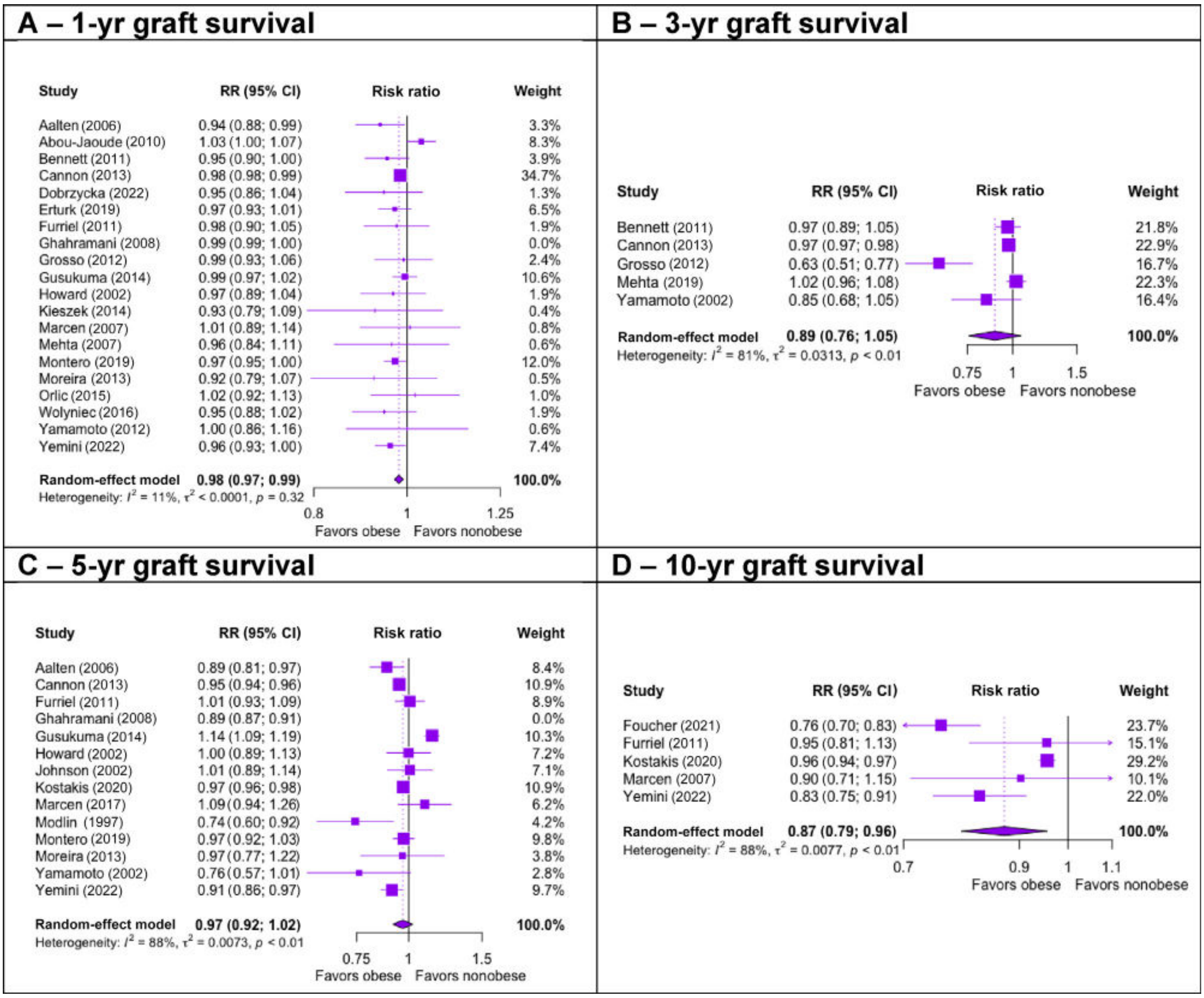

Fig. 2 – Forest plots of relative risk for graft survival at (A) 1 yr, (B) 3 yr, (C) 5 yr, and (D) 10 yr. CI = confidence interval; RR = relative risk.

3.9. *Sensitivity analysis*

The analysis conducted using the leave-one-out method and the influence diagnostic did not identify any specific studies that significantly altered the effect size estimates. By removing outliers based on the pooled and individual CIs, a noteworthy reduction in heterogeneity was achieved, while maintaining the same interpretation of the results. Detailed summaries of the adjusted effect sizes and measurements of heterogeneity can be found in Supplementary Table 4. Supplementary Figure 4 provides comprehensive influence diagnostic plots, such as Baujat and leave-one-out plots, Cook's distance, covariance ratio, and more, along with the resulting forest plots. GOSH plots were constructed for interesting outcomes, utilizing clustering methods such as K-means, DBSCAN, and Gaussian mixture model. GOSH plots were constructed, and several potential influential cases were identified. Identified studies were subsequently excluded, and the pooled effect size for each parameter was recalculated. The results of these recalculations are summarized in Supplementary Table 4.

3.10. *Discussion*

To the best of our knowledge, the present systematic review and meta-analysis describes the most updated outcomes of KT in obese (BMI $\geq$30 kg/m^2) versus nonobese (BMI <30 kg/m^2) recipients. The present study confirms existing literature, suggesting that obese recipients benefited greatly of KT but had worse graft and patient survival, and higher DGF and postoperative complication rates.

Obesity is a major public health issue in many countries [39]. In 2016, 650 million adults were obese worldwide, and obesity has tripled since 1975 [40]. Consequently, obesity increased among CKD and ESRD patients, some of whom will be considered for KT [2,21,41]. In the general population, obesity is associated with increased mortality risk primarily due to cardiovascular disease. In our meta-analysis, recipient obesity was also associated with an increased risk of death compared with a normal BMI. These results are different from those reported by Hill et al. [21] and Nicoletto et al. [19] in their systematic reviews. However, since that period, living donor KT has increased over the

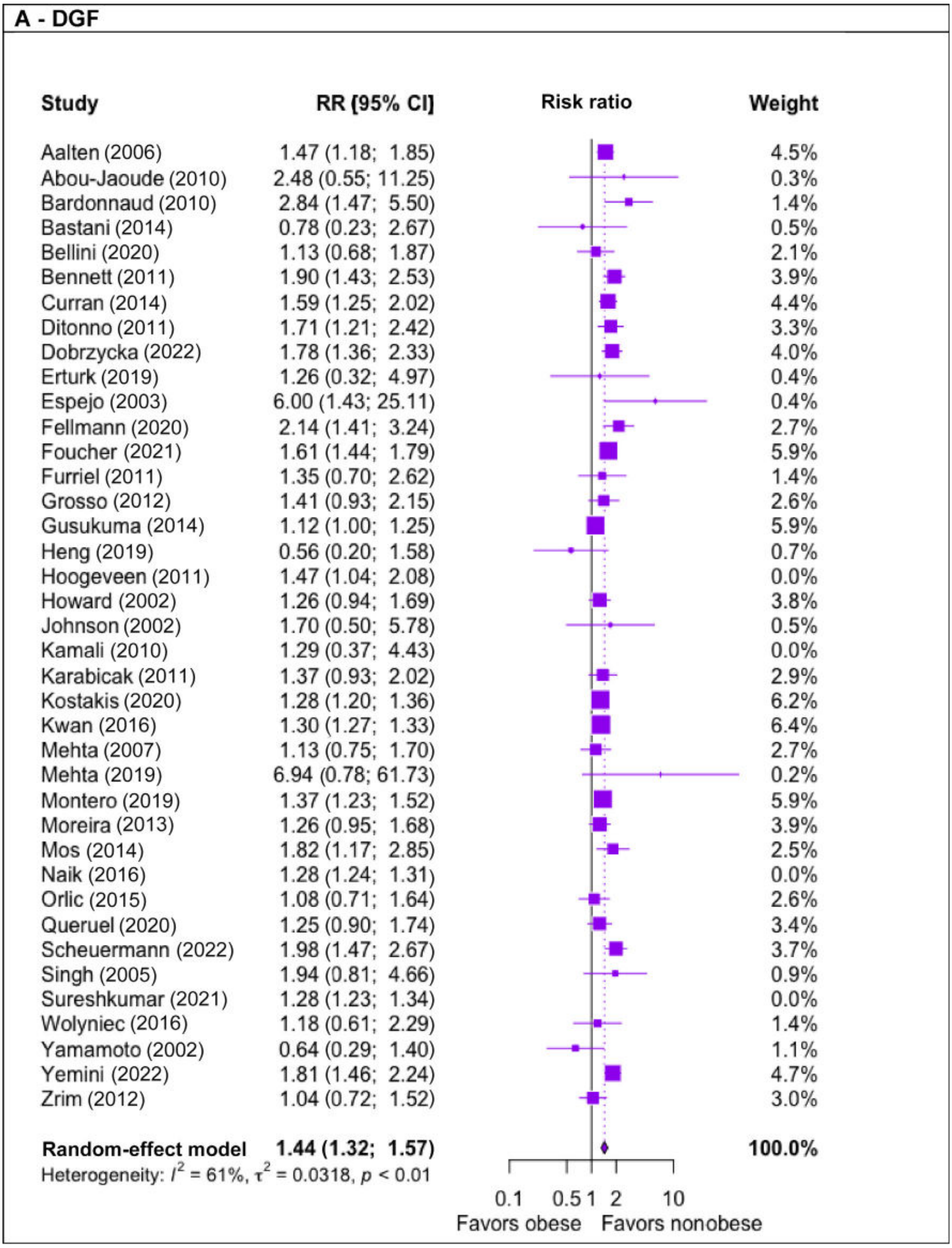

Fig. 3 – Forest plots of kidney function outcomes: (A) delayed graft function (DGF), (B) primary nonfunction (PNF), and (C) acute rejection (AR). CI = confidence interval; RR = relative risk.

years, providing better-quality grafts with improved graft and patient survival. Moreover, we reported lower patient survival in obese recipient population despite rigorous workup prior to activation on the waiting list, and candidates with significant comorbidities, such as cardiovascular disease, may not have been listed. In the absence of a randomized controlled trial, all transplant programs including obese recipients have selected the candidates according to medical or surgical comorbidities; thus, all studies showing a survival benefit of transplantation in obese recipients demonstrate, in fact, the satisfying results obtained after careful patient selection and controlling comorbidities.

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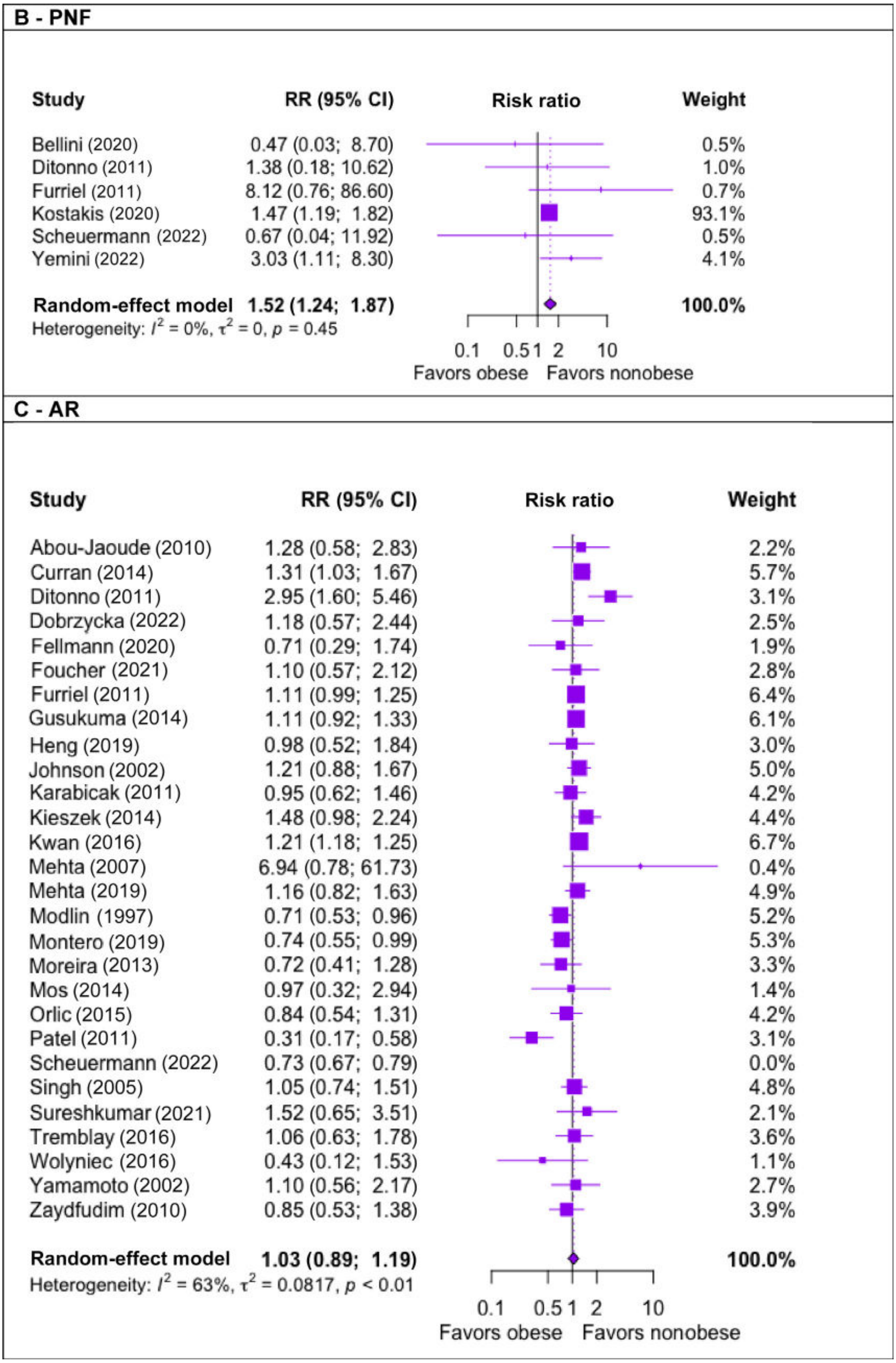

Fig. 3 (continued)

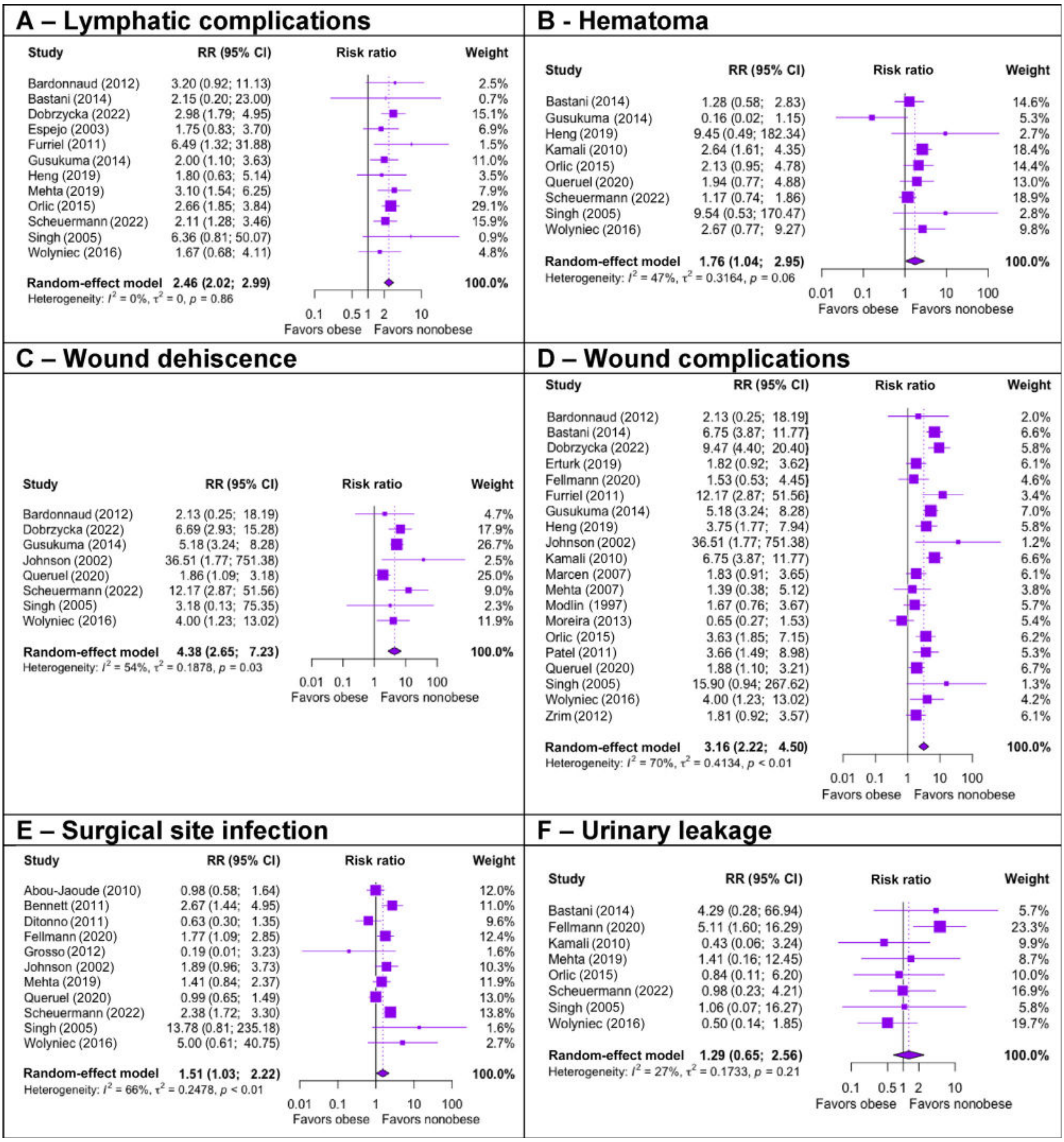

Fig. 4 – Forest plots of postoperative surgical and medical complications: (A) lymphatic complications, (B) hematoma, (C) wound dehiscence, (D) wound complications, (E) surgical site infection, (F) urinary leakage, (G) urinary complications, and (H) NODAT. CI = confidence interval; NODAT = new-onset diabetes after transplantation; RR = relative risk.

Obesity may dramatically increase perioperative risk and surgical complications when associated with other risk factors such as peripheral arterial disease [42].

In this meta-analysis, obesity was associated with an increased risk of DGF. This higher rate of DGF in obese recipients could be explained by the longer operation duration, which is itself associated with a higher DGF rate [43], but also by the combination of vasoconstriction, due to elevated sympathetic nervous system activity in obese recipients [44].

This meta-analysis also demonstrated an increased risk of surgical complications in obese recipients. These surgical complications lead to an increase of the hospital stay and medical cost. Moreover, the higher incidence of postoperative medical and surgical complications in obese recipients could increase the likelihood of DGF [21]. However, despite these complications, obese renal transplant recipients still demonstrate significant survival benefit from transplantation compared with dialysis [15].

Eventually, we reported that obesity prior to KT leads to impaired outcomes. Thus, losing weight prior to transplantation might be of great importance, although it is unclear whether this is advantageous for ESRD patients who remain

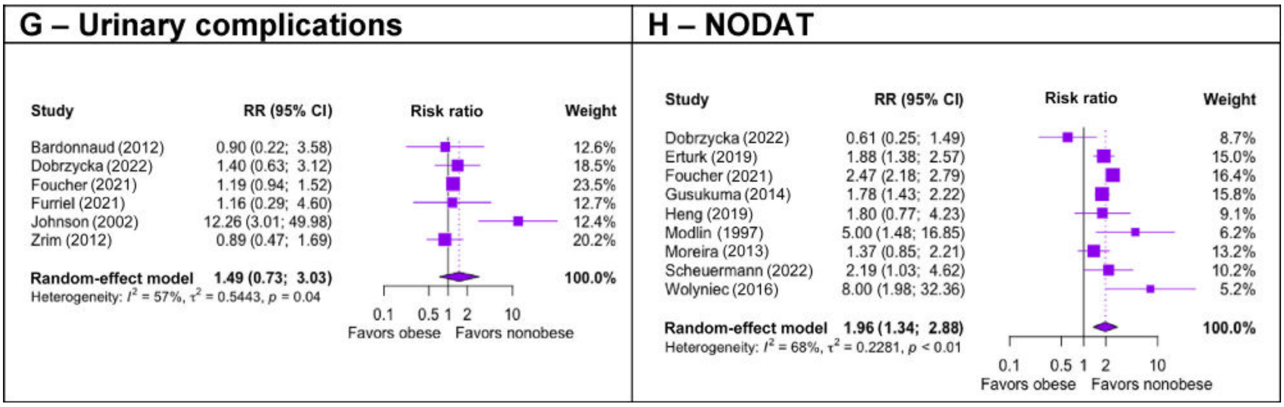

Fig. 4 (continued)

dependent on dialysis [45]. Therefore, several centers have proposed bariatric surgery before transplantation to optimize recipients and reduce time on the waiting list. Data from a large registry of obese patients with type 2 diabetes have already shown that bariatric surgery is associated with improved cardiovascular outcomes (including coronary arterial disease, peripheral arterial disease, and cerebrovascular disease) and lower mortality [46], suggesting that a similar benefit may be obtained in ESRD patients. Freeman et al. [47] reported outcomes of a prospective evaluation of laparoscopic sleeve gastrectomy in obese recipients, prior to transplantation. They reported a decrease of only 16% of BMI at 1 yr of follow-up. Similarly, conventional methods to lose weight, such as dietary advice, might not lead to the desired effect in obese candidates to KT [48].

The robotic-assisted kidney transplantation (RAKT) has been developed to reduce the surgical morbidity of KT in obese recipients [49–51]. Robotic surgery presented several advantages, such as lower wound infection occurrence [52]. However, RAKT has been developed mainly for living donor KT due to the “programmed” nature of these transplantations and requires selection of potential recipients (absence of atheroma on external iliac vessels, previous surgery, and others). Moreover, RAKT is a complex surgical procedure, with an estimated learning curve of 35 cases [53], but ensures good functional results when performed at high-volume referral centers by highly trained transplant teams.

This study has potential limitations. First, the main limitations are the low level of included studies, heterogeneity of evaluation between studies, and paucity of data. Indeed, data on several factors were poorly reported, in particular eGFR. We also reported high discrepancy in sample size between obese and nonobese recipients.

Moreover, only a few studies defined whether the transplanted kidneys were from live or deceased donors, which is a confounding factor in the pooled analysis of DGF. The rate of pre-emptive KT was poorly reported although it is of importance and had an impact on the outcomes after KT. More importantly, only BMI, as an obesity assessor, has been used. It would be interesting if future studies would include other parameters that consider the fat distribution of a recipient, such as waist circumference or hip-waist-ratio, and subcutaneous adipose tissue surface and visceral adipose tissue surface at computed tomography scans [54].

The major strength of this meta-analysis is the large number of transplant recipients included. A previous meta-analysis has aimed to address the impact of recipient obesity on outcomes following renal transplantation, but this is the largest study to investigate these outcomes [19–22]. Moreover, the studies included in this meta-analysis were also drawn from various countries, which increases its applicability across a number of healthcare systems and organ transplantation programs.

4. Conclusions

KT in obese recipients was associated with lower patient and graft survival, and higher DGF, and medical and surgical complications.

Obese renal transplant recipients should have careful optimization prior to KT to minimize postoperative morbidity and to reduce the likelihood of additional graft injury. In the current situation of organ shortage and increasing prevalence of obesity, ways to optimize KT in this setting should be investigated.

Author contributions: Thomas Prudhomme had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Prudhomme, Bento, Frontczak, Timsit, Boissier, Branchereau, Drouin, Mesnard, Bessede, Karam, Barrou, Badet, Kleinclauss, Terrier, Defortescu, Matillon, Doerfler, Alezra, Poinard, Thuret, Verhoest, Goujon, Gaillard, Millet, Delaporte, Sallusto, Boutin, Culty.
Acquisition of data: Prudhomme, Bento, Frontczak, Timsit, Boissier.
Analysis and interpretation of data: Prudhomme, Bento, Frontczak, Timsit, Boissier.
Drafting of the manuscript: Prudhomme, Bento, Frontczak.
Critical revision of the manuscript for important intellectual content: Timsit, Boissier.
Statistical analysis: Prudhomme, Bento, Frontczak.
Obtaining funding: None.
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Supervision: Timsit, Boissier.
Other: None.

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Appendix A. Supplementary data

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