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▶ **To cite this version:**

Grégoire Couvrat-Desvergnes, Yohann Foucher, Florent Le Borgne, Angelina Dion, Georges Mourad, et al.. Comparison of graft and patient survival according to the transplantation centre policy for 1-year screening biopsy among stable kidney recipients: a propensity score-based study. Nephrology Dialysis Transplantation, 2019, 34 (4), pp.703-711. 10.1093/ndt/gfy221 . inserm-02157631

HAL Id: inserm-02157631

https://inserm.hal.science/inserm-02157631

Submitted on 24 Sep 2021

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Comparison of graft and patient survival according to the transplantation center policy for 1-year screening biopsy among stable kidney recipients: a propensity score-based study

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Running title: Policy of 1-year screening kidney graft biopsies

Words counts: 3317

Abbreviations: BMI: Body Mass Index; CI: Confidence Interval; CIT: Cold Ischemia Time; CMV: cytomegalovirus; CNI: Calcineurin inhibitors; DGF: Delayed Graft Function; DIVAT: Données Informatisées et VAlidées en Transplantation; eGFR: estimated Glomerular Filtration Rate; HLA: Human Leukocyte Antigen; HR: Hazard Ratio; IFTA: Interstitial Fibrosis and Tubular Atrophy; IPW: Inverse Probability Weighted; MPA: Mycophenolic acid; MDRD: Modification of Diet in Renal Disease; SB: Screening Biopsy; SCR: subclinical rejection; SD: Standard Deviation.

Abstract

Clinical utility of screening biopsies (SB) at 1-year post-transplantation is still debated, especially for stable kidney graft recipients. Face to the heterogeneity of practices between transplantation centers, the objective was to compare graft and patient survival of stable patients depending if they are followed-up in a center having, or not, a SB policy at 1-year post-transplantation. From a multicentric French cohort, we studied 1573 kidney recipients alive with a functioning and stable graft function at 1-year post-transplantation, without acute rejection in their first year post-transplantation. From a propensity score-based analysis, we did not observe any significant difference in graft failure relative risk between patients from centers having a 1-year SB policy and patients from other centers (HR=1.15, 95% CI from 0.86 to 1.53). The corresponding adjusted survival probability at 8 years post-transplantation was 69% (95% CI from 61% to 74%) for patients from centers having a 1-year SB policy versus 74% (95% CI from 67% to 79%) for patients from other centers. One-year SB policy for stable patients may not lead to therapeutical taking care that may improve graft and patient survival. More studies describing the balanced benefit/risk of 1-year SB should be scheduled to demonstrate the long-term utility of this intervention.

Keywords: Kidney transplantation, Screening biopsy, Clinical utility, Graft failure, Long-term survival, Causal inference.

Introduction

Screening biopsies (SB) of kidney allografts were initially proposed in order to detect early allograft lesions which were potentially implicated in long-term graft failure risk.[1–3] For instance, subclinical rejection (SCR), defined by stable renal function with the presence of infiltrates, or chronic allograft nephropathy gathering chronic glomerular lesions, Interstitial Fibrosis and Tubular Atrophy (IFTA) seemed to be associated with a poor renal allograft survival.[4–7]

Whilst SBs provide important histological information for a better understanding of physio-pathological mechanisms, it remains clinically contentious from a patient-centered view,[8] mainly due to several reasons: 1) significant risks arise from biopsying grafts, including a potential risk of bleeding, hematoma, the requirement for packed red-blood cell transfusions, and ultimately, possible detriment to or loss of the kidney graft,[9,10] 2) the lack of consensus of the best timing to realize the biopsy (1-, 3-, 6- or 12-months), and 3) the lack of clear effective therapies face to most histological lesions identified on SB, such as borderline lesions, progressive IFTA lesions,[11,12] or inflammation in the microcirculation without Donor Specific Antibodies (DSA) or C4d.[13,14] Altogether, if 1-year SB could possibly be a useful tool for physician to better appreciate a kidneys transplant with a suboptimal function but also to improve the physiopathology knowledge, their long-term clinical utility and benefit could remained questionable particularly for recipients displaying stable renal function. This has resulted in a wide-ranging heterogeneity of practices between transplantation centers. Some transplantation centers systematically do not propose a 1-year SB. On the other hand, others transplantation centers make the choice of a SB policy at 1-year post-transplantation mainly to identify subclinical lesions and thus have an adapted

taking care to improve graft and patient outcomes, but also by historical habits or since they have translational research programs.

Several studies were interested in the SB benefit, but essentially using short term endpoints such as modification in immunosuppressive drugs or renal function changes after 6 months following the biopsy.[15–18] Even if a randomized clinical trial would be the gold standard study design to precisely estimate the long-term graft and patient outcomes, it seems ethically debatable and difficultly feasible.

Therefore, taking the opportunity of a large prospective, multicentric and observational cohort, the objective was to study the relevance of a 1-year SB policy among clinically and biologically stable patients at one year after the transplantation by comparing graft and patient survival between centers having, or not, a SB policy at 1-year post-transplantation.

Materials and methods

Study Population

Data were extracted from the French, multicentric, observational and prospective DIVAT cohort of kidney transplant recipients (www.divat.fr, CNIL final agreement, decision DR-2025-087 N°914184 the 15 February 2015). A total of 3344 patients met the following inclusion criteria: adults transplanted for the first or second time between January 2005 and December 2014 from heart-beating deceased donors, ABO-compatible, without previous non-renal transplantation, alive with a functional allograft at 1-year post-transplantation and receiving standard maintenance immunosuppressive therapy with calcineurin inhibitors (CNI such as Tacrolimus (68.2%) or cyclosporine (31.2%)), treated with mycofenolic acid derivatives and receiving corticosteroid regimen (92%). Within the first year post-transplantation, patients with an unstable renal function (more than 25% loss of estimated

Glomerular Filtration Rate -eGFR- calculated by the MDRD formula between 3-months and 12-months, n=858), and/or with a biopsy proven acute rejection episode (n=764), and/or with a BK virus viremia (n=110), and/or with de novo anti-HLA DSA occurrence (n=39) were not included, as they were considered not eligible for a SB, but rather an "indicated" biopsy. Note that we considered that patients may have a causal biopsy in the first year post-transplantation for various reasons (with finally various diagnoses as acute tubular necrosis, or CNI toxicity, etc.). If finally they recovered a stable renal function after this event, a 1-year biopsy can still be considered as screening biopsy. Finally, 1573 patients without any suspicious clinical signs during their first year post-transplantation were included.

Collected data

Recipient pre-transplantation variables were: age, gender, Body Mass Index (BMI), initial nephropathy (classified into relapsing disease or not), histories of either diabetes, hypertension, dyslipidemia, neoplasia, cardiac and/or vascular diseases, renal replacement therapy before transplantation (preemptive transplantation, hemodialysis, and peritoneal dialysis), and time spent on dialysis. Pre-transplantation immunization against class I or class II Anti-Human Leukocyte Antigen (HLA) was defined positive if at least one DSA was identified by Luminex® Single Antigen Bead technology within the 6 months pre-transplantation, unless if at least one DSA was not identified but a later determination performed by Luminex® screening or other technology (ELISA or CDC) was positive in pre-transplantation. Donor features were: age, last serum creatinine, gender, history of hypertension, cause of death (cerebrovascular vs. others). Transplantation features were: Cold Ischemia Time (CIT), HLA A-B-DR incompatibilities, rank of allograft, induction treatment (depleting vs. non-depleting). Follow-up transplantation features were: MDRD

eGFR at 3, 6 and 12 months post-transplantation, Delay Graft Function (DGF) defined by the need for dialysis in the first week post-transplantation, urinary infection, cytomegalovirus (CMV) infection or serious infection in the first year post-transplantation and causal biopsy in the first year post-transplantation.

Statistical analyses

The main judgment criteria was the time from 1-year post-transplantation (baseline) to graft failure, which was defined as the first event between return to dialysis, preemptive re-transplantation, and death with a functioning graft. In a secondary analysis, we also considered the time from 1-year post-transplantation to the first event between return-to-dialysis or preemptive re-transplantation (with death-censored). In both analyses, we respected the intention-to-treat principle used in randomized clinical trials, i.e. the results of an experiment is based on the initial treatment assignment and not on the treatment eventually received. Applied to our context, a patient transplanted in a center having a 1-year SB policy will remain in this group even if he/she did not actually have a 1-year SB. We therefore considered the 1-year SB policy (Policy of practicing 1-year SB vs. Policy of not practicing 1-year SB) as the main explicative variable.

Baseline comparisons regarding the 1-year SB policy were performed using Student's t-tests or Chi-square tests for quantitative or categorical variables, respectively. The median event-free follow-up time was calculated by the reverse Kaplan-Meier method.[19]

In order to estimate the population-average effect of 1-year SB policy, the Inverse Probability Weighted (IPW) estimator based on propensity score theory was used.[20,21] Propensity score is a balancing score[22] which straighten up the covariate differences by creating a pseudo-population in which the baseline covariate distributions are equivalent in

the two groups (practicing 1-year SB versus not practicing 1-year SB). In other words, it results in two identical groups except that in the first one all patients were managed in centers having a 1-year SB policy, while in the second all patients were managed in centers not practicing 1-year SB.

The propensity score was constructed in two steps. First, we selected a pool of variables only associated with graft failure in univariable survival analysis ($p<0.20$, Table S2 in web supplementary material). Second, this pool of selected variables was included in a multivariable logistic regression and, then, reduced to a lower number by using lasso penalization. This two-step variable selection leading to a parsimonious propensity score model allows to retain the efficient confounding variables and thus to limit the imprecision in the estimation.[23] Positivity assumption was graphically evaluated. Balance diagnostics was assessed from standardized differences on the pseudo-population, which could be considered as reasonable when they were lower or closer to 10%. In case of reasonably well-balanced diagnostics, the pseudo-population sample size should be closed to the original sample size.

Then, the weighted Kaplan–Meier estimator, the corresponding Log-Rank test, and the weighted Cox model with the robust variance estimator of Lin and Wei [24] were used. The log-linearity assumption for continuous variables was graphically verified and if necessary variables were categorized using thresholds traditionally used in the literature. Log-minus-log survival curves allowed graphical assessment of the proportional hazards assumption.

Following the same modeling strategy, we performed three sensitivity analyses having the objective to assess the robustness of our conclusion : (1) the comparison of patients biopsied at 1-year post-transplantation (n=388) and those followed in transplantation centers not having a 1-year SB policy (n=769), (2) the comparison of patients biopsied at 1-year post-

transplantation (n=388) and those not biopsied regardless of the 1-year SB policy of the transplantation center (n=1185), and (3) the comparison of patients biopsied at 1-year post-transplantation (n=388) and those not biopsied from transplantation centers having a 1-year SB policy (n=416).

All analyses were performed using the 3.0.2. version of the R software.[25] The IPW-based analyses were performed using the 0.4 version of the *IPWsurvival* package (www.labcom-risca.com).

Results

Description of kidney recipients

Among the 1573 included patients presenting a stable graft function at 1-year post-transplantation, without a biopsy proven acute rejection episode, without a BK virus viremia and without de novo anti-HLA donor specific antibody occurrence in their first year post-transplantation, 804 patients (51%) were from 3 transplantation centers having a 1-year SB policy while 769 patients (49%) were from 3 other centers. Importantly, none of these 769 patients ever received a 1-year SB, while among the 804 patients from centers with a 1-year SB policy, 388 recipients were actually biopsied (Figure 1). On the 1-year SB of these 388 patients, we diagnosed 66 normal histology, 127 IFTA grade 1, 51 IFTA grade 2, 20 IFTA grade 3, 6 recurrences of initial disease, 29 rejections, 30 vascular fibrous intimal thickening (cv>0) (isolated for 25, 5 associated with mild glomerulonephritis (g1)), 6 isolated chronic elementary lesions (5 tubulitis with ct1, 1 interstitial inflammation with ci1), 7 isolated acute elementary lesions (2 glomerulonephritis with g1, 3 tubilitis with ti>0, 2 acute interstitial inflammation with i1), 1 acute tubular necrosis, 2 thrombotic microangiopathy, while finally 43 histologies were unreadable or presented incomplete Banff scoring.

Demographic characteristics of donors and recipients and clinical features available during the first year post-transplantation are presented in Table 1. Patients from centers having a 1-year SB policy have longer organ CIT (20.1 hours vs. 18.7 hours, $p<0.01$). Patients with history of hypertension ($p<0.01$), dyslipidemia ($p<0.01$), donors presenting a history of hypertension ($p<0.01$), re-transplantation ($p=0.01$), having a causal biopsy during the first year post-transplantation ($p<0.01$), and presenting a DGF ($p<0.01$) belonged more frequently to transplantation centers having a 1-year SB policy. In contrast, patients receiving a depleting induction ($p<0.01$) belonged more frequently to transplantation centers not practicing 1-year SB.

Follow-up description

Among the studied population, 115 patients returned to dialysis (62 chronic graft dysfunctions, 32 allo-immune rejections, 4 infections and 17 from others causes) and 97 patients died with a functioning graft (32 cancers, 23 cardiovascular diseases, 19 infections and 23 from others causes). According to the histologic diagnosis, among the 29 patients presenting an acute rejection on their 1 year SB, 20 were not treated, 9 received steroid boluses (7 alone, 1 in association with plasma exchange, and 1 in association with rituximab and IvIg), 8 patients returned to dialysis and 2 died. Altogether, the cumulative follow-up covered 7273 patient–years. The median follow-up time was 5 years. The graft and patient survival probability at 2, 5 and 8 years post-transplantation were 98% (95% CI from 97% to 99%), 89% (95% CI from 87% to 91%) and 70% (95% CI from 66% to 75%) respectively.

Graft and patient survival analysis

The propensity score was composed of nine variables (Table S1 in web supplementary material). Respecting positivity assumption (Web Supplementary Figure S1), the propensity score-based analysis resulted in the comparison of two pseudo-groups of patients with similar characteristics as described in Table 2. Note that important standardized differences for a history of hypertension and graft rank do not represent a problem, since they are not showed here as relevant confounding factors being not significantly associated with graft failure (Table S2 in web supplementary material).

For the population described in Table 2, we estimated a 1.15-fold higher risk of graft failure for stable kidney recipients belonging to centers having a 1-year SB policy compared to others (HR=1.15, 95% CI from 0.86 to 1.53, p=0.3495) (Table 3). We may notably remark that this non-significant association may be interpreted independently of causal biopsy frequency in the first year post-transplantation since the initial imbalance (22.9% for patients from transplantation centers having 1-year SB policy versus 12.4% for patients from transplantation centers without 1-year SB policy as presented in Table 1) was straighten up to respectively 18.1% versus 18.6% as presented in Table 2. Estimated on the counterfactual population, Figure 2 represents the corresponding adjusted graft and patient survival probabilities if all centers had a policy of 1-year SB or if all centers had not such policy. The estimated graft and patient survival probability at 8 years post-transplantation was 69% (95% CI from 61% to 74%) for patients from centers having a 1-year SB policy versus 74% (95% CI from 67% to 79%) for patients from other centers.

Graft survival (with death-censored) analysis

We estimated the same risk of return in dialysis or preemptive re-transplantation for stable kidney recipients belonging to centers having a 1-year SB policy compared to others (HR=1.00, 95% CI from 0.68 to 1.47, p=0.9928) (Table 3). Figure S2 (Web supplementary material) represents the corresponding adjusted graft survival curves.[26,27] The death-censored graft survival probability at 8 years post-transplantation was 81% (95% CI from 74% to 87%) for patients from centers having a 1-year SB policy versus 82% (95% CI from 74% to 87%) for patients from other centers.

Sensitivity analyses

Firstly, we compared the 388 patients actually biopsied from transplantation centers having a 1-year SB policy, to the 769 patients from transplantation centers not having a 1-year SB policy. Details of the survival analysis are provided in the Web supplementary materials (Tables S3-S5, Figures S3-S5). We did not observe any difference in graft failure risk between the two groups (HR=1.00, 95% CI from 0.69 to 1.46, p=0.9944) (Table 3). Secondly, comparing the same 388 biopsied patients and the 1185 (416+769) patients not biopsied regardless of the 1-year SB transplantation center policy (Tables S6-S8 and Figures S6-S8 in Web supplementary materials), we did not observe a significant difference in graft failure risk (HR=0.89, 95% CI from 0.63 to 1.26, p=0.5073). Thirdly, we studied the same 388 biopsied patients and the 416 patients not biopsied from transplantation centers having 1-year SB policy (Tables S9-S11 and Figures S9-S11 in Web supplementary materials). Once again, we did not observe a significant difference in graft failure risk (HR=0.81, 95% CI from 0.53 to 1.24, p=0.3394).

Discussion

In kidney transplantation, whether long-term outcomes of stable patients without any suspicious clinical signs during their first year post-transplantation can be improved by practicing 1-year SB is still under debate. Arguments in favor of SB rely on histological information to assess physio-pathological mechanisms or to screen subclinical lesions which have been demonstrated to be associated with long-term outcomes.[3,28–30] However, it's potential usefulness could be counterbalanced by 1) the lack of consensus in changing patient therapy or follow-up faced with an abnormal histological diagnosis, 2) the risks of bleeding related to the invasive act, and 3) the percentage of 1-year SB biopsies finally revealing normal histological diagnosis.[3,7,18] Note that we did not observed abnormal bleeding compared to the literature with 1% of hematoma and serious bleeding and 0.05% isolated and rapidly recovering hematuria since 2006 in our whole cohort.[31,32] We were not able to described information concerning the changes of therapeutics in patients presented other diagnosis than acute rejection, since there is no common rule and it depends on each center and physician habits in particular for patients with normal histology who represent 17% of the cohort.

Since a randomized clinical trial is difficult to consider, we proposed a cohort-based study. By using a propensity score-based approach, we did not demonstrate any significant difference for graft and patient outcomes between stable kidney recipients from centers having a 1-year SB policy and those from centers that do not have such policy. Our results support the study of Moulin and al. focusing on short term endpoints.[18] They notably reported that renal function at 18-months post-transplantation seemed similar between their 154 patients having a 1-year SB and their 138 patients without biopsy, while the immunosuppressive regimen remained mainly unchanged.

In transplantation centers having a 1-year SB policy, all patients may not actually undergo this procedure. As illustrated in a recent survey through UNOS across 106 transplantation centers,[33] 17% performed SB for all kidney transplant recipients and 21% for selected recipients only. In our cohort, around half of the patients from these transplantation centers were finally not biopsied. This high percentage could be explained by non-observed confounders, such as warfarin administration, infection on the day of biopsy, doctor's omission or patient refusal, etc. The main consequence of these non-observed confounders is the difficulty in performing an individual comparison of patients receiving, or not, a 1-year SB without introducing selection bias. Similarly to randomized clinical trial analyses, we therefore respected the intention-to-treat principle: the results are based on the initial treatment decision and not on the treatment eventually received. This explains why we did not distinguish patients who actually had a 1-year SB and patients without 1-year SB. Nevertheless, we performed three different sensitivity analyses for validation of our results. Indeed, we did not observe any significant difference in graft failure risk between actually biopsied patients and the non-biopsied patients whether they were restricted to those of transplantation centers not having a 1-year SB policy, to those of transplantation centers having a 1-year SB policy, or to both. In the transplantation centers having 1-year SB policy, the 416 non biopsied patients were notably older and presented more frequent comorbidities than biopsied patients (Table S9 in web supplementary materials). We may have therefore expected that the survival probability among the biopsied patients was higher than for all patients of transplantation centers having 1-year SB policy. While we probably overestimated the survival probability of patients actually biopsied, since at-risk patients were non included, the clinical utility of a 1-year SB remains questionable, since we did not observe any significant difference on graft and patient survival between stable

biopsied kidney recipients from centers having a 1-year SB policy and those from centers not having a 1-year SB policy.

Another limitation of our study concerns the timing of the biopsy. There is currently no consensus on the best timing to perform this examination, as early biopsies (at 3- or 6-months post-transplantation) may identify SCR, while latter biopsies (at 1-year post-transplantation) could be more appropriate for assessing IFTA progression,[34–38] and this is why 1-year may be considered as too late. Using a prospective randomized study, Kurkoti et al. showed that early systematic biopsies at 1- and 3-months post-transplantation in patients receiving mainly ciclosporine and azathioprine as immunosuppressive regimens, afforded a benefit to renal function measured at 1-year of follow-up.[15] SCR was diagnosed in 17% of cases, which was treated with high doses of steroids. The early timing of biopsies (3-months) allows more frequent detection of SCR or inflammation according to previous reports[8,36,39] and these could be more accessible to a curative intervention than detecting histologic lesions at 1-year post-transplantation. However, SCR appears less frequently since the use of immunosuppressive strategies including tacrolimus and mycophenolic acid, and therefore the benefit of SCR treatment using steroids remains debatable.[16]

In conclusion, our study describes no difference on graft and patients outcomes between stable kidney recipients from centers having a 1-year SB policy and those from others centers. Our results suggest that 1-year SB policy to identify subclinical lesions may not lead to therapeutical taking care that may improve graft and patient survival and could thus be avoided in routine practice in clinically stable patients. But regarding the limitations we previously listed, additional studies aiming at describing the balanced benefit/risk of 1-year SB should be scheduled. Awaiting further evidence, biopsies could nevertheless benefit to patients with clinical warning during the first year post-transplantation and at risk of

histological lesions and in the frame of translational research programs or clinical trials to improve the transplantation sciences knowledge.

Acknowledgments

The authors would like to thank the members of the DIVAT consortium for their involvement into the study, the physicians who helped recruit patients, and all patients who participated in this study. We also thank the clinical research associates who participated in the data collection. Data were collected from the French DIVAT (Données Informatisées et VAlidées en Transplantation) multicentric prospective cohort of kidney and/or pancreatic transplant recipients (www.divat.fr, N° CNIL 914184). The analysis and interpretation of these data are the responsibility of the authors.

Funding information

This work was supported by the French Biomedicine Agency. We thank the Roche Pharma, Novartis and Sanofi laboratories for supporting the DIVAT cohort as the CENTAURE foundation (www.fondation-centaure.org).

Disclosure

The authors declare no conflict of interest.

References

1. Kasiske BL, Vazquez MA, Harmon WE, et al. Recommendations for the Outpatient Surveillance of Renal Transplant Recipients. *J Am Soc Nephrol*. 2000;11(suppl 1):S1-S86.

2. Yilmaz S, Tomlanovich S, Mathew T, et al. Protocol Core Needle Biopsy and Histologic Chronic Allograft Damage Index (CADI) as Surrogate End Point for Long-Term Graft Survival in Multicenter Studies. *J Am Soc Nephrol*. 2003;14(3):773-779. doi:10.1097/01.ASN.0000054496.68498.13

3. Cosio FG, Grande JP, Wadei H, Larson TS, Griffin MD, Stegall MD. Predicting Subsequent Decline in Kidney Allograft Function from Early Surveillance Biopsies. *Am J Transplant*. 2005;5(10):2464-2472. doi:10.1111/j.1600-6143.2005.01050.x

4. Thierry A, Thervet E, Vuiblet V, et al. Long-term Impact of Subclinical Inflammation Diagnosed by Protocol Biopsy One Year After Renal Transplantation. *Am J Transplant*. 2011;11(10):2153-2161. doi:10.1111/j.1600-6143.2011.03695.x

5. Moreso F, Ibernon M, Gomà M, et al. Subclinical Rejection Associated with Chronic Allograft Nephropathy in Protocol Biopsies as a Risk Factor for Late Graft Loss. *Am J Transplant*. 2006;6(4):747-752. doi:10.1111/j.1600-6143.2005.01230.x

6. Serón D, Moreso F, Fulladosa X, Hueso M, Carrera M, Grinyó JM. Reliability of chronic allograft nephropathy diagnosis in sequential protocol biopsies. *Kidney Int*. 2002;61(2):727-733. doi:10.1046/j.1523-1755.2002.00174.x

7. Cosio FG, El Ters M, Cornell LD, Schinstock CA, Stegall MD. Changing Kidney Allograft Histology Early Posttransplant: Prognostic Implications of 1-Year Protocol Biopsies. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg*. August 2015. doi:10.1111/ajt.13423

8. Wilkinson A. Protocol Transplant Biopsies: Are They Really Needed? *Clin J Am Soc Nephrol*. 2006;1(1):130-137. doi:10.2215/CJN.00350705

9. Whittier WL, Korbet SM. Timing of Complications in Percutaneous Renal Biopsy. *J Am Soc Nephrol*. 2004;15(1):142-147. doi:10.1097/01.ASN.0000102472.37947.14

10. Lefaucheur C, Nochy D, Bariety J. [Renal biopsy: procedures, contraindications, complications]. *Néphrologie Thérapeutique*. 2009;5(4):331-339. doi:10.1016/j.nephro.2009.02.005

11. Nankivell BJ, Borrows RJ, Fung CL-S, O'Connell PJ, Allen RDM, Chapman JR. The natural history of chronic allograft nephropathy. *N Engl J Med*. 2003;349(24):2326-2333. doi:10.1056/NEJMoa020009

12. El-Zoghby ZM, Stegall MD, Lager DJ, et al. Identifying Specific Causes of Kidney Allograft Loss. *Am J Transplant*. 2009;9(3):527-535. doi:10.1111/j.1600-6143.2008.02519.x

13. Sis B, Jhangri GS, Riopel J, et al. A New Diagnostic Algorithm for Antibody-Mediated Microcirculation Inflammation in Kidney Transplants. *Am J Transplant*. 2012;12(5):1168-1179. doi:10.1111/j.1600-6143.2011.03931.x

14. Loupy A, Vernerey D, Tinel C, et al. Subclinical Rejection Phenotypes at 1 Year Post-Transplant and Outcome of Kidney Allografts. *J Am Soc Nephrol JASN*. 2015;26(7):1721-1731. doi:10.1681/ASN.2014040399

15. Kurtkoti J, Sakhuja V, Sud K, et al. The Utility of 1- and 3-Month Protocol Biopsies on Renal Allograft Function: A Randomized Controlled Study. *Am J Transplant*. 2008;8(2):317–323. doi:10.1111/j.1600-6143.2007.02049.x

16. Rush D, Arlen D, Boucher A, et al. Lack of Benefit of Early Protocol Biopsies in Renal Transplant Patients Receiving TAC and MMF: A Randomized Study. *Am J Transplant*. 2007;7(11):2538-2545. doi:10.1111/j.1600-6143.2007.01979.x

17. Kee TY-S, Chapman JR, O'Connell PJ, et al. Treatment of subclinical rejection diagnosed by protocol biopsy of kidney transplants. *Transplantation*. 2006;82(1):36-42. doi:10.1097/01.tp.0000225783.86950.c2

18. Moulin B, Merville P, Renaudin K, et al. Evaluation of Protocol Biopsy Utility 12 Months after Renal Transplantation: A Multicenter Observational Analysis. *J Transplant*. 2012;2012:1-9. doi:10.1155/2012/781263

19. Schemper M, Smith TL. A note on quantifying follow-up in studies of failure time. *Control Clin Trials*. 1996;17(4):343-346.

20. Rosenbaum PR, Rubin DB. Reducing bias in observational studies using subclassification on the propensity score. *J Am Stat Assoc*. 1984;79(387):516–524.

21. Gayat E, Resche-Rigon M, Mary J-Y, Porcher R. Propensity score applied to survival data analysis through proportional hazards models: a Monte Carlo study. *Pharm Stat*. 2012;11(3):222-229. doi:10.1002/pst.537

22. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41–55.

23. Heinze G, Jüni P. An overview of the objectives of and the approaches to propensity score analyses. *Eur Heart J*. 2011;32(14):1704-1708. doi:10.1093/eurheartj/ehr031

24. Lin DY, Wei L-J. The robust inference for the Cox proportional hazards model. *J Am Stat Assoc*. 1989;84(408):1074–1078.

25. R Development Core Team . *R: A Language and Environment for Statistical Computing*. (Computing RF for S, ed.). Vienna, Austria; 2010. http://www.R-project.org/.

26. Xie J, Liu C. Adjusted Kaplan-Meier estimator and log-rank test with inverse probability of treatment weighting for survival data. *Stat Med*. 2005;24(20):3089-3110. doi:10.1002/sim.2174

27. Le Borgne F, Giraudeau B, Querard AH, Giral M, Foucher Y. Comparisons of the performance of different statistical tests for time-to-event analysis with confounding factors: practical illustrations in kidney transplantation. *Stat Med*. October 2015. doi:10.1002/sim.6777

28. Yilmaz S, Tomlanovich S, Mathew T, et al. Protocol Core Needle Biopsy and Histologic Chronic Allograft Damage Index (CADI) as Surrogate End Point for Long-Term Graft Survival in Multicenter Studies. *J Am Soc Nephrol*. 2003;14(3):773-779. doi:10.1097/01.ASN.0000054496.68498.13

29. Nankivell BJ, Borrows RJ, Fung CL-S, O'Connell PJ, Allen RDM, Chapman JR. The Natural History of Chronic Allograft Nephropathy. *N Engl J Med*. 2003;349(24):2326-2333. doi:10.1056/NEJMoa020009

30. Hertig A, Anglicheau D, Verine J, et al. Early epithelial phenotypic changes predict graft fibrosis. *J Am Soc Nephrol JASN*. 2008;19(8):1584-1591. doi:10.1681/ASN.2007101160

31. Hergesell O, Felten H, Andrassy K, Kühn K, Ritz E. Safety of ultrasound-guided percutaneous renal biopsy-retrospective analysis of 1090 consecutive cases. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc*. 1998;13(4):975-977.

32. Furness PN, Philpott CM, Chorbadjian MT, et al. Protocol biopsy of the stable renal transplant: a multicenter study of methods and complication rates. *Transplantation*. 2003;76(6):969-973. doi:10.1097/01.TP.0000082542.99416.11

33. Mehta R, Cherikh W, Sood P, Hariharan S. Kidney allograft surveillance biopsy practices across US transplant centers: A UNOS survey. *Clin Transplant*. 2017;31(5). doi:10.1111/ctr.12945

34. Shishido S, Asanuma H, Nakai H, et al. The Impact of Repeated Subclinical Acute Rejection on the Progression of Chronic Allograft Nephropathy. *J Am Soc Nephrol*. 2003;14(4):1046-1052. doi:10.1097/01.ASN.0000056189.02819.32

35. Nankivell BJ, Borrows RJ, Fung CL-S, O'Connell PJ, Allen RDM, Chapman JR. Natural History, Risk Factors, and Impact of Subclinical Rejection in Kidney Transplantation. [Miscellaneous Article]. *Transplant July 27 2004*. 2004;78(2):242-249. doi:10.1097/01.TP.0000128167.60172.CC

36. Nankivell BJ, Fenton-Lee CA, Kuypers DR, et al. Effect of histological damage on long-term kidney transplant outcome. *Transplantation*. 2001;71(4):515-523.

37. de Sandes-Freitas TV, Felipe CR, Campos ÉF, et al. Subclinical Lesions and Donor-Specific Antibodies in Kidney Transplant Recipients Receiving Tacrolimus-Based Immunosuppressive Regimen Followed by Early Conversion to Sirolimus. *Transplantation*. April 2015. doi:10.1097/TP.0000000000000748

38. Servais A, Meas-Yedid V, Noël LH, et al. Interstitial Fibrosis Evolution on Early Sequential Screening Renal Allograft Biopsies Using Quantitative Image Analysis. *Am J Transplant*. 2011;11(7):1456-1463. doi:10.1111/j.1600-6143.2011.03594.x

39. Rush D, Nickerson P, Gough J, et al. Beneficial effects of treatment of early subclinical rejection: a randomized study. *J Am Soc Nephrol*. 1998;9(11):2129-2134.

Table 1: Description of recipient, donor, transplantation characteristics and follow-up parameters in the first year post-transplantation for the sample of patients (n=1573) according to 1-year SB policy.

	Missing data	Global N=1573	Patients from transplantation centers without a 1-year SB policy N=769 (49%)	Patients from transplantation centers having a 1-year SB N=804 (51%)	p-value	Standardized difference (%)
Quantitative characteristics : Mean ± SD (1st quartile - 3rd quartile)						
Recipient age (years)	0	50.4±13.0 (42 – 60)	50.0±12.9 (42 – 60)	50.8±13.1 (41 – 61)	0.2378	5.96
Recipient BMI (kg/m²)	7	24.0±4.2 (21.0 – 26.6)	23.9±4.1 (21.0 – 26.3)	24.1±4.4 (21.0 – 26.6)	0.3179	5.05
Time spent on dialysis (years)	3	3.2±3.3 (1.1 – 4.3)	3.0±3.0 (1.1 – 4.0)	3.4±3.6 (1.0 – 4.5)	0.0161	12.14
Donor age (years)	0	50.4±15.8 (40 – 62)	49.0±15.5 (38 – 61)	51.8±16.0 (42 – 63)	0.0006	17.44
Last donor serum creatinine (µmol/L)	11	91.0±58.5 (60 – 105)	90.8±53.5 (61 – 103)	91.2±62.8 (59 – 106)	0.9022	0.62
CIT (hours)	0	19.4±7.3 (14.0 – 23.5)	18.7±6.9 (13.6– 22.5)	20.1±7.7 (14.4 – 24.0)	0.0001	19.37
3-month eGFR (µmol/L)	0	55.2±18.4 (42.5 – 65.4)	54.8±17.6 (42.5 – 64.5)	55.5±19.1 (42.4 – 66.6)	0.4592	3.74
6-month eGFR (µmol/L)	25	55.1±19.0 (42.0 – 65.4)	55.3±19.0 (42.2 – 65.6)	55.0±19.0 (41.7 – 65.1)	0.7695	1.49
12-month eGFR (µmol/L)	79	55.1±18.4 (41.8 – 66.1)	55.2±18.0 (42.0 – 66.5)	55.1±18.7 (41.5 – 65.6)	0.9982	0.12
Categorical characteristics : N (%)						
Recipient men	0	976 (62.0)	474 (61.6)	502 (62.4)	0.7836	1.65
History of diabetes	0	180 (11.4)	83 (10.8)	97 (12.1)	0.4761	4.00
History of hypertension	0	1244 (79.1)	556 (72.3)	688 (85.6)	<0.0001	32.98
History of dyslipidemia	0	519 (33.0)	204 (26.5)	315 (39.2)	<0.0001	27.18
History of neoplasia	0	140 (8.9)	60 (7.8)	80 (10.0)	0.1595	7.56
History of cardiovascular diseases	0	509 (32.4)	226 (29.4)	283 (35.2)	0.0160	12.45
Dialysis technique	0				0.3826	7.00
Pre-emptive transplantation		149 (9.5)	65 (8.5)	84 (10.4)		
Peritoneal dialysis		137 (8.7)	66 (8.6)	71 (8.8)		
Hemodialysis		1287 (81.8)	638 (83.0)	649 (80.7)		
Relapsing initial disease	0	465 (29.6)	233 (30.3)	232 (28.9)	0.5674	3.16
Daily anti-HLA immunization of class I	507	274 (25.7)	119 (27.5)	155 (24.5)	0.3039	6.84
Daily anti-HLA immunization of class II	548	253 (24.7)	98 (24.2)	155 (25.0)	0.8280	1.86
Donor men	0	969 (61.6)	457 (59.4)	512 (63.7)	0.0925	8.75
Donor history of hypertension	0	421 (26.8)	179 (23.3)	242 (30.1)	0.0027	15.47
Cerebro-vascular donor death	2	853 (54.3)	412 (53.6)	441 (54.9)	0.6486	2.56
More than 5 HLA A-B-DR incompatibilities	0	164 (10.4)	73 (9.5)	91 (11.3)	0.2705	5.98
Second graft	0	279 (17.7)	115 (15.0)	164 (20.4)	0.0058	14.31
Depleting induction	0	767 (48.8)	429 (55.8)	338 (42.0)	<0.0001	27.76
DGF	11	390 (25.0)	149 (19.5)	241 (30.2)	<0.0001	24.95
Urinary infection in the first year	0	188 (12.0)	103 (13.4)	85 (10.6)	0.0996	8.70
CMV infection in the first year	0	221 (14.0)	124 (16.1)	97 (12.1)	0.0248	11.69
Serious infection in the first year	0	311 (19.8)	156 (20.3)	155 (19.3)	0.6612	2.53
Causal biopsy in the first year	0	279 (17.7)	95 (12.4)	184 (22.9)	<0.0001	27.91

Table 2: Description of recipient, donor, transplantation characteristics and follow-up parameters in the first year post-transplantation for the pseudo-population obtained after Inverse Probability Weighting (Bold labels correspond to variables retained in the propensity score) according to 1-year SB policy.

	Patients from transplantation centers without a 1-year SB policy in the pseudo-population N=766 (49%)	Patients from transplantation centers having a 1-year SB in the pseudo-population N=805 (51%)	Standardized difference (%)
Quantitative characteristics : Mean ± SD			
Recipient age (years)	50.7±12.9	50.6±13.2	0.68
Recipient BMI (kg/m²)	23.9±4.1	24.0±4.3	0.98
Time spent on dialysis (years)	3.2±3.4	3.2±3.3	0.15
Donor age (years)	50.3±15.3	50.3±16.6	0.04
Last donor serum creatinine (µmol/L)	91.4±53.0	90.2±60.6	2.04
CIT (hours)	19.2±6.9	19.2±7.7	0.08
3-month eGFR (µmol/L)	55.3±18.2	55.4±18.6	0.14
6-month eGFR (µmol/L)	55.6±19.3	55.1±18.7	2.87
12-month eGFR (µmol/L)	55.3±18.2	55.4±18.6	1.63
Categorical characteristics : N (%)			
Recipient men	483 (63.0)	484 (60.1)	6.01
History of diabetes	89 (11.6)	89 (11.0)	1.84
History of hypertension	559 (73.0)	685 (85.1)	30.15
History of dyslipidemia	253 (33.1)	265 (32.8)	0.48
History of neoplasia	60 (7.8)	80 (10.0)	7.58
History of cardiovascular diseases	236 (30.8)	269 (33.4)	5.39
Dialysis technique			10.64
Pre-emptive transplantation	60 (7.9)	88 (10.9)	
Peritoneal dialysis	67 (8.8)	71 (8.8)	
Hemodialysis	638 (83.4)	646 (80.2)	
Relapsing initial disease	231 (30.2)	236 (29.3)	1.97
Daily anti-HLA immunization of class I	119 (26.8)	162 (26.3)	1.01
Daily anti-HLA immunization of class II	99 (23.7)	162 (27.0)	7.75
Donor men	480 (62.7)	505 (62.7)	0.13
Donor history of hypertension	192 (25.1)	227 (28.2)	7.04
Cerebro-vascular donor death	414 (54.1)	429 (53.4)	1.51
More than 5 HLA A-B-DR incompatibilities	67 (8.8)	87 (10.9)	6.87
Second graft	118 (15.4)	184 (22.8)	19.11
Depleting induction	376 (49.1)	397 (49.3)	0.35
DGF	169 (22.3)	221 (27.6)	12.26
Urinary infection in the first year	105 (13.8)	82 (10.2)	11.12
CMV infection in the first year	122 (15.9)	104 (12.9)	8.54
Serious infection in the first year	157 (20.5)	147 (18.3)	5.53
Causal biopsy in the first year	142 (18.6)	146 (18.1)	1.24

Table 3: Summary of the results given the different performed IPW survival analyses.

	Risk factor of interest	Survival outcomes	Hazard Ratio	95% Confidence Interval	p- value
Principal analysis	With 1-year SB policy (n=804) vs. without 1-year SB policy (n=769)	Graft and patient survival	1.15	[0.86 – 1.53]	0.3495
Secondary analysis		Graft survival (death-censored)	1.00	[0.68 – 1.47]	0.9928
Sensitivity analysis 1	Biopsied patients (n=388) vs. without 1-year SB policy (n=769)	Graft and patient survival	1.00	[0.69 – 1.46]	0.9944
		Graft survival (death-censored)	0.76	[0.45 – 1.27]	0.2916
Sensitivity analysis 2	Biopsied patients (n=388) vs. not biopsied regardless of1-year SB policy (n=1185)	Graft and patient survival	0.89	[0.63 – 1.26]	0.5073
		Graft survival (death-censored)	0.79	[0.48 – 1.31]	0.3618
Sensitivity analysis 3	Biopsied patients (n=388) vs. not biopsied from transplantation centers having a 1-year SB policy (n=416)	Graft and patient survival	0.81	[0.53 – 1.24]	0.3394
		Graft survival (death-censored)	0.88	[0.47 – 1.65]	0.6930

Figure 1: Flowchart picturing selection of the studied patients and their partition given the 1-year SB policy.

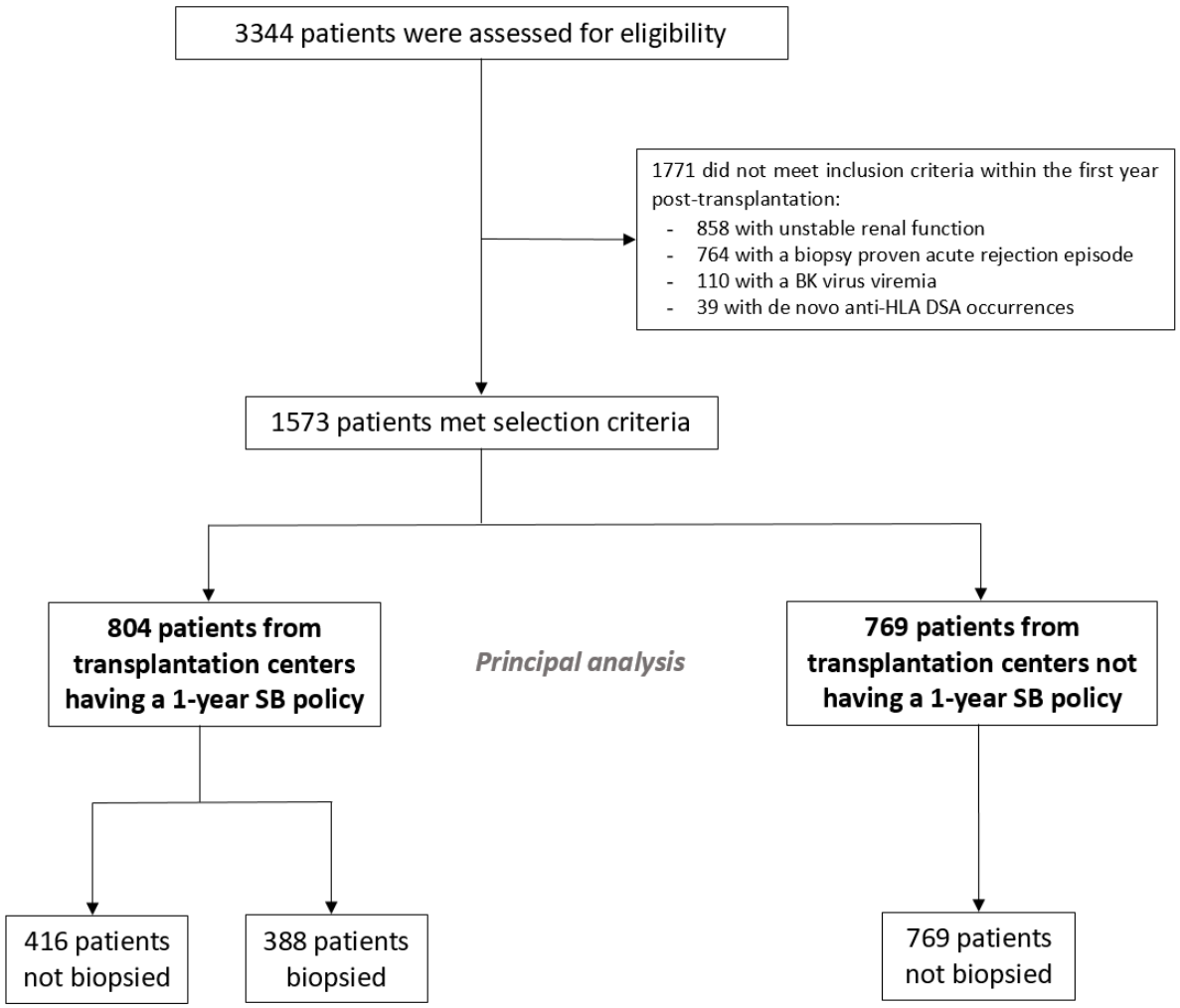
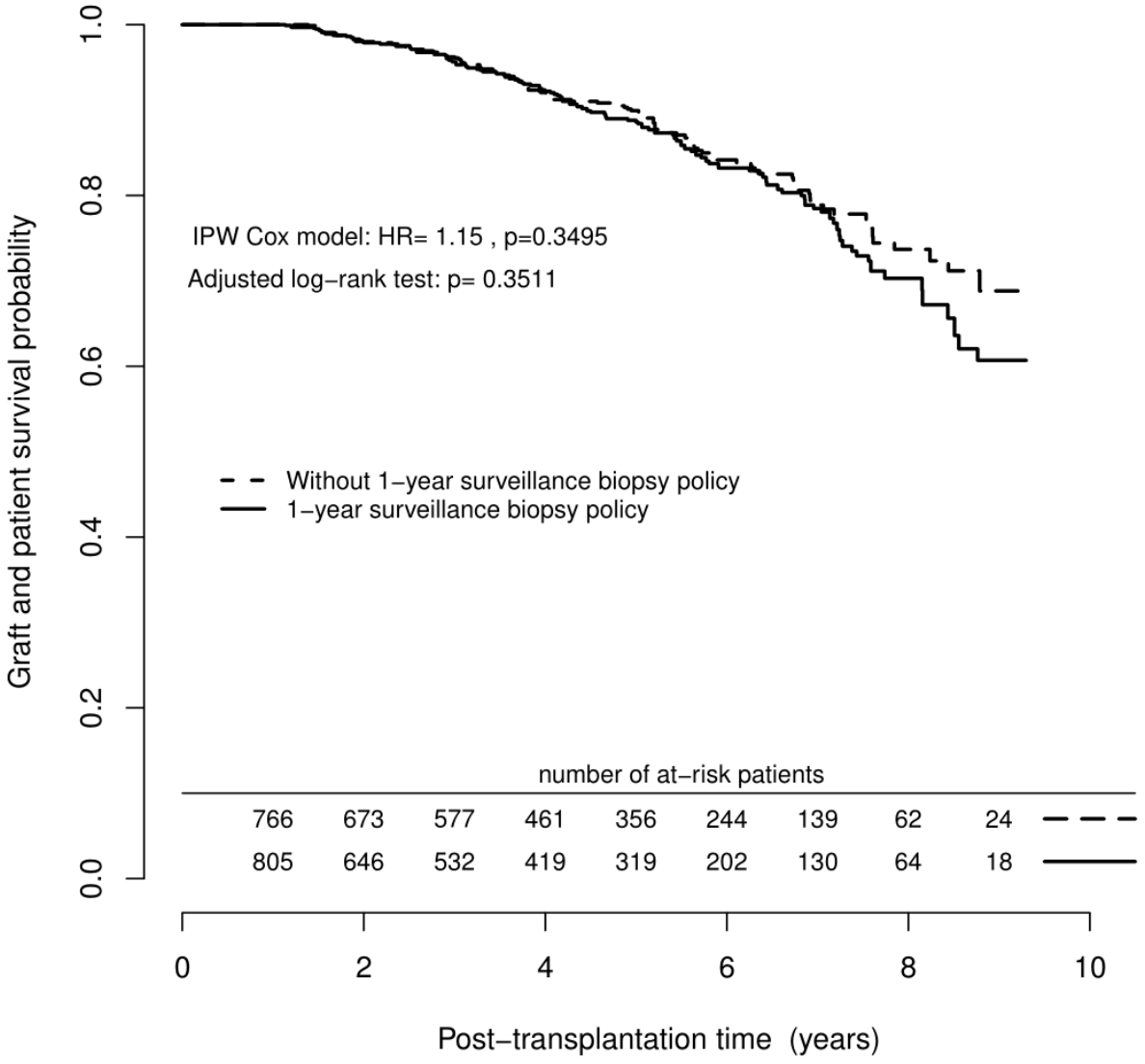


Figure 2: Adjusted graft and patient survival curves estimated by the IPW Kaplan–Meier estimator for kidney recipients according to the 1-year SB policy (transplantation centers without 1-year SB (dashed line) and transplantation centers with 1-year SB policy (solid line)) (n= 1570, 3 observations deleted due to missing data concerning covariates).



Web supplementary materials

1- Principal analysis: Graft and patient survival analysis (804 patients from transplantations centers having 1-year SB policy versus 769 patients from transplantations centers not having 1-year SB policy)

Table S1: Multivariable logistic regression used for definition of the propensity score (n=1570, 3 patients excluded due to missing data).

	Odds Ratio	95% Confidence Interval	p- value
Recipient age (years)	0.99	[0.97 – 1.00]	0.0193
Donor age (years)	1.02	[1.01 – 1.03]	<0.0001
Time spent on dialysis (years)	1.03	[1.00 – 1.07]	0.0433
CIT (hours)	1.03	[1.01 – 1.04]	0.0004
3-month eGFR (ml/min/1.73m²)	1.01	[1.01 – 1.02]	0.0005
History of dyslipidemia (positive vs. negative)	1.83	[1.46 – 2.30]	<0.0001
Donor gender (men vs. women)	1.28	[1.03 – 1.58]	0.0268
Induction therapy (depleting vs. non depleting)	0.57	[0.46 – 0.70]	<0.0001
Causal biopsy in the first year post-transplantation (yes vs. no)	2.08	[1.56 – 2.77]	0.0001

Figure S1: Distribution of the propensity score according to the 1-year SB policy (With 1-year SB policy versus Without 1-year SB policy) (n= 1570, 3 observations deleted due to missing data concerning covariates).

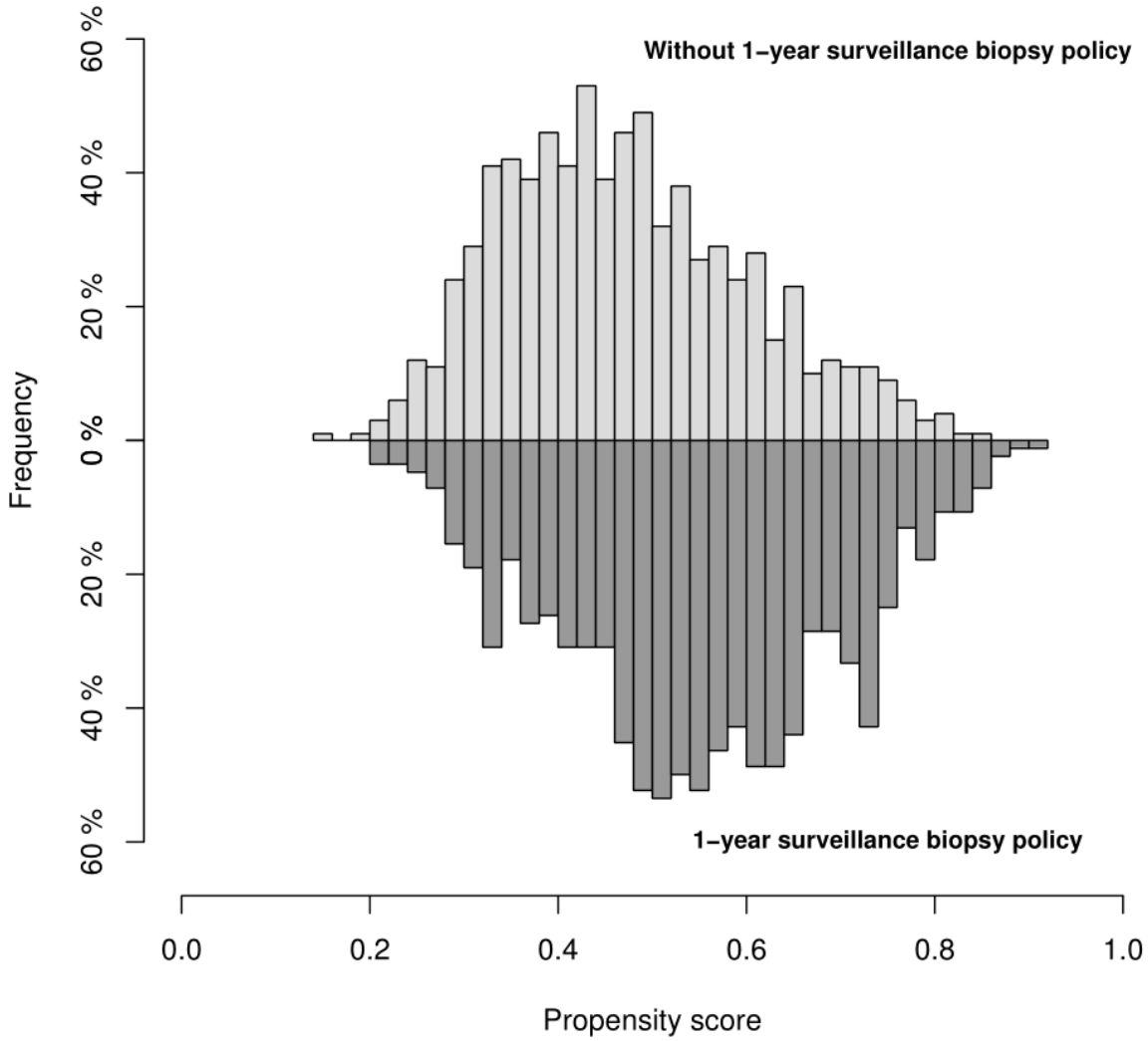
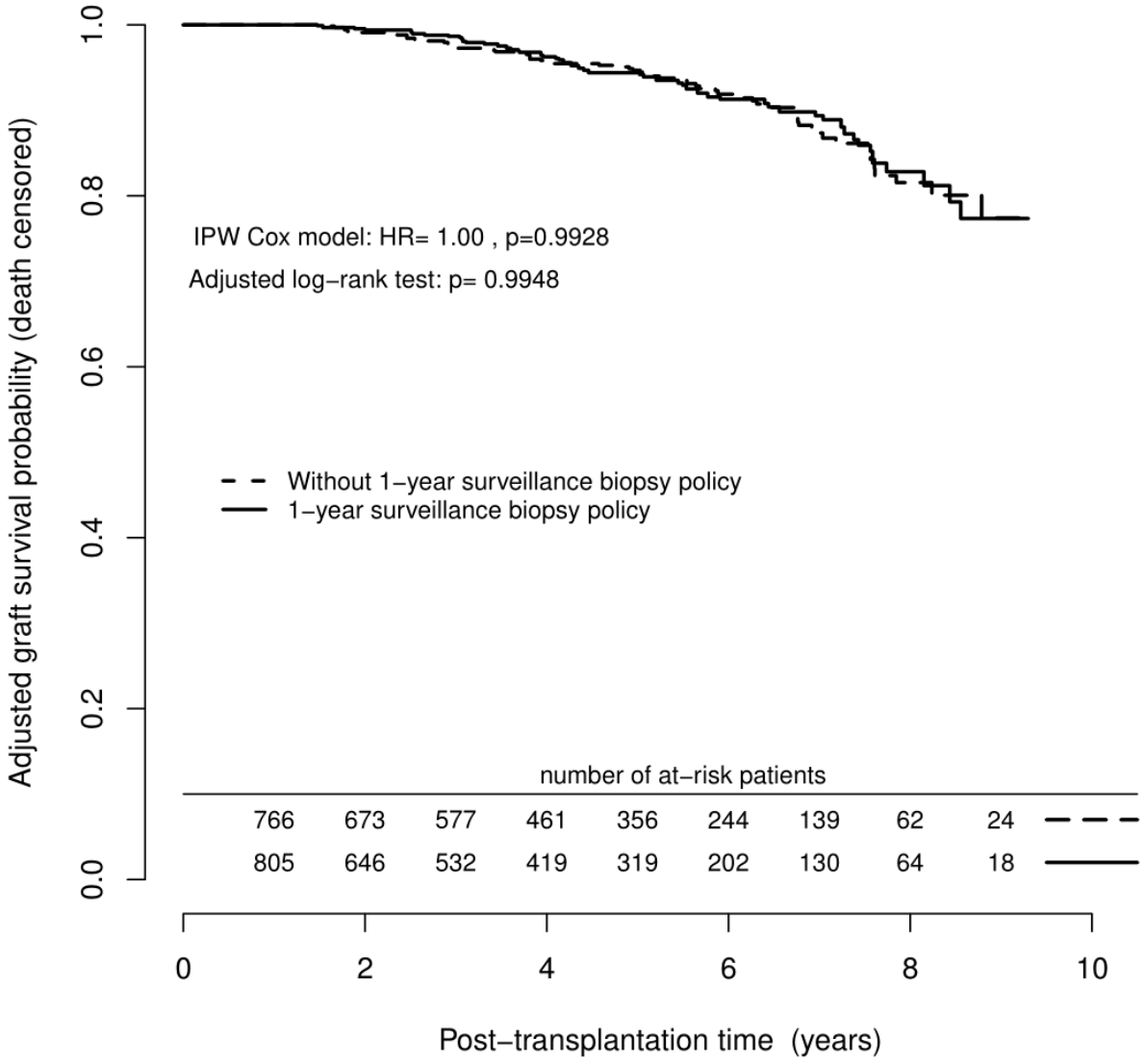


Table S2: Univariable graft and patient survival analyses for each possible confounding variable: significant variables were considered eligible for the propensity score from the sample of patients (n=1573) (p<0.20).

	Hazard Ratio	95% Confidence Interval	p
1-year SB policy (practicing vs. not practicing)	1.28	[0.98 - 1.68]	0.0741
Recipient age (years)	1.03	[1.02 – 1.04]	<0.0001
Recipient BMI			0.7698
18.5-30 kg/m² vs. ≤18.5 kg/m²	0.94	[0.57 – 1.55]	
>30 kg/m² vs. ≤18.5 kg/m²	1.11	[0.59 – 2.09]	
Donor age (years)	1.03	[1.02 – 1.04]	<0.0001
Last donor serum creatinine (>132.75 µmol/L vs. ≤132.75 µmol/L)	1.34	[0.91 – 1.99]	0.1400
Time spent on dialysis (years)	1.03	[0.99 – 1.06]	0.1384
Cold Ischemia Time (hours)	1.01	[0.99 – 1.03]	0.1074
3-month eGFR (µmol/L)	0.97	[0.96 – 0.98]	<0.0001
6-month eGFR (µmol/L)	0.97	[0.96 – 0.98]	<0.0001
12-month eGFR (µmol/L)	0.97	[0.96 – 0.98]	<0.0001
Recipient gender (male vs. female)	1.38	[1.04 – 1.83]	0.0274
Relapsing initial disease (yes vs. no)	0.73	[0.53 – 1.00]	0.0533
History of diabetes (positive vs. negative)	2.11	[1.47 – 3.04]	<0.0001
History of hypertension (positive vs. negative)	1.16	[0.80 – 1.67]	0.4309
History of cardiovascular diseases (positive vs. negative)	1.90	[1.45 – 2.49]	<0.0001
History of dyslipidemia (positive vs. negative)	1.54	[1.17 – 2.03]	0.0021
History of neoplasia (positive vs. negative)	1.78	[1.20 – 2.65]	0.0045
Dialysis technique			0.2414
Peritoneal dialysis vs. Pre-emptive transplantation	0.76	[0.33 – 1.75]	
Hemodialysis vs. Pre-emptive transplantation	1.27	[0.75 – 2.15]	
HLA A-B-DR incompatibilities (>4 vs. ≤ 4)	0.90	[0.57 – 1.41]	0.6457
Detectable daily anti-HLA immunization of class I (positive vs. negative)	1.42	[0.97 – 2.06]	0.0693
Detectable daily anti-HLA immunization of class II (positive vs. negative)	0.82	[0.51 – 1.30]	0.3997
Donor gender (male vs. female)	0.75	[0.57 – 0.98]	0.0366
Donor type (cerebrovascular death vs. non cerebro-vascular death)	1.25	[0.95 – 1.65]	0.1138
Donor history of hypertension (positive vs. negative)	1.46	[1.08 – 1.96]	0.0127
Induction treatment (depleting vs. non depleting)	0.79	[0.60 – 1.04]	0.0935
Delayed Graft Function (positive vs. negative)	1.49	[1.12 – 1.98]	0.0059
Urinary infection during the first year post-transplantation (positive vs. negative)	1.30	[0.90 – 1.88]	0.1663
CMV infection during the first year post-transplantation (positive vs. negative)	1.08	[0.74 – 1.59]	0.6882
Serious infection during the first year post-transplantation (positive vs. negative)	1.44	[1.06 – 1.95]	0.0195
Number of transplantation (second vs. first)	1.15	[0.82 – 1.60]	0.4201
Causal biopsy in the first year post-transplantation (yes vs. no)	1.56	[1.13 – 2.17]	0.0075

2- Secondary analysis: Graft survival (with death-censored) analysis (804 patients from transplantations centers having 1-year SB policy versus 769 patients from transplantations centers not having 1-year SB policy)

Figure S2: Adjusted graft survival curves (with death-censored) estimated by the IPW Kaplan–Meier estimator for kidney recipients according to the 1-year SB policy (transplantation centers without 1-year SB policy (dashed line) and transplantation centers with a 1-year SB policy (solid line)) (n= 1570, 3 observations deleted due to missing data concerning covariates).



3- Sensitivity analysis 1 (388 biopsied patients from transplantations centers having 1-year SB policy versus 769 patients from transplantations centers not having 1-year SB policy)

Demographic characteristics of donors and recipients and clinical features available during the first year post-transplantation are presented in Table S3. The propensity score was composed of height variables (Table S4). Respecting positivity assumption (Figure S3), the propensity score-based analysis resulted in the comparison of two pseudo-groups of patients with similar characteristics (Table S5). Note that important standardized differences for a history of hypertension, induction treatment and CMV infection in the first year do not represent a problem, since they are not showed as relevant confounding factors being not significantly associated with graft failure (data not shown). We did not observe a significant difference of graft failure risk between biopsied patients and patients from transplantation centers without 1-year SB policy (HR=1.00, 95% CI from 0.69 to 1.46, p=0.9944). Estimated on the counterfactual population, the corresponding adjusted graft and patient survival probabilities were not significantly different (Figure S4). The adjusted graft and patient survival probability at 8 years post-transplantation was 69% (95% CI from 57% to 78%) for patients from centers having a 1-year SB policy versus 75% (95% CI from 68% to 80%) for patients from other centers. Estimated on the counterfactual population, the corresponding adjusted graft survival probabilities (with death-censored) were not significantly different between biopsied patients and patients from transplantation centers without 1-year SB policy (HR=0.76, 95% CI from 0.45 to 1.27, p=0.2916) (Figure S5).

Table S3: Description of the sample of patients (n=1157, 416 patients from centers with 1-year SB policy and finally not biopsied were not included).

	Missing data	Global N=1157	Patients from transplantation centers without a 1-year SB policy N=769 (66%)	Biopsied patients from transplantation centers having a 1-year SB N=388 (34%)	p-value	Standardized difference (%)
Quantitative characteristics : Mean ± SD (1st quartile - 3rd quartile)						
Recipient age (years)	0	49.8±12.8 (41 – 60)	50.0±12.9 (42 – 60)	49.3±12.8 (40 – 58)	0.3467	5.85
Recipient BMI (kg/m²)	7	24.0±4.2 (21.0 – 26.5)	23.9±4.1 (21.0 – 26.3)	24.2±4.4 (21.0 – 26.6)	0.3301	6.15
Time spent on dialysis (years)	2	3.2±3.2 (1.1 – 4.3)	3.0±3.0 (1.1 – 4.0)	3.6±3.6 (1.1 – 4.9)	0.0027	19.27
Donor age (years)	0	49.4±15.6 (39 – 61)	49.0±15.5 (38 – 61)	50.2±15.9 (40 – 61)	0.2251	7.60
Last donor serum creatinine (µmol/L)	9	92.9±62.6 (61 – 105)	90.8±53.5 (61 – 103)	97.1±77.2 (60 – 108)	0.1554	9.37
CIT (hours)	0	19.2±7.2 (14.0 – 23.5)	18.7±6.9 (13.6– 22.5)	20.3±7.7 (15.0 – 24.2)	0.0004	22.74
3-month eGFR (µmol/L)	0	55.7±18.1 (42.7 – 66.0)	54.8±17.6 (42.5 – 64.5)	57.4±19.0 (43.4 – 69.3)	0.0285	13.83
6-month eGFR (µmol/L)	12	55.6±18.7 (42.4 – 66.1)	55.3±19.0 (42.2 – 65.6)	56.1±18.2 (42.6 – 66.9)	0.4437	4.77
12-month eGFR (µmol/L)	68	55.7±17.9 (42.6 – 66.8)	55.2±18.0 (42.0 – 66.5)	56.8±17.7 (43.7 – 67.3)	0.1494	9.29
Categorical characteristics : N (%)						
Recipient men	0	723 (62.5)	474 (61.6)	249 (64.2)	0.4371	5.25
History of diabetes	0	136 (11.8)	83 (10.8)	53 (13.7)	0.1827	8.76
History of hypertension	0	889 (76.8)	556 (72.3)	333 (85.8)	<0.0001	33.71
History of dyslipidemia	0	345 (29.8)	204 (26.5)	141 (36.3)	0.0007	21.25
History of neoplasia	0	89 (7.7)	60 (7.8)	29 (7.5)	0.9355	1.24
History of cardiovascular diseases	0	354 (30.6)	226 (29.4)	128 (33.0)	0.2351	7.78
Dialysis technique	0				0.4646	7.61
Pre-emptive transplantation		106 (9.2)	65 (8.5)	41 (10.6)		
Peritoneal dialysis		96 (8.3)	66 (8.6)	30 (7.7)		
Hemodialysis		955 (82.5)	638 (83.0)	317 (81.7)		
Relapsing initial disease	0	340 (29.4)	233 (30.3)	107 (27.6)	0.3728	6.00
Daily anti-HLA immunization of class I	367	213 (27.0)	119 (27.5)	94 (26.3)	0.7775	2.60
Daily anti-HLA immunization of class II	398	187 (24.6)	98 (24.2)	89 (25.1)	0.8285	2.19
Donor men	0	698 (60.3)	457 (59.4)	241 (62.1)	0.4134	5.50
Donor history of hypertension	0	290 (25.1)	179 (23.3)	111 (28.6)	0.0570	2.19
Cerebro-vascular donor death	1	624 (54.0)	412 (53.6)	212 (54.6)	0.7968	1.99
More than 5 HLA A-B-DR incompatibilities	0	112 (9.7)	73 (9.5)	39 (10.1)	0.8429	1.88
Second graft	0	173 (15.0)	115 (15.0)	58 (14.9)	0.9999	0.02
Depleting induction	0	545 (47.1)	429 (55.8)	116 (29.9)	<0.0001	54.21
DGF	6	267 (23.2)	149 (19.5)	118 (30.5)	<0.0001	25.58
Urinary infection in the first year	0	138 (11.9)	103 (13.4)	35 (9.0)	0.0384	13.90
CMV infection in the first year	0	151 (13.1)	124 (16.1)	27 (7.0)	<0.0001	28.99
Serious infection in the first year	0	222 (19.2)	156 (20.3)	66 (17.0)	0.2088	8.42
Causal biopsy in the first year	0	184 (15.9)	95 (12.4)	89 (22.9)	<0.0001	28.04

Table S4: Multivariable logistic regression used for definition of the propensity score (n=1149, 8 patients excluded due to missing data).

	Odds Ratio	95% Confidence Interval	p- value
Recipient age (years)	0.98	[0.96 – 0.99]	0.0057
Donor age (years)	1.02	[1.01 – 1.04]	0.0003
Time spent on dialysis (years)	1.07	[1.02 – 1.11]	0.0024
3-month eGFR (ml/min/1.73m²)	1.02	[1.01 – 1.03]	<0.0001
Dialysis technique			0.0154
Peritoneal dialysis vs. Pre-emptive transplantation	0.54	[0.30 – 0.99]	0.0480
Hemodialysis vs. Pre-emptive transplantation	0.50	[0.32 – 0.80]	0.0034
History of dyslipidemia (positive vs. negative)	1.68	[1.27 – 2.23]	0.0003
DGF (positive vs. negative)	1.79	[1.31 – 2.43]	0.0002
Causal biopsy in the first year post-transplantation (yes vs. no)	2.10	[1.49 – 2.96]	<0.0001

Figure S3: Distribution of the propensity score for biopsied patients from transplantation center with 1-year SB policy and for patients from transplantation centers without 1-year SB policy (n=1149, 8 observations deleted due to missing data concerning covariates).

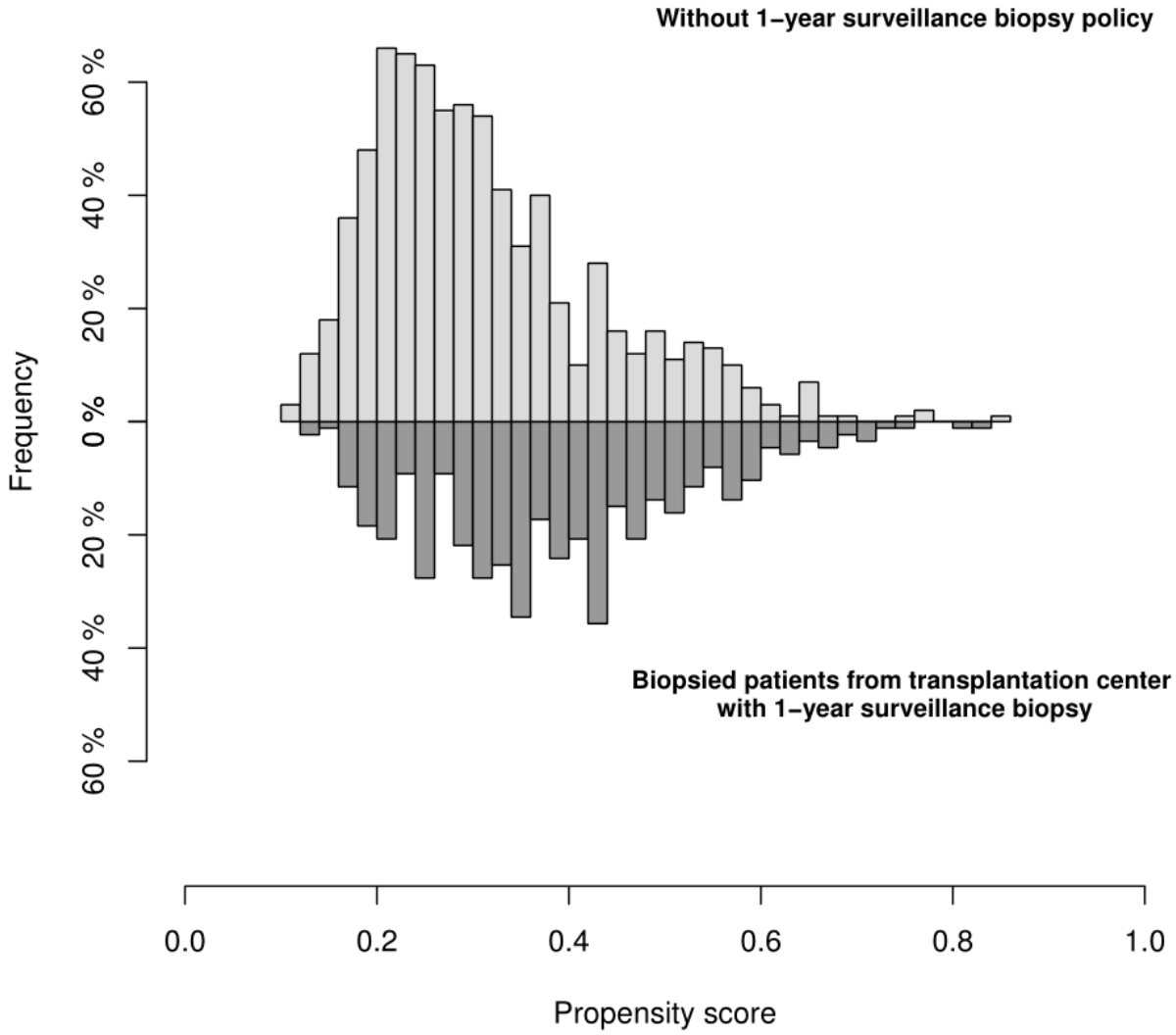


Table S5: Description of recipient, donor, transplantation characteristics and follow-up parameters in the first year post-transplantation for the pseudo-population obtained after Inverse Probability Weighting (Bold labels correspond to variables retained in the propensity score).

	Patients from transplantation centers without a 1-year SB policy in the pseudo-population N=767 (67%)	Biopsied patients from transplantation centers having a 1-year SB in the pseudo-population N=384 (33%)	Standardized difference (%)
Quantitative characteristics : Mean ± SD			
Recipient age (years)	49.8±12.9	50.1±12.5	1.94
Recipient BMI (kg/m²)	23.9±4.2	24.1±4.3	4.71
Time spent on dialysis (years)	3.3±4.0	3.2±3.1	4.18
Donor age (years)	49.2±15.3	49.2±16.3	0.19
Last donor serum creatinine (µmol/L)	92.4±56.3	94.5±69.1	3.27
CIT (hours)	18.8±6.9	19.8±7.6	13.91
3-month eGFR (µmol/L)	56.0±18.2	56.3±18.3	1.30
6-month eGFR (µmol/L)	56.0±19.6	55.6±17.7	3.10
12-month eGFR (µmol/L)	56.0±18.8	56.3±18.3	1.07
Categorical characteristics : N (%)			
Recipient men	479 (62.5)	237 (61.7)	1.63
History of diabetes	84 (11.0)	49 (12.7)	5.24
History of hypertension	554 (72.2)	324 (84.4)	30.02
History of dyslipidemia	228 (29.8)	114 (29.7)	0.24
History of neoplasia	63 (8.2)	30 (7.8)	1.51
History of cardiovascular diseases	232 (30.2)	122 (31.8)	3.47
Dialysis technique			2.41
Pre-emptive transplantation	71 (9.3)	38 (10.0)	
Peritoneal dialysis	63 (8.2)	32 (8.3)	
Hemodialysis	632 (82.5)	313 (81.7)	
Relapsing initial disease	231 (30.2)	106 (27.7)	5.46
Daily anti-HLA immunization of class I	125 (28.3)	92 (26.3)	4.77
Daily anti-HLA immunization of class II	100 (24.4)	87 (24.8)	0.81
Donor men	463 (60.4)	239 (62.2)	3.75
Donor history of hypertension	182 (23.8)	108 (28.2)	10.12
Cerebro-vascular donor death	404 (52.8)	209 (54.5)	3.35
More than 5 HLA A-B-DR incompatibilities	71 (9.2)	36 (9.4)	0.60
Second graft	121 (15.7)	56 (14.7)	2.89
Depleting induction	431 (56.2)	119 (31.0)	52.63
DGF	182 (23.7)	91 (23.8)	0.33
Urinary infection in the first year	103 (13.5)	35 (9.1)	13.77
CMV infection in the first year	124 (16.2)	28 (7.2)	28.41
Serious infection in the first year	159 (20.7)	63 (16.4)	11.06
Causal biopsy in the first year	125 (16.3)	64 (16.6)	0.73

Figure S4: Adjusted graft and patient survival curves estimated by the IPW Kaplan–Meier estimator for biopsied patients from transplantation center with 1-year SB policy (solid line) and for patients from transplantation centers without 1-year SB policy (dashed line) (n=1149, 8 observations deleted due to missing data concerning covariates).

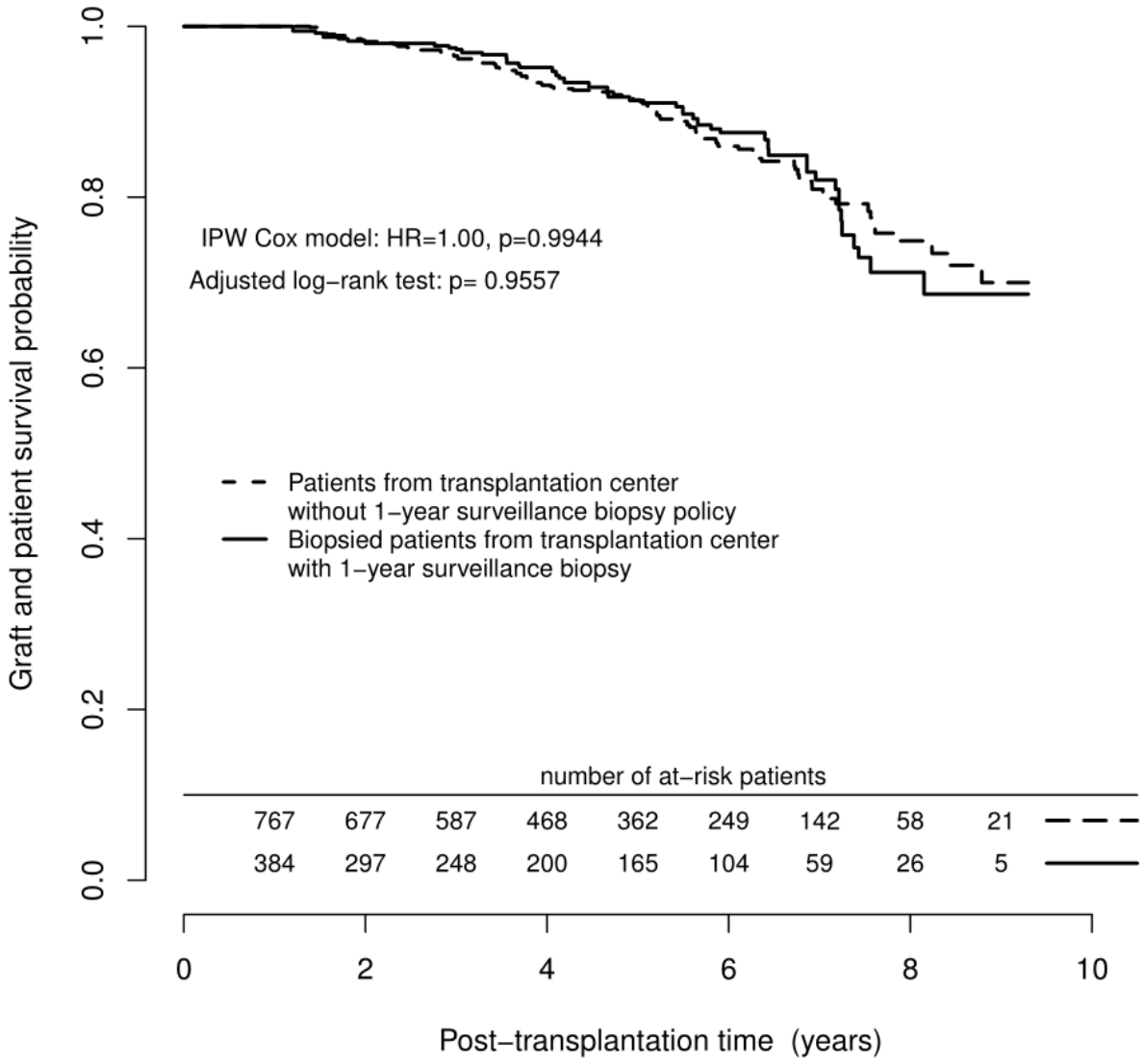
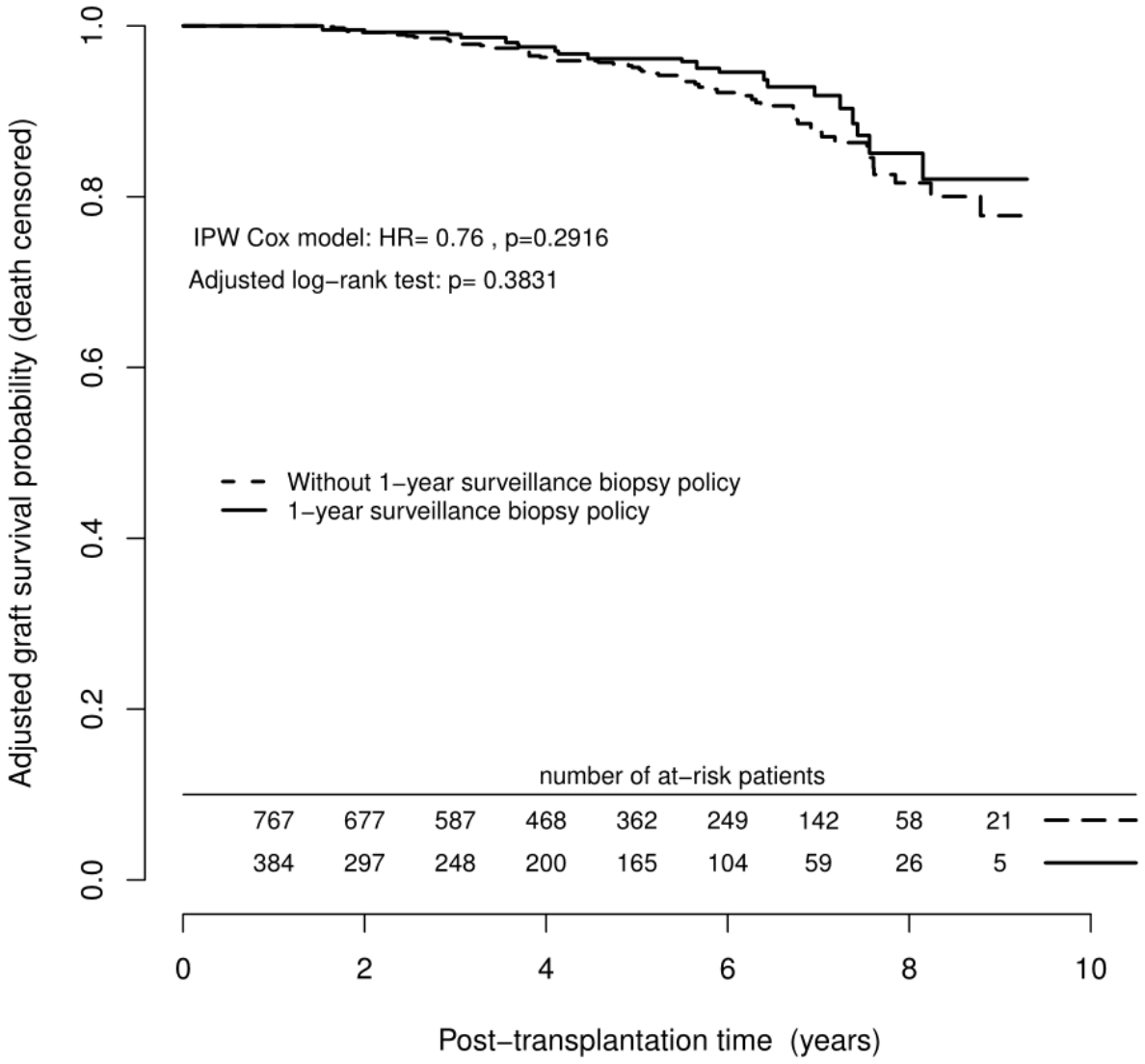


Figure S5: Adjusted graft survival curves (with death-censored) estimated by the IPW Kaplan–Meier estimator for biopsied patients from transplantation center with 1-year SB policy (solid line) and for patients from transplantation centers without 1-year SB policy (dashed line) (n=1149, 8 observations deleted due to missing data concerning covariates).



4- Sensitivity analysis 2 (388 biopsied patients from transplantations centers having 1-year SB policy versus 1185 patients not biopsied regardless of the 1-SB policy)

Demographic characteristics of donors and recipients and clinical features available during the first year post-transplantation are presented in Table S6. The propensity score was composed of seven variables (Table S7). Respecting positivity assumption (Figure S6~~S5~~), the propensity score-based analysis resulted in the comparison of two pseudo-groups of patients with similar characteristics (Table S8). Note that important standardized differences for a history of hypertension and CMV infection in the first year do not represent a problem, since they are not showed as relevant confounding factors being not significantly associated with graft failure (data not shown). We did not observe a significant difference of graft failure risk between biopsied patients and patients not biopsied regardless of the 1-SB policy (HR=0.89, 95% CI from 0.63 to 1.26, p=0.5073). Estimated on the counterfactual population, the corresponding adjusted graft and patient survival probabilities were not significantly different (Figure S7). The adjusted graft and patient survival probability at 8 years post-transplantation was 66% (95% CI from 54% to 77%) for patients from centers having a 1-year SB policy versus 71% (95% CI from 66% to 75%) for patients from other centers. Estimated on the counterfactual population, the corresponding adjusted graft survival probabilities (with death-censored) were not significantly different between biopsied patients and patients not biopsied regardless of the 1-SB policy (HR=0.79, 95% CI from 0.48 to 1.31, p=0.3618) (Figure S8).

Table S6: Description of the sample of patients (n=1573).

	Missing data	Global N=1573	Patients not biopsied regardless of the 1-SB policy N=1185 (66%)	Biopsied patients from transplantation centers having a 1-year SB N=388 (34%)	p-value	Standardized difference (%)
Quantitative characteristics : Mean ± SD (1st quartile - 3rd quartile)						
Recipient age (years)	0	50.4±13.0 (42 – 60)	50.8±13.1 (42 – 61)	49.3±12.8 (40 – 58)	0.0431	11.78
Recipient BMI (kg/m²)	7	24.0±4.2 (21.0 – 26.6)	24.0±4.2 (21.0 – 26.5)	24.2±4.4 (21.0 – 26.6)	0.4266	4.72
Time spent on dialysis (years)	3	3.2±3.3 (1.1 – 4.3)	3.1±3.2 (1.1 – 4.0)	3.6±3.6 (1.1 – 4.9)	0.0051	16.81
Donor age (years)	0	50.4±15.8 (40 – 62)	50.5±15.8 (40 – 62)	50.2±15.9 (40 – 61)	0.7632	1.77
Last donor serum creatinine (µmol/L)	11	91.0±58.5 (61 – 105)	89.0±50.6 (60 – 103)	97.1±77.2 (60 – 108)	0.0558	12.30
CIT (hours)	0	19.4±7.3 (14.0 – 23.5)	19.1±7.2 (13.8– 22.9)	20.3±7.7 (15.0 – 24.2)	0.0052	16.70
3-month eGFR (µmol/L)	0	55.2±18.4 (42.4 – 65.4)	54.5±18.1 (42.1 – 64.0)	57.4±19.0 (43.4 – 69.3)	0.0086	15.60
6-month eGFR (µmol/L)	25	55.1±19.0 (42.0 – 65.4)	54.8±19.2 (41.6 – 64.7)	56.1±18.2 (42.6 – 66.9)	0.2099	7.31
12-month eGFR (µmol/L)	79	55.1±18.4 (41.8 – 66.1)	54.6±18.6 (41.4 – 65.6)	56.8±17.7 (43.7 – 67.3)	0.0453	12.02
Categorical characteristics : N (%)						
Recipient men	0	976 (62.0)	727 (61.4)	249 (64.2)	0.3498	5.85
History of diabetes	0	180 (11.4)	127 (10.7)	53 (13.7)	0.1366	9.00
History of hypertension	0	1244 (79.1)	911 (76.9)	333 (85.8)	0.0002	23.12
History of dyslipidemia	0	519 (33.0)	378 (31.9)	141 (36.3)	0.1205	9.38
History of neoplasia	0	140 (8.9)	111 (9.4)	29 (7.5)	0.3012	6.82
History of cardiovascular diseases	0	509 (32.4)	381 (32.2)	128 (33.0)	0.8075	1.79
Dialysis technique	0				0.5440	6.45
Pre-emptive transplantation		149 (9.5)	108 (9.1)	41 (10.6)		
Peritoneal dialysis		137 (8.7)	107 (9.0)	30 (7.7)		
Hemodialysis		1287 (81.8)	970 (81.9)	317 (81.7)		
Relapsing initial disease	0	465 (29.6)	358 (30.2)	107 (27.6)	0.3562	5.81
Daily anti-HLA immunization of class I	507	274 (25.7)	180 (25.4)	94 (26.3)	0.7963	2.15
Daily anti-HLA immunization of class II	548	253 (24.7)	164 (24.4)	89 (25.1)	0.8642	1.62
Donor men	0	969 (61.6)	728 (61.4)	241 (62.1)	0.8583	1.40
Donor history of hypertension	0	421 (26.8)	310 (26.2)	111 (28.6)	0.3793	5.49
Cerebro-vascular donor death	2	853 (54.3)	641 (54.2)	212 (54.6)	0.9224	0.91
More than 5 HLA A-B-DR incompatibilities	0	164 (10.4)	125 (10.5)	39 (10.1)	0.8553	1.88
Second graft	0	279 (17.7)	221 (18.6)	58 (14.9)	0.1141	9.81
Depleting induction	0	767 (48.8)	651 (54.9)	116 (29.9)	<0.0001	52.37
DGF	11	390 (25.0)	272 (23.1)	118 (30.5)	0.0047	16.63
Urinary infection in the first year	0	188 (12.0)	153 (12.9)	35 (9.0)	0.0499	12.48
CMV infection in the first year	0	221 (14.0)	194 (16.4)	27 (7.0)	<0.0001	29.64
Serious infection in the first year	0	311 (19.8)	245 (20.7)	66 (17.0)	0.1337	9.38
Causal biopsy in the first year	0	279 (17.7)	190 (16.0)	89 (22.9)	0.0026	17.50

Table S7: Multivariable logistic regression used for definition of the propensity score (n=1545, 28 patients excluded due to missing data).

	Odds Ratio	95% Confidence Interval	p- value
Recipient age (years)	0.98	[0.97 – 1.00]	0.0297
Donor age (years)	1.01	[1.00 – 1.02]	0.0528
Time spent on dialysis (years)	1.05	[1.01 – 1.08]	0.0083
3-month eGFR (ml/min/1.73m²)	1.02	[1.01 – 1.04]	0.0007
6-month eGFR (ml/min/1.73m²)	0.99	[0.98 – 1.00]	0.0435
Induction therapy (depleting vs. non depleting)	0.35	[0.27 – 0.45]	<0.0001
Causal biopsy in the first year post-transplantation (yes vs. no)	1.55	[1.14 – 2.11]	0.0049

Figure S6: Distribution of the propensity score for biopsied patients from transplantation center with 1-year SB policy and for patients not biopsied regardless of the 1-year SB policy of the transplantation center (n=1545, 28 observations deleted due to missing data concerning covariates).

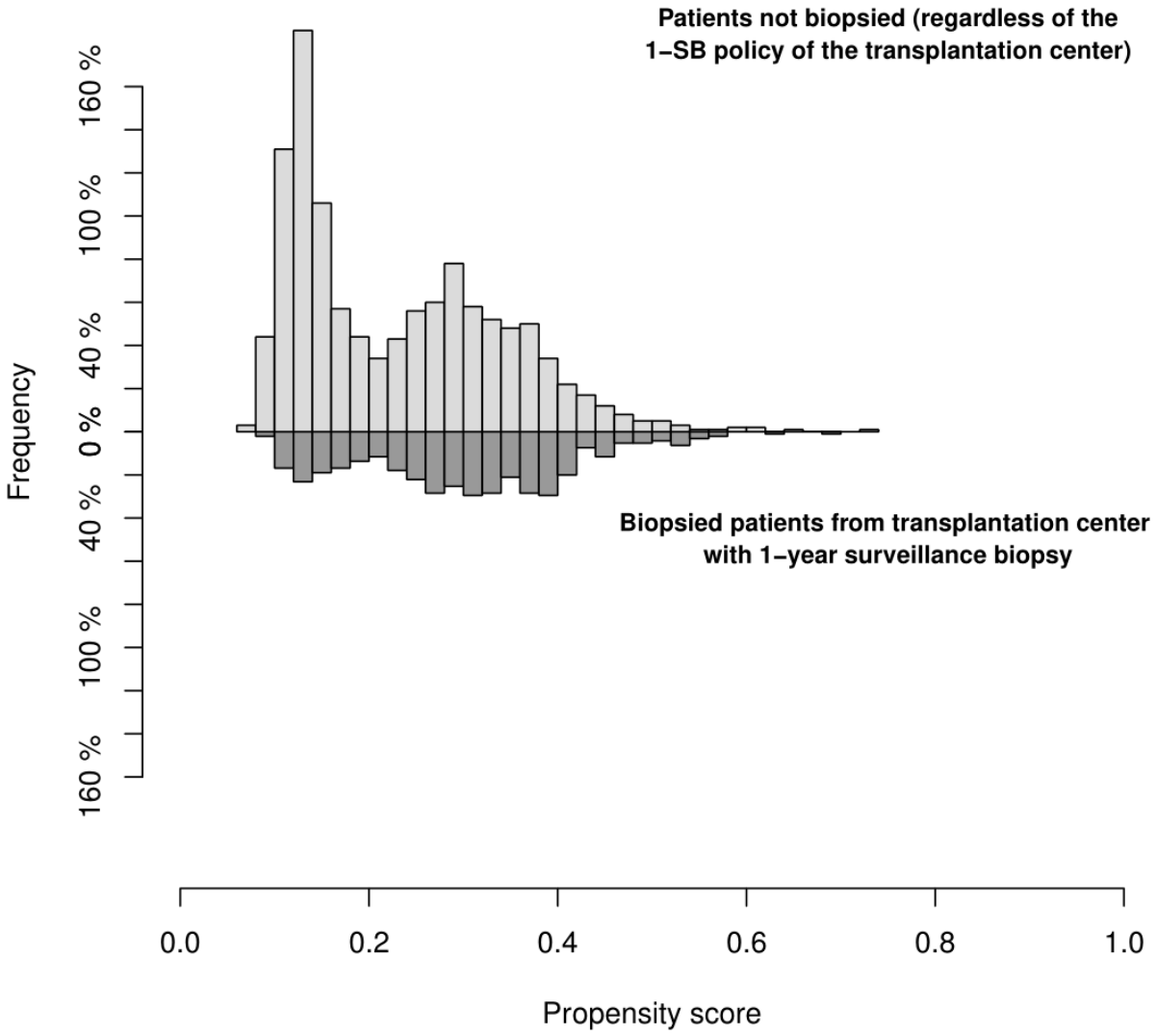


Table S8: Description of recipient, donor, transplantation characteristics and follow-up parameters in the first year post-transplantation for the pseudo-population obtained after Inverse Probability Weighting (Bold labels correspond to variables retained in the propensity score).

	Patients not biopsied regardless of the 1-SB policy in the pseudo-population N=1166 (76%)	Biopsied patients from transplantation centers having a 1-year SB in the pseudo-population N=376 (24%)	Standardized difference (%)
Quantitative characteristics : Mean ± SD			
Recipient age (years)	50.5±13.3	50.7±12.6	1.66
Recipient BMI (kg/m²)	23.9±4.2	24.4±4.4	11.78
Time spent on dialysis (years)	3.2±3.7	3.2±3.3	0.96
Donor age (years)	50.5±15.9	50.5±16.2	0.08
Last donor serum creatinine (µmol/L)	88.98±50.6	95.8±73.3	10.85
CIT (hours)	18.9±7.1	19.7±7.7	9.99
3-month eGFR (µmol/L)	55.3±19.1	56.1±18.2	4.00
6-month eGFR (µmol/L)	55.22±19.8	55.7±18.2	2.39
12-month eGFR (µmol/L)	55.3±19.1	56.1±18.2	4.87
Categorical characteristics : N (%)			
Recipient men	724 (62.1)	233 (61.8)	0.58
History of diabetes	122 (10.5)	52 (13.9)	10.43
History of hypertension	886 (76.0)	327 (86.8)	28.08
History of dyslipidemia	364 (31.2)	137 (36.4)	10.92
History of neoplasia	110 (9.4)	28.2 (7.5)	7.01
History of cardiovascular diseases	373 (32.0)	123 (32.8)	1.59
Dialysis technique			10.64
Pre-emptive transplantation	105 (9.0)	44 (11.8)	
Peritoneal dialysis	104 (8.9)	31 (8.2)	
Hemodialysis	957 (82.1)	301 (80.0)	
Relapsing initial disease	346 (29.7)	108 (28.8)	1.80
Daily anti-HLA immunization of class I	169 (24.0)	106 (30.1)	15.53
Daily anti-HLA immunization of class II	153 (22.9)	101 (29.8)	15.72
Donor men	715 (61.3)	231(61.4)	0.15
Donor history of hypertension	306 (26.2)	113 (30.0)	8.50
Cerebro-vascular donor death	635 (54.5)	206 (54.8)	0.57
More than 5 HLA A-B-DR incompatibilities	127 (10.9)	33 (8.7)	7.36
Second graft	205 (17.5)	73 (19.5)	4.97
Depleting induction	566 (48.6)	179 (47.5)	2.17
DGF	268 (23.2)	106 (28.1)	11.21
Urinary infection in the first year	153 (13.1)	31 (8.2)	15.84
CMV infection in the first year	183 (15.7)	32 (8.6)	21.82
Serious infection in the first year	241 (20.7)	57 (15.3)	14.12
Causal biopsy in the first year	208 (17.9)	68 (18.0)	0.43

Figure S7: Adjusted graft and patient survival curves estimated by the IPW Kaplan–Meier estimator for kidney recipients biopsied at 1-year post-transplantation (solid line) and for patients not biopsied regardless of the 1-year SB policy of the transplantation center (dashed line) (n=1545, 28 observations deleted due to missing data concerning covariates).

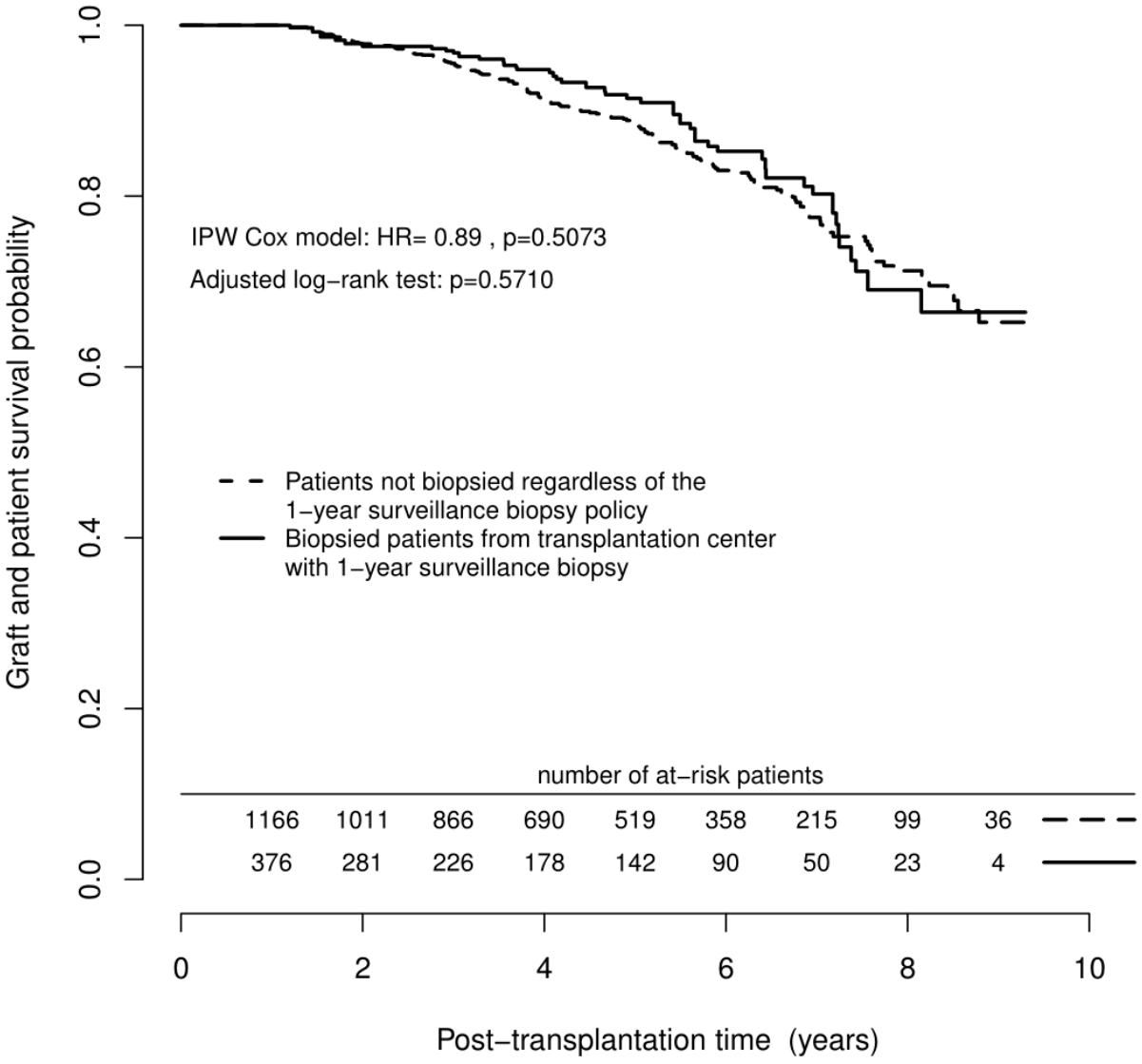
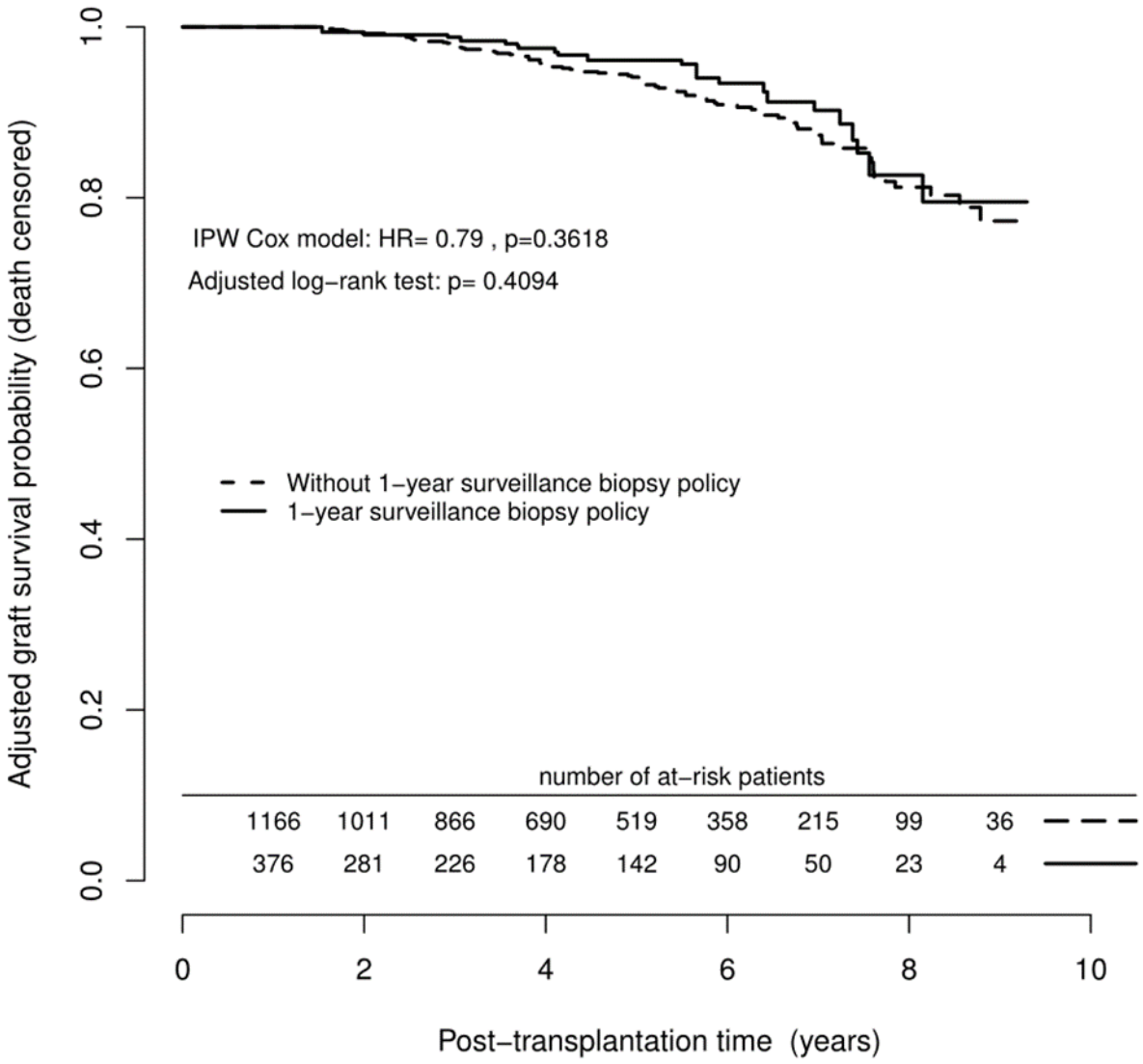


Figure S7: Adjusted graft survival curves (witht death-censored) estimated by the IPW Kaplan–Meier estimator for kidney recipients biopsied at 1-year post-transplantation (solid line) and for patients not biopsied regardless of the 1-year SB policy of the transplantation center (dashed line) (n=1545, 28 observations deleted due to missing data concerning covariates).



5- Sensitivity analysis 3 (388 biopsied patients from transplantations centers having 1-year SB policy versus 416 patients not biopsied from transplantations centers having 1-year SB policy)

Demographic characteristics of donors and recipients and clinical features available during the first year post-transplantation are presented in Table S9. The propensity score was composed of ten variables (Table S10). Respecting positivity assumption (Figure S9~~S7~~), the propensity score-based analysis resulted in the comparison of two pseudo-groups of patients with similar characteristics (Table S11). Note that important standardized differences for time spent in dialysis, graft rank, induction treatment and CMV infection in the first do not represent a problem, since they are not showed as relevant confounding factors being not significantly associated with graft failure (data not shown). We did not observe a significant difference of graft failure risk between biopsied patients and patients not biopsied from transplantations centers having 1-year policy (HR=0.81, 95% CI from 0.53 to 1.24, p=0.3394). Estimated on the counterfactual population, the corresponding adjusted graft and patient survival probabilities were not significantly different (Figure S10). The adjusted graft and patient survival probability at 8 years post-transplantation was 67% (95% CI from 56% to 77%) for patients from centers having a 1-year SB policy versus 68% (95% CI from 55% to 76%) for patients from other centers. Estimated on the counterfactual population, the corresponding adjusted graft survival probabilities (with death-censored) were not significantly different between biopsied patients and patients not biopsied from transplantations centers having 1-year policy (HR=0.88, 95% CI from 0.47 to 1.65, p=0.6930) (Figure S11).

Table S9: Description of the sample of patients from transplantation centers having 1-year SB policy (n=804, 769 patients from centers without a 1-year SB policy were not included).

	Missing data	Global N=804	Non-biopsied patients from transplantation centers having a 1-year SB N=416 (52%)	Biopsied patients from transplantation centers having a 1-year SB N=388 (48%)	p-value	Standardized difference (%)
Quantitative characteristics : Mean ± SD (1st quartile - 3rd quartile)						
Recipient age (years)	0	50.8±13.1 (41 – 61)	52.2±13.3 (43 – 62)	49.3±12.8 (40 – 58)	0.0014	22.63
Recipient BMI (kg/m²)	0	24.1±4.2 (21.0 – 26.6)	24.1±4.3 (21.0 – 26.7)	24.2±4.4 (21.0 – 26.6)	0.7591	2.17
Time spent on dialysis (years)	1	3.4±3.6 (1.0 – 4.5)	3.2±3.0 (1.0 – 4.1)	3.6±3.6 (1.1 – 4.9)	0.0738	12.64
Donor age (years)	0	51.7±16.0 (42 – 63)	53.2±16.0 (44 – 64)	50.2±15.9 (40 – 61)	0.0078	18.82
Last donor serum creatinine (µmol/L)	2	91.2±62.8 (59 – 106)	85.7±44.8 (59 – 105)	97.1±77.2 (60 – 108)	0.0118	17.99
CIT (hours)	0	20.1±7.7 (14.4 – 24.0)	19.8±7.7 (14.0– 23.7)	20.3±7.7 (15.0 – 24.2)	0.3815	6.18
3-month eGFR (µmol/L)	0	55.5±19.1 (42.4 – 66.6)	53.8±19.1 (41.5 – 62.5)	57.4±19.0 (43.4 – 69.3)	0.0081	18.73
6-month eGFR (µmol/L)	20	55.0±19.0 (41.7 – 65.1)	53.9±19.6 (40.4 – 64.1)	56.1±18.2 (42.6 – 66.9)	0.0924	12.03
12-month eGFR (µmol/L)	43	55.1±18.7 (41.5 – 65.6)	53.7±19.5 (41.1 – 63.2)	56.8±17.7 (43.7 – 67.3)	0.0209	16.77
Categorical characteristics : N (%)						
Recipient men	0	502 (62.4)	253 (60.8)	249 (64.2)	0.3630	6.94
History of diabetes	0	97 (12.1)	44 (10.6)	53 (13.7)	0.2177	9.46
History of hypertension	0	688 (85.6)	355 (85.3)	333 (85.8)	0.9232	1.39
History of dyslipidemia	0	315 (39.2)	174 (41.8)	141 (36.3)	0.1284	11.26
History of neoplasia	0	80 (10.0)	51 (12.3)	29 (7.5)	0.0318	16.10
History of cardiovascular diseases	0	283 (35.2)	155 (37.3)	128 (33.0)	0.2329	8.95
Dialysis technique	0				0.5698	7.50
Pre-emptive transplantation		84 (10.4)	43 (10.3)	41 (10.6)		
Peritoneal dialysis		71 (8.8)	41 (9.9)	30 (7.7)		
Hemodialysis		649 (80.7)	332 (79.8)	317 (81.7)		
Relapsing initial disease	0	232 (28.9)	125 (30.0)	107 (27.6)	0.4872	5.46
Daily anti-HLA immunization of class I	171	155 (24.5)	61 (22.1)	94 (26.3)	0.2569	9.88
Daily anti-HLA immunization of class II	184	155 (25.0)	66 (24.8)	89 (25.1)	0.9999	0.76
Donor men	0	512 (63.7)	271 (65.1)	241 (62.1)	0.4125	6.30
Donor history of hypertension	0	242 (30.1)	131 (31.5)	111 (28.6)	0.4160	6.29
Cerebro-vascular donor death	1	441 (54.9)	229 (55.2)	212 (54.6)	0.9337	1.09
More than 5 HLA A-B-DR incompatibilities	0	91 (11.3)	52 (12.5)	39 (10.1)	0.3253	7.75
Second graft	0	164 (20.4)	106 (25.5)	58 (14.9)	0.0003	26.45
Depleting induction	0	338 (42.0)	222 (53.4)	116 (29.9)	<0.0001	49.02
DGF	6	241 (30.2)	123 (29.9)	118 (30.5)	0.9233	1.23
Urinary infection in the first year	0	85 (10.6)	50 (12.0)	35 (9.0)	0.2052	9.78
CMV infection in the first year	0	97 (12.1)	70 (16.8)	27 (7.0)	<0.0001	30.85
Serious infection in the first year	0	155 (19.3)	89 (21.4)	66 (17.0)	0.1375	11.15
Causal biopsy in the first year	0	184 (22.9)	95 (22.8)	89 (22.9)	0.9999	0.24

Table S10: Multivariable logistic regression used for definition of the propensity score (n=618, 186 patients excluded due to missing data).

	Odds Ratio	95% Confidence Interval	p- value
Recipient age (years)	1.00	[0.98 – 1.01]	0.6558
Donor age (years)	0.99	[0.97 – 1.01]	0.2447
CIT (hours)	1.01	[0.99 – 1.03]	0.5384
3-month eGFR (ml/min/1.73m²)	1.02	[1.00 – 1.04]	0.0292
6-month eGFR (ml/min/1.73m²)	0.99	[0.97 – 1.00]	0.1212
Gender recipient (men vs. women)	1.34	[0.76 – 2.37]	0.0993
History of cardiovascular diseases (positive vs. negative)	0.76	[0.44 – 1.31]	0.1151
HLA A-B-DR incompatibilities (≥ 5 vs <5)	0.65	[0.28 – 1.52]	0.0847
Daily anti-HLA immunization of class I (positive vs. negative)	1.37	[0.92 – 2.03]	0.1225
Gender donor (men vs. women)	0.75	[0.53 – 1.06]	0.1035

Figure S9: Distribution of the propensity score according to the 1-year SB (With 1-year SB versus Without 1-year SB) among patients from transplantation centers having 1-SB policy (n=804).

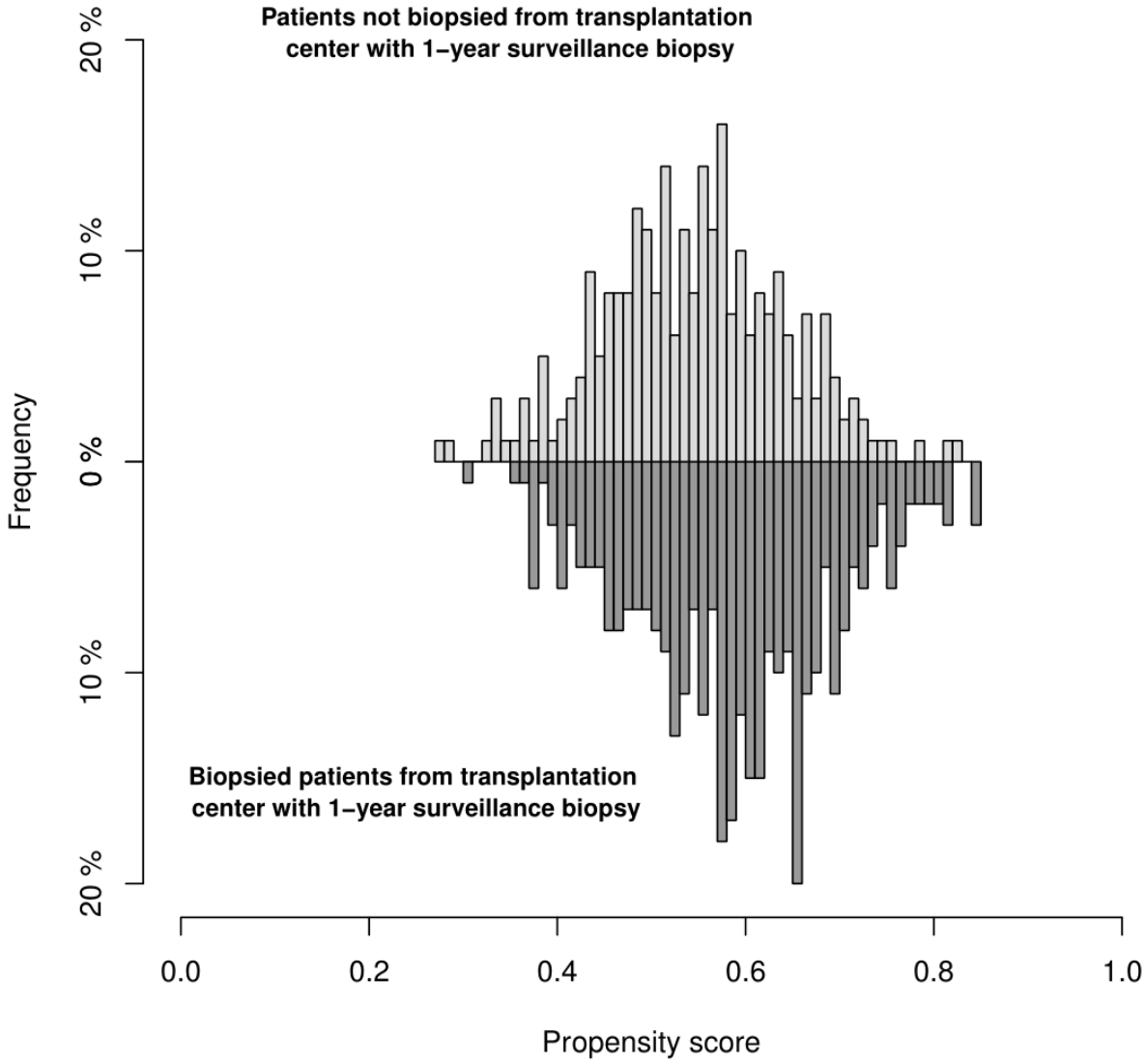


Table S11: Description of recipient, donor, transplantation characteristics and follow-up parameters in the first year post-transplantation for the pseudo-population obtained after Inverse Probability Weighting (Bold labels correspond to variables retained in the propensity score).

	Non-biopsied patients from transplantation centers having a 1-year SB in the pseudo-population N=265 (43%)	Biopsied patients from transplantation centers having a 1-year SB in the pseudo-population N=353 (57%)	Standardized difference (%)
Quantitative characteristics : Mean ± SD			
Recipient age (years)	50.7±13.6	50.7±12.6	0.48
Recipient BMI (kg/m²)	24.0±4.3	24.1±4.4	2.45
Time spent on dialysis (years)	3.0±2.8	3.6±3.6	18.69
Donor age (years)	52.0±16.6	52.1±15.8	0.50
Last donor serum creatinine (µmol/L)	88.0±45.2	97.7±78.3	15.11
CIT (hours)	20.2±7.7	20.3±7.8	0.36
3-month eGFR (µmol/L)	56.0±19.0	56.2±18.6	1.35
6-month eGFR (µmol/L)	55.3±19.8	55.4±18.2	0.55
12-month eGFR (µmol/L)	56.0±19.0	56.2±18.6	1.24
Categorical characteristics : N (%)			
Recipient men	161 (60.6)	215 (61.0)	0.86
History of diabetes	28 (10.5)	45 (12.9)	7.54
History of hypertension	220 (83.2)	302 (85.7)	6.85
History of dyslipidemia	106 (40.2)	132 (37.4)	5.66
History of neoplasia	28 (10.4)	29 (8.3)	7.46
History of cardiovascular diseases	98 (37.1)	131 (37.3)	0.27
Dialysis technique			2.13
Pre-emptive transplantation	31 (11.8)	39 (11.2)	
Peritoneal dialysis	22 (8.2)	29 (8.3)	
Hemodialysis	212 (80.0)	284 (80.5)	
Relapsing initial disease	76 (28.6)	93 (26.4)	4.85
Daily anti-HLA immunization of class I	64 (24.2)	85 (24.0)	0.31
Daily anti-HLA immunization of class II	64 (25.5)	87 (24.9)	1.24
Donor men	166 (62.3)	221 (62.7)	0.33
Donor history of hypertension	84 (31.6)	106 (30.5)	2.40
Cerebro-vascular donor death	137 (51.7)	198 (56.1)	8.77
More than 5 HLA A-B-DR incompatibilities	34 (12.7)	44 (12.5)	0.66
Second graft	68 (25.5)	45 (12.8)	32.85
Depleting induction	122 (46.1)	96 (27.3)	40.00
DGF	68 (26.0)	103 (29.4)	7.82
Urinary infection in the first year	31 (11.8)	34 (9.6)	7.13
CMV infection in the first year	40 (15.0)	24 (6.9)	26.37
Serious infection in the first year	54 (20.5)	64 (18.1)	6.10
Causal biopsy in the first year	65 (24.4)	84 (23.8)	1.50

Figure S10: Adjusted graft and patient survival curves estimated by the IPW Kaplan–Meier estimator for kidney recipients biopsied from transplantation with 1-year SB policy (solid line) and not biopsied patients from transplantation centers with 1-year SB policy (dashed) (n=618, 186 patients excluded due to missing data).

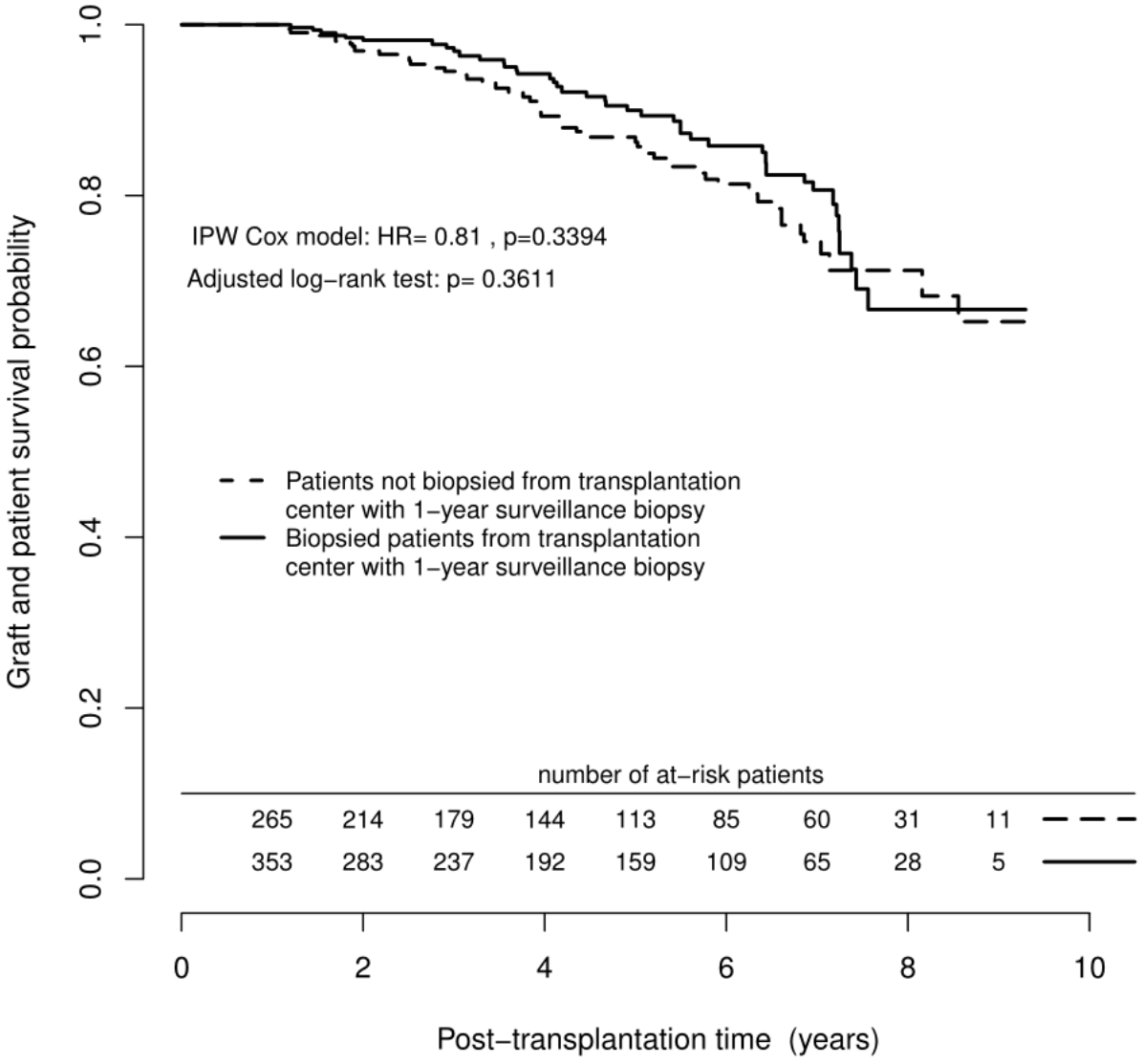


Figure S11: Adjusted graft survival curves (with death-censored) estimated by the IPW Kaplan–Meier estimator for kidney recipients biopsied from transplantation with 1-year SB policy (solid line) and not biopsied patients from transplantation centers with 1-year SB policy (dashed) (n=618, 186 patients excluded due to missing data).

