

Rapport Activités du Collège – Project 2018-2019

Study project 2018-2019

What are the obstacles to put dialysis patients, aged between 18 and 64 years of age, on the transplant waiting list ?

1.1 Introduction

Renal transplantation is considered the best form of renal replacement therapy in terms of both efficiency and quality of life, albeit non-curative, at a less expensive cost, compared to any type of dialysis.

The importance of "kidney transplantation" has been acknowledged by the Ministry of Health; the current agreement about "dialysis financing" incorporates the number of transplants of the last 3 years, as part of the formula for calculating the percentage of "low care / low cost" renal replacement therapies.

For all post-mortal organ transplants, Belgium cooperates with the organ exchange organization Eurotransplant International [ET] (located in Leiden, The Netherlands), together with The Netherlands, Luxembourg, Germany, Austria, Slovenia, Croatia and Hungary. There is a specific allocation program for each organ, taking into account the principles of justice, urgency and efficiency. In order to be considered by the allocation program, the patient should not only be registered on the waiting list, but additionally flagged as "actively waiting" – they can be "called up" when a suitable donor organ is available. Sometimes the patients are flagged as "passively waiting" upon an intervening event (medical, non-medical); they are "non-transplantable" [NT] and are ignored by the organ allocation program.

In the past, the NBVN as well as the GNFB registry have repeatedly shown that on average "only one third" of the dialysis patients aged 18 to 65 years are **actively** waiting on the ET kidney transplant waiting list, whereas, intuitively, a much higher percentage would be expected in this age category. Comparing 2012-2018, there might even be a decreasing trend [Table 1].

*Table 1: Prevalence of the active ET kidney (Ki) transplant waiting list and dialysis patients covered in the NBVN and GNFB registries – all ages and age category 18-64 years
 Ki-only : kidney-only transplant; Ki+Pa : kidney+pancreas transplant*

Belgium	All ages active total Ki WL Belgium	All ages active Ki-only WL Belgium	All ages active Ki+Pa WL Belgium	18-64 yrs active Ki-only WL Belgium	18-64 yrs dialysis patients Belgium	18-64 yrs dialysis patients NBVN	18-64 yrs dialysis patients GNFB	18-64 years % dialysis patients active on the WL
01/01/2012	883	837	19	740	2204	1277	927	33.5% (Belgium)
01/01/2013	791	748	26	648		1199	NA	
01/01/2014	770	721	31	632		1210	NA	
01/01/2015	878	821	40	691		1197	NA	36% (NBVN)
01/01/2016	871	813	37	687		1182	NA	32% (NBVN)
01/01/2017	797	742	30	640		1155	NA	
01/01/2018	849	793	25	677	2688	1134	1554	25.0% (Belgium)

1.2 Aim

1. Survey of the reasons, prohibiting dialysis patients from being listed on the kidney transplant waiting list – age category – 18-64 years of age – reference date = January 1, 2018 [NBVN].
2. Survey of the time flow, starting from the proposal “transplant option” to the final transplantation, considering all 'intermediate stations' (start investigations, registration transplant center, start dialysis, additional interventions, registration at Eurotransplant, ...) [GNFB].

1.3 Results

1.3.1 – CAUSES OF NON-LISTING ON THE ET WAITING LIST – NBVN (& GNFB & BELGIUM)

A. Background:

On January 1, 2018, 1138 patients – aged 18-64 years – were treated with dialysis, either hemodialysis or peritoneal dialysis, in the NBVN organization. This population corresponds to only 24% of the total dialysis population [N=4701].

Since one large dialysis center was not able to submit the requested data (N=77 patients – aged 18—64 years), the analysis was done on the total of 1061 patients.

The number of actively waiting dialysis patients (“callable”) decreased slightly over the recent years. The large difference between the categories “Not-Transplantable” and “Not on the ET Waiting list” might be due to a misconception of the word “not transplantable”, mixing its clinical and administrative meaning – see Figure 1.

NBVN Age: 18-64 years	<u>ET-Waiting list</u> Transplantable “callable”	<u>ET-Waiting list</u> Not-Transplantable “not callable”	Not on the ET Waiting list	Total	Centers
1/1/2015	378 – 36%	201 – 19%	466 – 45%	1045	25 / 26
1/1/2016	323 – 32%	147 – 15%	531 – 53%	1001	23 / 26
1/1/2018	331 – 31%	90 – 9%	640 – 60%	1061	25 / 26

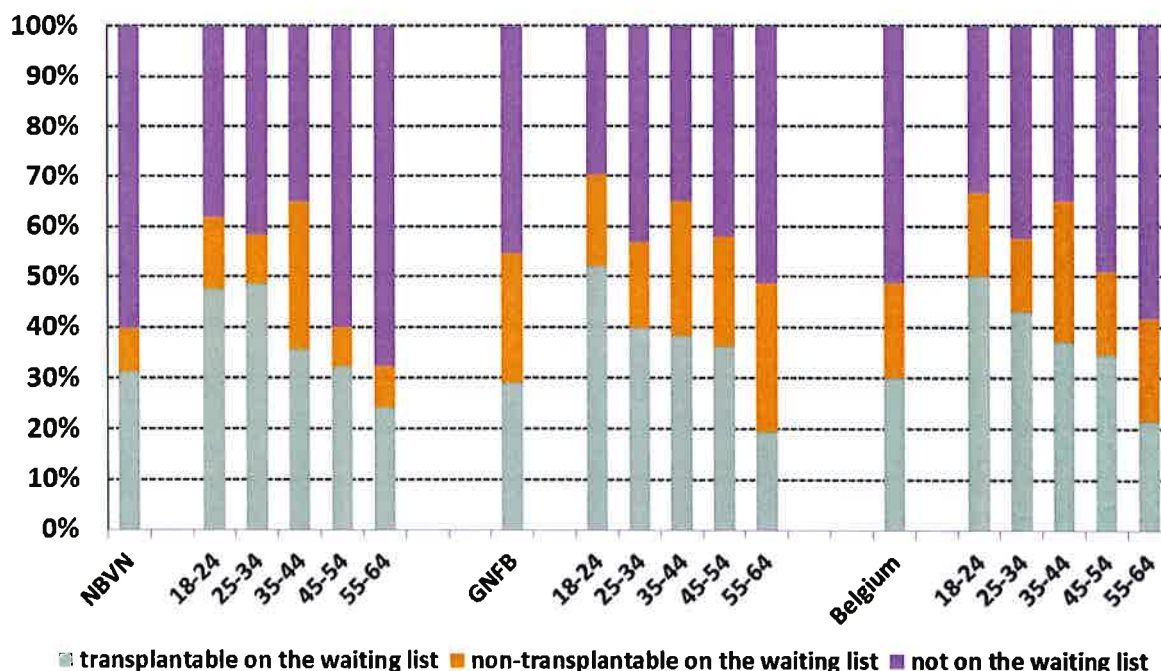
Figure 1 also shows the corresponding data of the GNFB organization.

The GNFB data match the NBVN data well, with regard to the percentage patients active on the waiting list (29% - N=449/1549).

Only the proportion of patients not actively waiting on the waiting list is much larger (26% GNFB versus 9% in NBVN); the might be the reflection of another practice: patients are listed on the waiting list prior to the full evaluation of the patients suitability as renal transplant candidate.

On the level of Belgium, 50% of the dialysis patients aged 18-64 years is not on the renal transplant waiting list. The other half is on the ET waiting list, 50% actively waiting and 50% passively waiting.

Figure 1 : Distribution of the dialysis patients on the waiting list for kidney transplantation in NBVN, GNFB and Belgium



B. Characteristics of the dialysis population aged 18-64 years

The age group 55-64 years is the largest group of the dialysis population 18-64 years [N=544; 57%] and has the highest percentage dialysis patients not being listed on the transplant waiting list [N=369; 68%] – see also Figure 1. The GNFB data match the NBVN data.

NBVN Age group	Transplantable "callable"	Not-Transplantable "not callable"	Not on the waiting list	Total dialysis patients	
	N - %	N	N - %	N	%
18-24	10 – 48%	3	8 – 38%	21	2%
25-34	35 – 49%	7	30 – 42%	72	7%
35-44	62 – 45%	15	61 – 44%	138	13%
45-54	92 – 32%	22	172 – 60%	286	27%
55-64	132 – 24%	43	369 – 68%	544	57%
Total	331 – 31%	90 – 9%	640 – 60%	1061	100%

There is no difference regarding gender.

The distribution of the underlying kidney disease varies considerably per age category, but the percentage "Not on the waiting list" is explained to a better extent by the age group than by the underlying renal disease.

Patients with cystic kidneys (ADPKD), immunological kidney diseases and diabetic nephropathy in the context of type 1 diabetes mellitus are often younger and have the lowest percentage "Not on the waiting list".

Patients with diabetic nephropathy in the context of type 2 diabetes mellitus are older and have, as such, a clearly higher percentage "Not on the waiting list".

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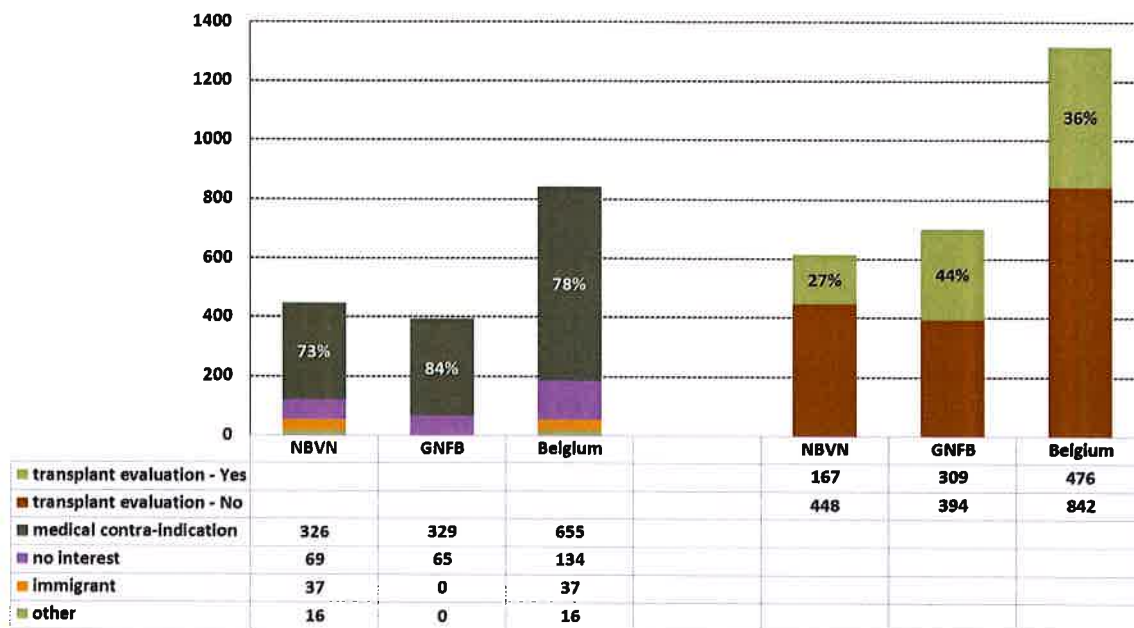
NBVN Renal disease	Transplantable "callable"	Not-Transplantable "not callable"	Not on the waiting list	Total dialysis patients	
	N	N	N - %	N=	%
Cystic kidneys	46	13	33 – 36%	92	9%
Immunological glomerulonephritis	94	17	119 – 52%	230	22%
Type 1 diabetes	24	5	41 – 59%	70	7%
Hereditary renal disease	17	3	31 – 60%	51	5%
Other renal disease	23	5	48 – 63%	76	7%
Unknown cause	31	11	72 – 63%	114	11%
Vascular disease	31	12	75 – 64%	118	11%
Tubulo-interstitial nephritis	39	7	93 – 67%	139	13%
Type 2 diabetes	23	13	102 – 74%	138	13%
Irreversible acute kidney failure	2	3	18 – 78%	23	2%
Cardiorenal syndrome	1	1	8 – 80%	10	1%
Total	331 – 31%	90 – 9%	640 – 60%	1061	100%

No analysis was done with regard to the time the patients were already on dialysis [dialysis vintage].

It should be noted that, in the NBVN organization, potential candidates for a kidney transplant are seldomly put on the ET transplant waiting list before starting dialysis.

In 1999 the allocation factor "waiting time" was redefined in the ET allocation program. The waiting time [being a high impact selection factor] no longer starts from the date of registration on the waiting list, but starts from the date the patient started the last dialysis episode. Technically speaking, no waiting time is accumulated prior to the start of dialysis; so, the placement on the waiting list prior to the start of dialysis is less mandatory to speed up a selection because the waiting time is "zero".

Figure 2 : Distribution of the reasons why the dialysis patients are not on the renal transplant waiting list



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C. Reasons – Not on the waiting list

The College survey (completed by 23 of 26 dialysis centers) showed some corrections about transplantability status with regard to the earlier NBVN survey. Even lesser patients were on the renal transplant waiting list than initially reported.

The total patients not being on the waiting list amounted to 632 patients – no information was available for 17 patients. The analysis population consisted of 615 patients – see Figure 2.

Luckily, 27% of these NBVN dialysis patients is either currently involved in an assessment of the candidacy for a renal transplantation (22% - N=136) or awaiting the final registration at the Eurotransplant waiting list (5% - N=31). Not surprisingly these patients are aged less than 45 years and/or have either a renal cystic disease or immunological renal disease.

NBVN: Reasons of non-listing on the transplant waiting list (N, %)		
Ongoing transplant evaluation	88	14%
Transplant evaluation finished – awaiting evaluation by the transplant center	7	2%
Following visit transplant center, extra examinations ongoing / additional surgery planned	41	6%
Awaiting registration on the ET waiting list	31	5%
No ongoing transplant evaluation	448	73%
Total	615	100%

Compared to the NBVN (27%), there is a higher proportion of patients, being evaluated by the dialysis centers (44% GNFB) – see Figure 2. There is no good explanation for this difference; it is plausible that it just comes down to a different interpretation of the concept "transplant evaluation".

Of the NBVN dialysis patients not involved in an evaluation for a transplant (N=448), a medical contra-indication is the main reason – 69%; either truly somatic or rather mental issues.

NBVN: No ongoing transplant evaluation due to (N, %) :		
Medical contra-indication : somatic and/or mental illness, persistent non-compliant behavior (smoking, use of alcohol, use of illicit drugs, ...)	307	69%
Decline by the transplant center after visit	19	4%
No interest of the patient, though potential candidate	69	15%
Immigrant – no legal residence permit	37	8%
Other - potential recovery of renal function - just transferred from another dialysis center - on waiting list outside Belgium	16	4%
Total	448	100%

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Several centers mentioned the problem of the “unchangeable non-compliant behavior” with regard to smoking, excessive drinking of alcohol or the use of illicit drugs. This problematic behavior prohibited the commencement of an a priori successful evaluation as renal transplant candidate.

Some patients (4%) had been evaluated by the dialysis centers but were ultimately declined as suitable transplant candidate following the final evaluation by the transplant center. The current analysis does not provide information on the acceptance and refusal rate by the transplant centers.

Fifteen percent of the patients declared themselves not to be interested to get a transplant. This also was present among relatively young patients.

Figure 2 shows that also in the GNFB region medical contra-indications and no interest are the most important reasons for not evaluating transplant candidacy.

Several dialysis patients could not be evaluated due to their immigrant status, and their corresponding lack of an official health insurance. As long as these patients don't have a residence permit, the Belgian transplant centers are obliged to refrain them from any transplant evaluation. As such, many (mainly young) patients are condemned to a long (and more expensive) dialysis period, due to the lengthy assessment procedure at the Immigration Office.

On the other hand, as long as the return to their land of origin is pending, it might not be wise to transplant the patients in the meantime, since anti-rejection medication might not be available in their land of origin. So, if they have to go back after being transplanted; the fate of their renal transplant might be endangered by the lack of immunosuppressive medication. One should also be aware of so-called transplant tourism.

Finally, for some patients, an evaluation of transplant candidacy is not appropriate / too early since there is a reasonable chance of recovery of their renal function, with a life without further dialysis need.

1.3.2 – TRAJECTORY FROM PATIENT SELECTION TILL TRANSPLANTATION – GNFB

The GNFB organization evaluated the workflow from the transplant proposal to the realization of a transplant in a patient cohort, starting dialysis between 2011 and 2018.

Two scenarios were evaluated:

- pre-emptive listing prior to the start of dialysis [112 patients]
- listing after the start of dialysis [349 patients].

In this analysis there was no age restriction.

1.3.2a. Successful listing on the kidney transplant waiting list – prior to the start of dialysis.

On average the patients were listed 10 months (IQR 3 – 15 months; median 7 months) before the start of dialysis.

Forty-nine patients got their transplant in the period 2011-2018 – 50% of the patients was transplanted after a dialysis time of 36 months.

1.3.2b. Successful listing on the kidney transplant waiting list – after the start of dialysis.

The time between the start of dialysis and the registration on the transplant waiting list averaged 19 months (IQR 6 – 24 months, median 13 months). No information was present on the exact time point upon which one initiated the pre-transplant work-up after the start of dialysis.

The total dialysis time till transplant of 50% of the 154 patients amounted to 48 months.

In conclusion, having the patient listed on the transplant waiting list prior to their start of dialysis results lesser waiting time on dialysis of about 12 months to get a transplant. Lesser time on dialysis means an economical benefit [level of society] and more quality of life [patient level]. The organization of the pre-transplant work-up is also more complex during the dialysis period due to intervening dialysis sessions.

*Table 2 : Time line till transplant, following listing on the waiting list before or after the start of dialysis
 The time is expressed as median with interquartile range [IQR].*

Listing before the start of dialysis			
	Listing waiting list	Dialysis	Transplantation
N=112	7 months [IQR, 3 – 15]		
		23 months [IQR, 3 – 44] – N=49 transplants median transplant rate = 36 months	
Listing after the start of dialysis			
		Dialysis	Listing waiting list Transplantation
N=349		13 months [IQR, 6 – 24]	
		35 months [IQR, 2 – 50] – N=154 transplants median transplant rate = 48 months	

1.4 Discussion

The option "kidney transplantation – with survival benefit" can only be offered to a carefully selected dialysis population. For this analysis, a simple age criterion [18-64 years] was used.

On average, 25% - 30% of the dialysis patients are actively waiting list for a kidney transplant; 10% – 25% is passively on the waiting list and is, per definition, ignored in the allocation algorithm. About 45% - 60% is not on the transplant waiting list.

Of these patients, the preparations for listing are on the way in about one-third. In the other group, medical contraindications and also unchangeable non-compliance behavior are the main reasons prohibiting pre-transplant work-up.

Fortunately, about one third of the Belgian dialysis patients not on the waiting list is indeed in an active evaluation process or just finished it. Although one might be disappointed by this low percentage, there is a constant flow in the assessment of dialysis patients as potential transplant candidates, demonstrating a positive attitude towards renal transplantation among the Belgian nephrologists.

One can also point out that patients are indeed carefully screened, in order to get the maximum benefit of a renal transplantation. All Belgian kidney transplant centers have a guideline for examining a patient with late stage of chronic kidney disease or a dialysis patient for the purpose of a successful kidney transplant. In addition, practical information how to select suitable patients aiming at such a successful kidney transplantation is also available in the European Renal Best Practice, written under the auspices of the ERA-EDTA organization¹. One should avoid unnecessary wait-listing of unsuitable patients.

Looking at the GNFB analysis, one could formulate a recommendation to start the transplantation work-up and wait-list the patient prior to the start of dialysis. Wait-listing is possible as of a renal function below 15 ml/min/1,73 m². A lucky few will get their transplant prior to the start of dialysis; the benefit of the other patients is a potential shorter dialysis time till transplantation and less cumbersome dialysis period (due to the lack of the more extended transplant work-up and difficult planning of the different examinations, in between the dialysis sessions).

¹ Abramowicz D, Cochat P, Claas FH, Heemann U, Pascual J, Dudley C, Harden P, Hourmant M, Maggiore U, Salvadori M, Spasovski G, Squifflet JP, Steiger J, Torres A, Viklicky O, Zeier M, Vanholder R, Van Biesen W, Nagler E. European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care. *Nephrol Dial Transplant.* 2015;11:1790-1797

There is also an economical benefit, due to the lesser time on dialysis.

A more structured questionnaire why the "kidney transplant" option was not offered could provide more information on the selection process at the dialysis center, and could lead to an additional quality indicator of the care performance of a dialysis center. However, the College doubted the added value of such an interrogation on the center level.

Even when the patient is listed on the kidney transplant waiting list, the nephrologist should constantly assess whether the patient remains to be a suitable renal transplant candidate. In doubt, the patient should be re-evaluated by the transplant center. In anticipation various kidney transplant centers have opted for a "return day" in order to "check" this recipient suitability, but also to refresh the information for the patient what to do upon the call that a donor kidney is available and after the transplantation.

In conclusion, according to this study, the Belgian nephrologists are well aware to the option of renal transplantation. Although only one third of the dialysis patients aged below 65 years is actively waiting for a renal transplant, the College finds no indication that suitable dialysis patients are unnecessarily refrained from the option "transplantation".

1.5 Recommendation of the College

The College formulates 2 recommendations for the Belgian nephrologists :

- 1. Chronic kidney patients with nearly end-stage kidney failure [CKD stage 5] and who are probable good candidates for a renal transplant, should be evaluated [and listed] prior to the start of dialysis.**
- 2. Patients should be registered on the kidney transplant waiting list, only as of the moment they are truly suitable candidates and they can be actively waiting for a renal transplant.**

Namens het college,
Au nom du collège

Dr. Johan De Meester
Internist-nefroloog
Dr. Johan De Meester
Nefrologie
1-45255-53-580
AZ Nikolaas vzw

19 02 2020