

# RISK FACTORS AND INCIDENCE OF NEOPLASIA AFTER KIDNEY TRANSPLANTATION IN ADULTS: EXTENSIVE SINGLE EXPERIENCE CENTER

Mario Jimenez Hernandez, Ignacio Revuelta, Fritz Diekmann, Federic Oppenheimer, Jose Maria Campistol, Nephrology and Renal Transplantation Unit, Barcelona, Hospital Clinic de Barcelona, Spain.

## Background:

The incidence and risk of malignancy is high in solid organ transplant recipients compared to the general population. There is a possible relationship with the kind, intensity and duration of immunosuppressive therapy and developing of cancer after transplantation. Currently the cancer is considered as the second cause of death in the transplant population. To date, there are no records of neoplasms in the renal transplant population at the level of Catalonia and the rest of Spain.

## Objectives:

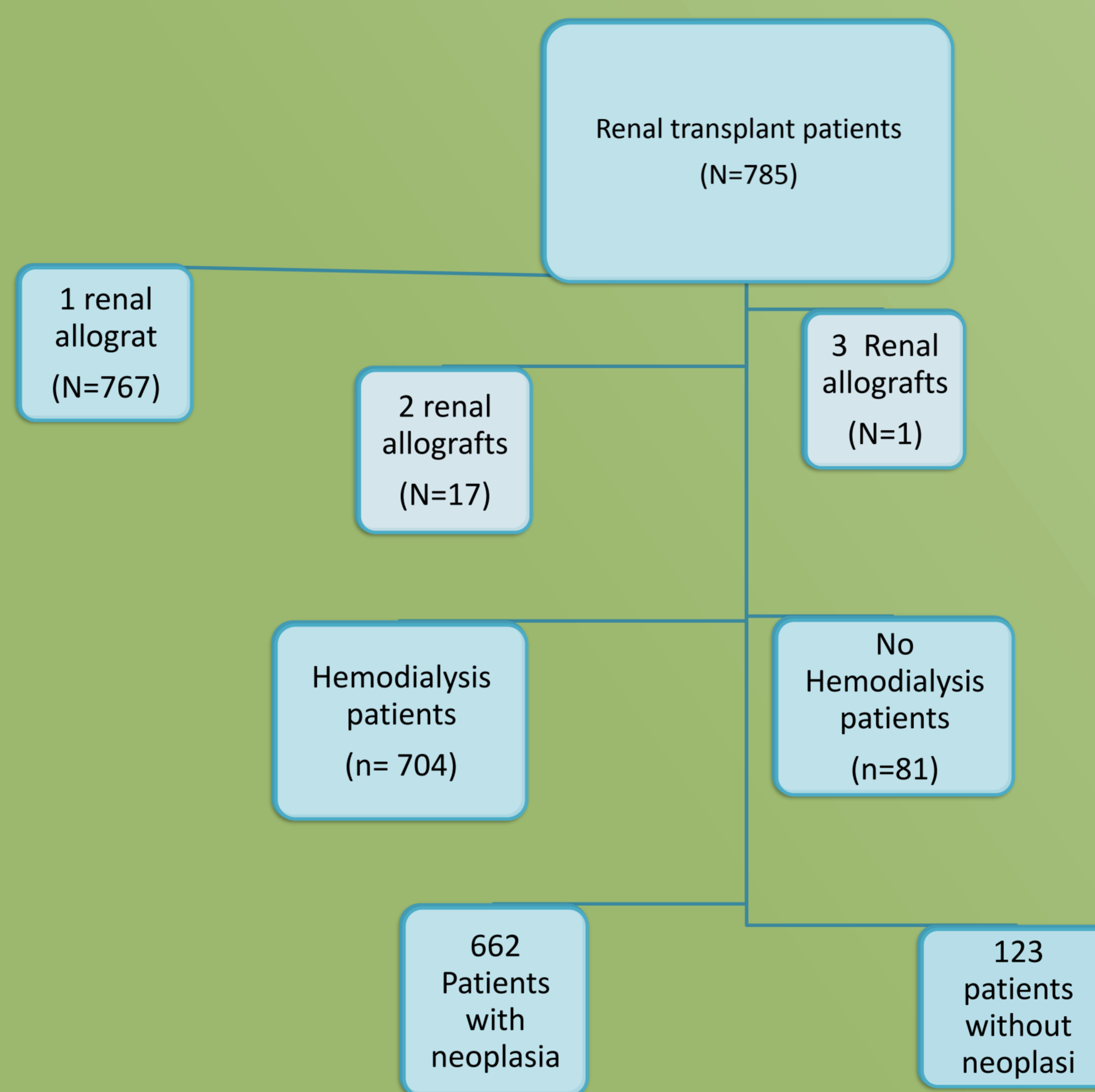
- To determine incidence and prevalence of cancer in patients with renal transplantation in our Renal Transplant Unit at Hospital Clinic of Barcelona from January 1, 2003 to December 21, 2009.
- To find out risk factors with the appearance of cancer in renal transplant patients.
- To determine cancer mortality in the study population.

## Methods:

Observational, retrospective cohort study. We included all patients whom received a renal transplant from 2003 to 2009 at our center, performing the statistical analysis at each transplant. Anthropometric data, comorbidities, appearance of new neoplasia and possible risk factors for its development were recorded.

## Results:

803 kidney transplants were recorded in 785 patients (767 with 1 TR, 17 with 2 TR, 1 with 3 TR). Males represent 59% of patients. The mean age was 58.2 years  $\pm$  14.06 years of age. 123 (15,67%) patients developed neoplasia de novo. The incidence rate of neoplasia of 15.27% patient-years and a prevalence of 15.66% during the observation period. Skin cancer was the most common. Age ( $p = 0.0001$ ) and use of CIN ( $p = 0.02$ ) as immunosuppression were associated as risk factors for the development of neoplasms. No significant association was found with dialysis time or with type or type of renal graft rejection. The mortality attributed to the neoplasia was 14.4% with RR of 1.7



| Variable                 | No Neoplasia (N=664) | Neoplasia (N=121)    | P Value |
|--------------------------|----------------------|----------------------|---------|
| Sex                      |                      |                      |         |
| Female                   | 275 (41,5%)          | 47 (38,3%)           | NS      |
| Male                     | 387 (58,5%)          | 76 (61,7%)           |         |
| Age (years SD $\pm$ )    | 57,03 ( $\pm$ 14,34) | 64,56 ( $\pm$ 10,39) | 0.000*  |
| Weight (Kg SD $\pm$ )    | 69,68 ( $\pm$ 14,80) | 69,18 ( $\pm$ 13,84) | NS      |
| Height (cm SD $\pm$ )    | 165,79 ( $\pm$ 9,49) | 165,74 ( $\pm$ 8,32) | NS      |
| BMI (Kg/m <sup>2</sup> ) | 25,31 ( $\pm$ 4,96)  | 25,11 ( $\pm$ 4,27)  | NS      |
| Smoking                  |                      |                      |         |
| Non smoker               | 416 (62,7%)          | 69 (57%)             | NS      |
| Smoker                   | 109 (16,4%)          | 17 (14%)             |         |
| Ex smoker                | 139 (20,9%)          | 35 (28,9%)           |         |
| Alcoholism               |                      |                      |         |
| No alcoholism            | 509 (76,7%)          | 84 (69,4%)           | NS      |
| Ex alcoholism            | 88 (13,3%)           | 25 (20,7%)           |         |
| Habitual Consumption     | 67 (10,1%)           | 12 (9,9%)            |         |
| Diabetes Mellitus        |                      |                      |         |
| Presence                 | 544 (81,9%)          | 95 (78,5%)           | NS      |
| Absence                  | 120 (18,1%)          | 26 (21,5%)           |         |
| Hypertension             |                      |                      |         |
| Presence                 | 573 (86,3%)          | 108 (89,3%)          | NS      |
| Absence                  | 91 (13,7%)           | 13 (10,7%)           |         |
| Dyslipidemia             |                      |                      |         |
| Presence                 | 392 (59%)            | 63 (52,1%)           | NS      |
| Absence                  | 272 (41%)            | 58 (47,9%)           |         |

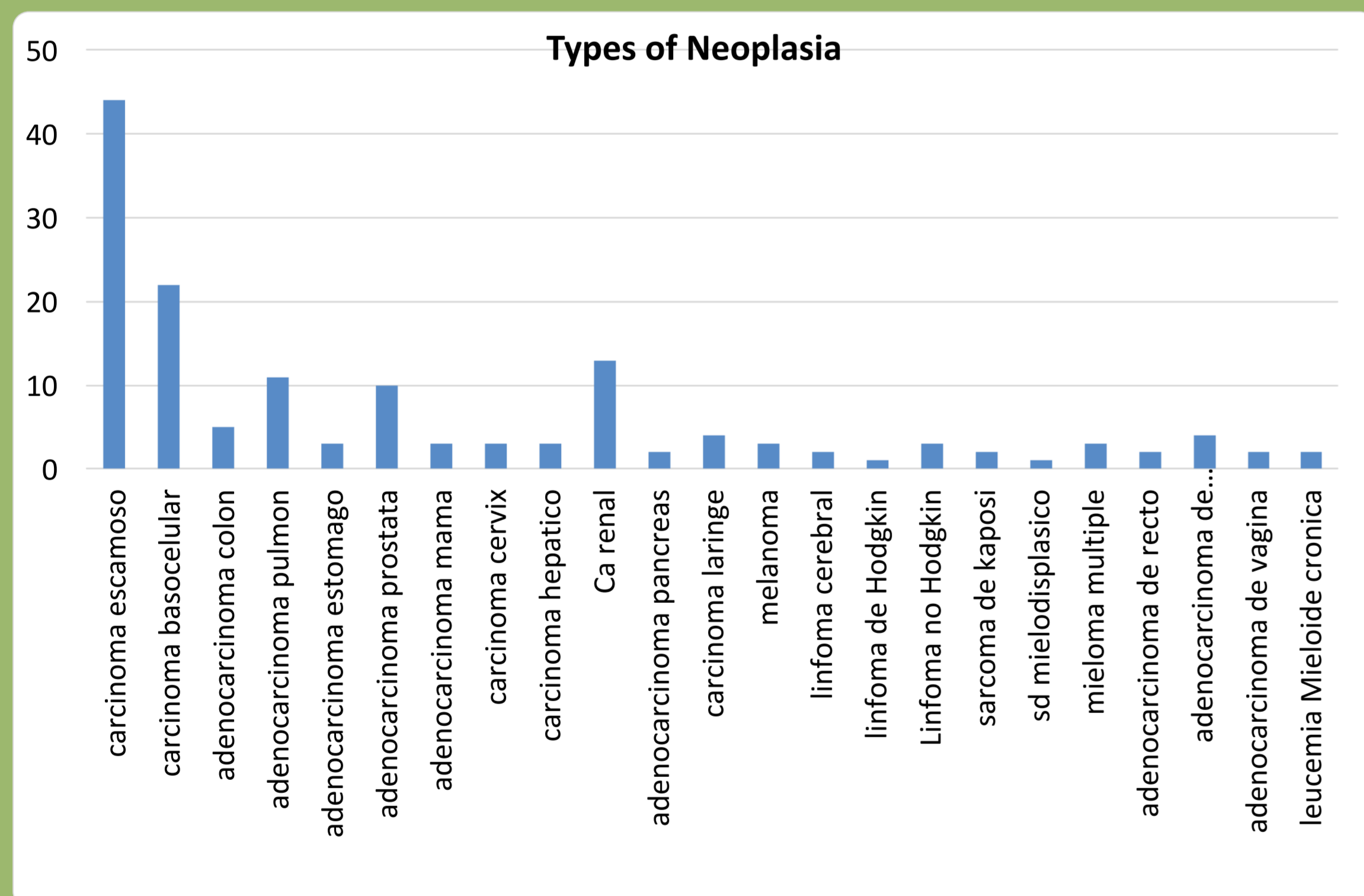


Figure 1. Cancer distribution according to Chronic kidney disease (etiology)

## Possible risk factors for the development of Neoplasia

Relation between immunosuppression treatment with cancer developing

| Induction therapy | Induction therapy |             |              |            |           | Total  | Valor p |
|-------------------|-------------------|-------------|--------------|------------|-----------|--------|---------|
|                   | No inducción      | Basiliximab | Timoglobulin | Daclizumab | Alefacept |        |         |
| Neo no neoplasia  | 157               | 279         | 225          | 10         | 9         | 680    | 0.263   |
| neoplasia         | 23,1%             | 41,0%       | 33,1%        | 1,5%       | 1,3%      | 100,0% |         |
| Total             | 177               | 336         | 270          | 11         | 9         | 803    |         |
|                   | 22,0%             | 41,8%       | 33,6%        | 1,4%       | 1,1%      | 100,0% |         |

| Immunosuppressor therapy        | Neo          |              | Total | Valor p |
|---------------------------------|--------------|--------------|-------|---------|
|                                 | No neoplasia | Si neoplasia |       |         |
| calcineurin inhibitors (CNIs)   | 494 (86,5%)  | 77 (13,5%)   | 571   | 0.0245  |
| Mammalian TOR (mTOR) inhibitors | 229 (82,7%)  | 48 (17,3%)   | 277   | 0.2516  |

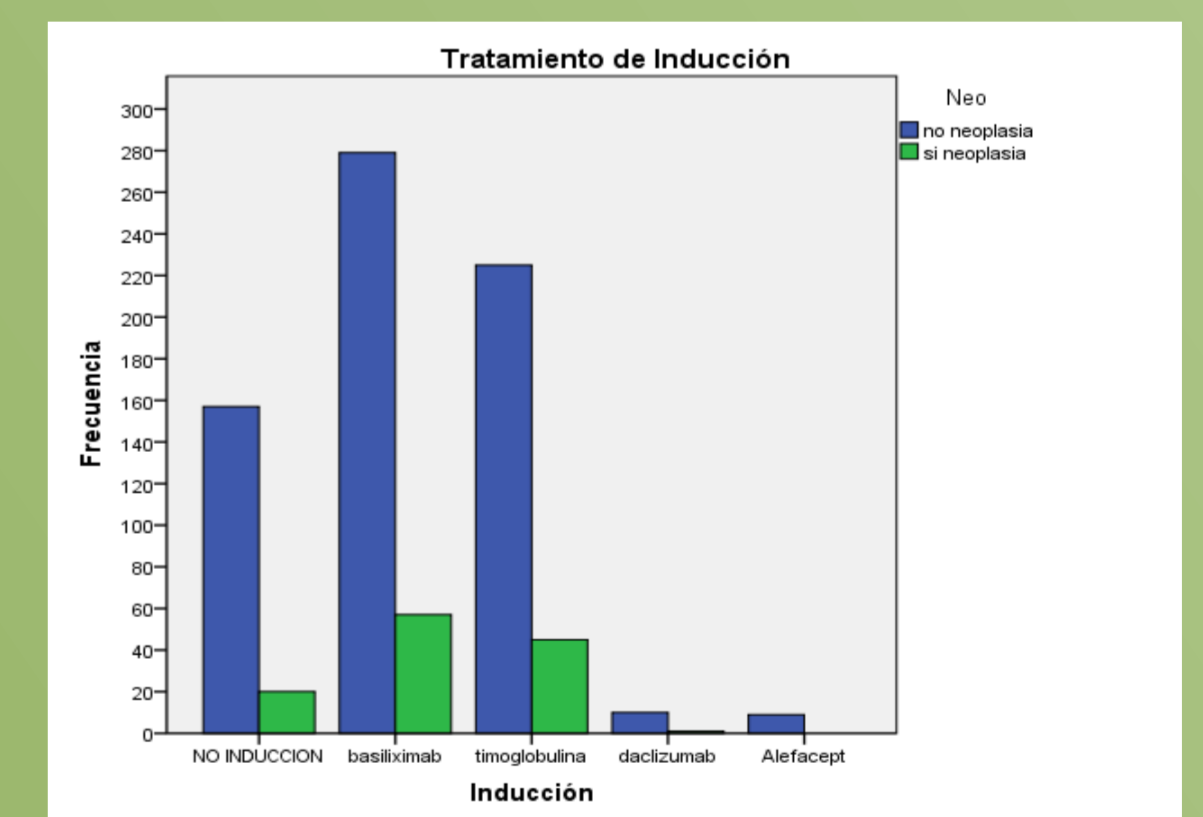
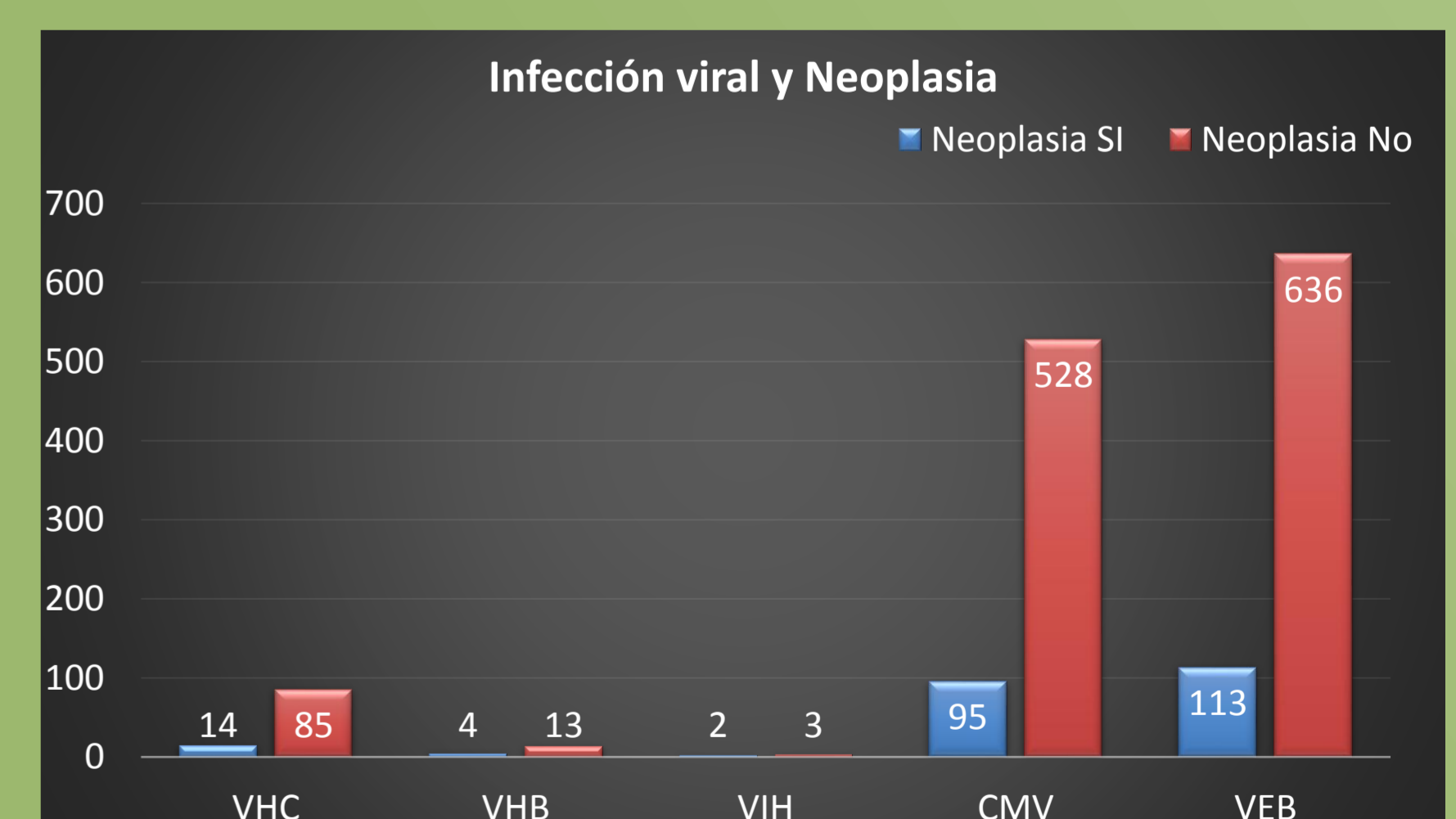


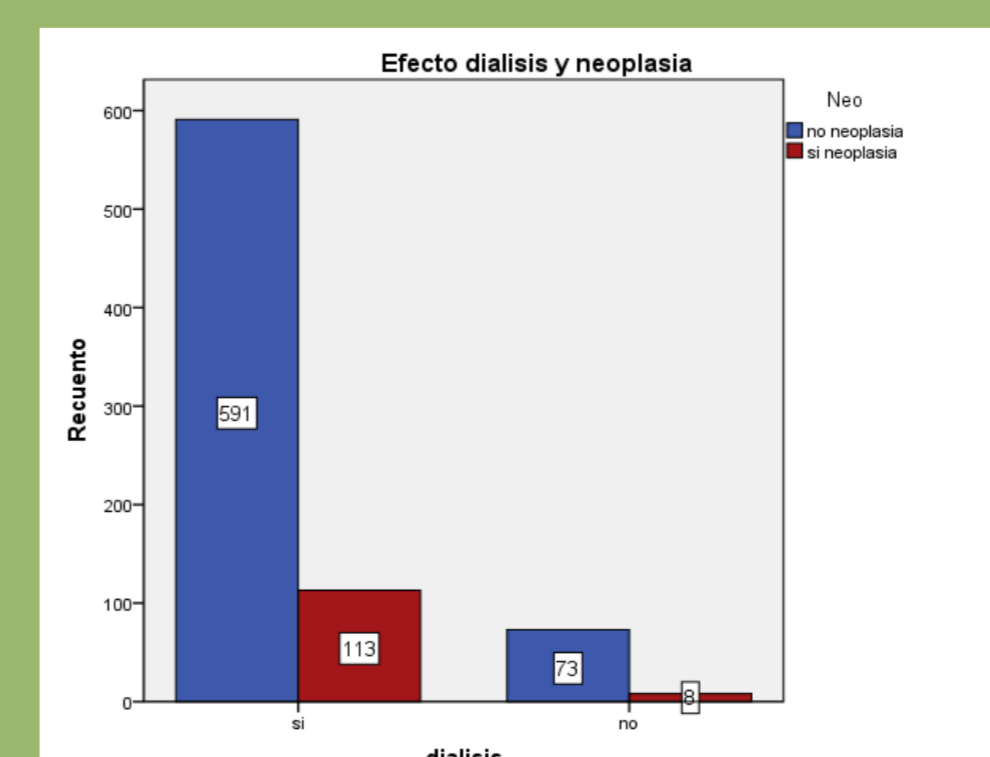
Figure 4. Viral infection as a possible risk for the development of Neoplasia

Relationship of rejection episodes, rejection type and presence of Neoplasia

|   | No neoplasia | Si neoplasia | Valor p            |
|---|--------------|--------------|--------------------|
| Rechazo humoral agudo (% de pacientes)          | 50           | 7            | p=0.402<br>p=0.410 |
| Rechazo celular agudo (% de pacientes)          | 81           | 15           | p=0.285<br>p=0.092 |
| Rechazo humoral cronico activo (% de pacientes) | 61           | 8            | p=0.305            |
| Rechazo Broderline (% de pacientes)             | 31           | 12           | p=0.540<br>p=0.325 |



Effect of dialysis as a possible risk factor for the development of cancer



## Conclusions

Currently, cancer, after cardiovascular disease, is one of the main causes of morbidity and mortality in renal transplantation in relation to the general population of the same age and sex. Evidence has confirmed that the incidence of cancer increased significantly in post-transplant. The etiology behind this increased risk is multifactorial, but in most cases it is related to prolonged immunosuppression. Despite the increased risk of cancer, information remains limited in order to achieve the development of strategies to improve treatment efficacy and prognosis in this population.

