# TNF-alpha Inhibitors in Organ Transplant Recipients: A Retrospective Cohort Study

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# Abstract

Tumor necrosis factor-alpha inhibitors (TNFi) can be an effective treatment for organ transplant recipients (OTR) with various diseases but can increase the risk of infection and drug interactions.[1] There is also a potential for acute graft rejection while on TNFi with an unclear causal relationship. Two patients experienced acute graft rejection out of sixteen in a retrospective study of kidney transplant patients on TNFi, but the rejections were deemed unlikely to be related to biologic use.[4] The purpose of this larger, multicenter study was to evaluate the safety of TNFi use in OTR by assessing rates of complications in patients treated with TNFi post-transplant.

# Full Text

Following IRB approval at Vanderbilt University Medical Center (VUMC) and Johns Hopkins Hospital (JHH), we queried both electronic health records and identified OTR who were prescribed a TNFi post-transplant. Chart review was conducted to retrieve patient demographics, transplant type, biologic type, baseline and follow-up labs, and complication history. The primary outcome was the occurrence of any infection, hospitalization for infection, sepsis, or rejection after starting a TNFi. R v4.0.2 was used for all analyses.

We identified 223 OTR from VUMC prescribed a biologic after their transplant, 48 of whom started a TNFi. Of the 73 OTR from JHM on biologics, 39 patients were treated with a TNFi. The majority of patients were male with a mean age of 54±15 years. The types of organ transplants received by patients included: 50 kidney, 18 liver, 14 lung, 3 heart, and 2 pancreas (Table 1).

Thirty-eight patients (44%) experienced at least one infectious complication post-transplant. Of the patients who developed an infection, twenty-two (25%) were hospitalized for infection and eight (9.2%) developed sepsis. Seventeen patients (20%) discontinued TNFi, and seven patients (8%) underwent modification of immunosuppressants secondary to TNFi use. Three patients (3.4%) experienced rejection while receiving TNFi. Mean leukocyte, hemoglobin, and platelet counts (Table 2) were not significantly changed from baseline when trended over the course of two years post-transplant.

Adverse effects of TNFi have previously been described in post-marketing studies. TNFi have shown infection rates ranging from 35% to 52.7% in otherwise immunocompetent patients with most occurring within one year of initiation.[3] There are currently no reports in the literature to compare baseline rates of hospitalizations or sepsis in OTR specifically taking TNFi.

Several limitations may impact our results. All included patients were treated at tertiary care academic centers with high-volume transplant centers, which may not be representative of the general population. Additionally, VUMC and JHM participate in an open healthcare system, and the charts reviewed might not have captured all of the potential complications. Lastly, we do not have evidence that any of the experienced complications were directly caused by TNFi, and we cannot predict if these complications would have occurred regardless of TNFi treatment.

Findings from this retrospective cohort study have demonstrated results similar to previously described adverse effects in post-marketing studies for TNFi. These results add further evidence regarding the safety of TNFi in OTR.

## Abbreviations

TNFi – TNF-alpha inhibitors

OTR – organ transplant recipients

VUMC – Vanderbilt University Medical Center

JHM – Johns Hopkins Medicine

## Declarations

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Study approved as exempt non-human subjects research, VUMC IRB #200335, JHM IRB #IRB00398143)

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## Tables

Table 1. Baseline characteristics and complication rates of transplant patients treated with TNF-alpha inhibitors

| Characteristic | N = 87[1] |
|---|---|
| Demographics | |
| **Sex** | |
| F | 40 (46%) |
| M | 47 (54%) |
| **Race** | |
| Black | 10 (11%) |
| Hispanic | 1 (1.1%) |
| Multiracial | 1 (1.1%) |
| Native Hawaiian or Other Pacific Islander | 2 (2.3%) |
| White | 73 (84%) |
| **Ethnicity** | |
| Hispanic/Latino | 2 (2.3%) |
| Not Hispanic/Latino | 84 (97%) |
| Unknown | 1 (1.1%) |
| **Age** | 54 (15) |
| **Organ** | |
| Heart | 3 (3.4%) |
| Kidney | 50 (57%) |
| Liver | 18 (21%) |
| Lung | 14 (16%) |
| Pancreas/GI | 2 (2.3%) |
| **TNF Inhibitors** | |
| Etanercept | 19 (22%) |
| Adalimumab | 45 (52%) |
| Infliximab | 23 (26%) |
| **Indication for TNF Inhibitor** | |
| Crohn's Disease | 19 (22%) |
| Hidradenitis Suppurativa | 1 (1.1%) |

| Characteristic | N = 87[1] |
|---|---|
| Psoriasis | 16 (18%) |
| Psoriatic Arthritis | 7 (8.0%) |
| Rheumatoid Arthritis | 13 (15%) |
| Ulcerative Colitis | 16 (18%) |
| Other | 15 (17%) |
| Complications | |
| Rejection while taking TNF Inhibitor | 3 (3.4%) |
| Immunosuppressive medications adjusted | 7 (8.0%) |
| TNF Inhibitor discontinued | 17 (20%) |
| Infection | 38 (44%) |
| Hospitalization | 22 (25%) |
| Sepsis | 8 (9.2%) |

[1]n (%); Mean (SD)

Table 2. Rates of complications in transplant patients treated with TNF-alpha inhibitors

| Laboratory Values | Baseline (n=73)[1] | Post-Transplant (n=73)[1] | p-value[2] |
|---|---|---|---|
| Hemoglobin (g/dL) | 11.50 (2.26) | 11.79 (1.89) | 0.5 |
| Platelets (103/mL) | 193 (130) | 189 (75) | 0.6 |
| Leukocyte count (103/mL)[3] | 6.7 (3.6) | 7.3 (2.7) | 0.058 |

[1]Mean (SD)

[2]Wilcoxon rank sum test

[3]Baseline data available for 66 of 77 patients.