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Review Article

Gamma Delta T Cells and Organ Transplantation: A Review of Recent Studies

Rumeysa Yegin, Aeisha Ahmed, Gulam Hekimoglu

[1]Hamidiye International School of Medicine, University of Health Sciences, Senior Medical Student, İstanbul, Türkiye
[2]Hamidiye International School of Medicine, University of Health Sciences, Department of Histology and Embryology, İstanbul, Türkiye

Abstract

Gamma delta (γδ) T cells have gained a lot of attention in the field of cancer immunotherapy due to their unique innate and adaptive immune properties. However, until recently, their potential significance in organ transplantation went unnoticed. This review highlights the effector roles and potential advantages of γδ T cells in organ transplantation by examining recent studies examining the connection between T cells and organ transplantation. Recent studies have shown that high γδ T-cell immune reconstitution following organ transplantation is associated with a significantly greater overall survival rate and a lower incidence of acute graft-versus-host disease (GVHD), despite prior studies' contradictory findings. These results suggest that γδ T cells might be a useful addition to the current transplantation procedures. The effector activities of γδ T cells and their putative modes of action following organ transplantation will be covered in this review. We also provide a summary of the most recent research on the connection between γδ T cells and organ transplant outcomes, such as acute GVHD and graft survival. Finally, we point out the areas that still need to be studied in order to fully comprehend how γδ T cells function after organ donation.

Keywords: Phase angle, diabetes mellitus, fasting glucose, hemoglobin A1c

INTRODUCTION

A distinct subpopulation of lymphocytes known as gamma delta (γδ) T cells possess both innate and adaptive immunological features. In contrast to the alpha-beta (αβ) TCR expressed by typical T cells, they express a T-cell receptor (TCR) made up of gamma and delta chains (1). It is well recognized that γδ T cells are essential for a number of immunological responses, including tumor surveillance, pathogen removal, and tissue homeostasis (2). γδ T cells may play a part in organ transplantation, according to recent investigations (3).

The most successful course of action for end-stage organ failure is organ transplantation. Immune rejection, in which the recipient's immune system perceives the transplanted organ as foreign and develops an immunological response against it, limits the success of organ transplantation. Drugs that suppress the immune system are used to prevent immunological rejection, but long-term usage is linked to a number of problems, including infections and cancers (4). To enhance the results of organ transplantation, it is, therefore, necessary to investigate new immunotherapy options.

γδ T cells may have a function in organ transplantation, according to current studies. The effects of γδ T cells on organ transplantation have been studied in the past, but the findings have been mixed. While some research indicated that γδ T cells had a positive effect, other investigations found no effect or possibly a negative effect (5,6). To better appreciate the potential advantages

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Corresponding Author: Gulam Hekimoglu, Hamidiye International School of Medicine, University of Health Sciences, Department of Histology and Embryology, İstanbul, Türkiye
E-mail: gulam.hekimoglu@sbu.edu.tr

and disadvantages of γδ T cells and organ donation, it is necessary to analyze the available evidence.

In this essay, we examine the most recent research on the function of γδ T cells after organ donation. We talk about the effector capabilities of γδ T cells and possible organ transplantation strategies they might employ. We also provide a summary of the most recent research on the association between γδ T cells and organ transplant outcomes, such as acute GVHD and graft survival. Finally, we point out the areas that still need to be studied to fully comprehend how γδ T cells function after organ donation.

γδ T cells

T lymphocytes have a special subgroup known as γδ T cells, which contain TCR γ and δ chains (7). γδ T cells can detect antigens in a TCR-dependent or -independent way, in contrast to traditional αβ T cells (8). The liver, gut, and epithelial tissues are only a few of the tissues where they can be found (9).

Based on how their TCRs are expressed, Vγ9Vδ2 T cells and non-Vγ9Vδ2 T cells are the two main categories of γδ T cells (10). The most prevalent type of γδ T-cell subset in peripheral blood is Vγ9Vδ2 T cells, which accounts for up to 5% of circulating T cells in healthy people (11). They detect phosphorylated non-peptidic antigens produced by different bacteria and tumor cells, such as isopentenyl pyrophosphate (IPP) (12). Although less well understood, non-Vγ9Vδ2 T cells are capable of recognizing a wide range of antigens, including self-antigens and stress-induced molecules (13).

Recent research has also raised the possibility of tissue-resident γδ T cells, which are essential for immune surveillance and tissue homeostasis (14). These tissue-resident γδ T cells differ from the circulating γδ T cells in that they have a high level of tissue selectivity (15).

γδ T cells and organ transplantation

Early studies on the organ transplant effect of γδ T cells: the role of γδ T cells in organ transplantation has been investigated since the 1990s. Early studies suggested that γδ T cells might contribute to graft rejection due to their potent cytotoxic activity and pro-inflammatory cytokine production (16). However, other studies reported conflicting results, with some indicating that γδ T cells might have a protective role in graft survival (17).

Recent studies on γδ T cells immune reconstitution after organ transplantation: the favorable impact of γδ T cells in organ transplantation has been demonstrated by more recent investigations. Studies have confirmed that patients, who received bone marrow transplantation and had high levels of γδ T cells experienced considerably lower incidences of GVHD and greater overall survival rates (18). Similar findings were made regarding kidney transplant recipients, where it was discovered that higher levels of circulating γδ T cells were linked to improved graft function and a lower risk of acute rejection (19).

γδ T cells have also been demonstrated to be important in the immune system's recovery following organ transplantation. The recovery of γδ T cells in peripheral blood was linked to a lower risk of post-transplant infections in a study of liver transplant recipients (20). Similarly, early γδ T cells recovery after heart transplantation was linked to a lower risk of infection and better graft survival (21).

These studies collectively imply that γδ T cells might be useful in organ transplantation. To clarify the underlying mechanisms and decide when and how much to provide γδ T cells-based treatments, more investigation is required.

Effector mechanisms, subtypes in several organ transplantations

A diverse group of T cells known as γδ T cells possess both innate and adaptive immunological capabilities. They are capable of identifying and reacting to a variety of antigens, including self-antigens produced by stress and non-peptidic antigens delivered by non-classical major histocompatibility complex (MHC) molecules (22, 23).

The effector mechanisms and γδ T cell subtypes in the setting of organ transplantation have been the subject of numerous research. According to one study, Vδ1 T cells, a subtype of γδ T cells, were protective against acute rejection and were selectively increased in the peripheral blood of kidney transplant recipients (23). The most common T-cell subset in human blood, Vδ2 T cells, was discovered to play a cytotoxic role in the rejection of liver transplants in another investigation (24).

Furthermore, diverse subsets of γδ T cells have been discovered to have various effector capabilities. For instance, some γδ T-cell subsets create anti-inflammatory cytokines like interleukin (IL)-10, while others produce pro-inflammatory cytokines like interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) (25). Additionally, it has been discovered that some T-cell subsets possess regulatory abilities, such as the capacity to inhibit T-cell growth and control dendritic cell activity (26).

Liver transplantation is a life-saving treatment for diverse etiologies of end-stage liver disease. Immunosuppression (IS) therapy must be administered for the remainder of a patient's life to maintain the function of an allograft liver. Patients on lifelong IS therapy had a higher mortality rate than the normal population because of infections, cancers, cardiovascular problems, and incomplete liver function preservation (27). γδ T cells after liver transplantation have both good and bad consequences, according to studies. Patients with liver transplant rejection have been found to have the presence of γδ2+ T cells, and it is considered that these γδ2 T cells may be the cause of allograft rejection. As one of T cells' beneficial effects, they lower the likelihood of GVHD, which worsens with organ damage as a result of an intense immune response mediated by healthy T lymphocytes. Intolerant liver recipients show an increase in γδ1+ T cell infiltration. It has been observed that it causes the release of interleukin (IL)-4 and IL-10, which results in the protection of allografts, particularly in the liver (28) (Figure 1).

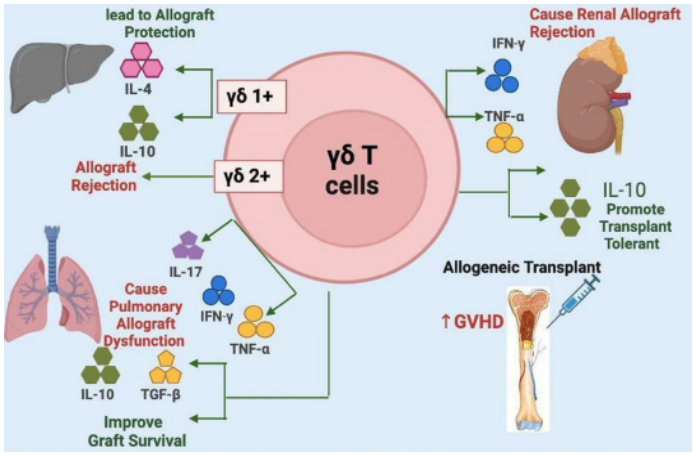

Figure 1: γδ T cells following liver transplantation have both good and bad consequences. Rejection of liver allografts has been linked to the presence of γδ2+ T cells. However, IL-4 and IL-10 are secreted when a γδ1+ T cells is activated, protecting the liver allograft. IL-17 from γδ T cells contributes to acute and chronic allograft dysfunction in lung transplants. The acute rejection of lung allografts and the early phases of renal allograft rejection is accompanied by an increase in TNF-α and IFN-γ production. In hematopoietic stem cell transplantation, acute GVHD is more common and is correlated with γδ T cells

Renal transplantation is chosen in individuals with end-stage renal failure as a therapeutic option. Transplantation necessitates long-term chronic immunosuppression to prevent acute rejection and increase graft survival. Studies have demonstrated that by releasing pro-inflammatory cytokines such as IFN-γ and TNF-α, γδ T cells can influence the early stages of renal allograft rejection (29). Additionally, during acute rejection episodes, it has been observed that γδ T cells infiltrate the renal graft, indicating their possible role in the etiology of renal allograft rejection (30).

On the other side, it has also been demonstrated that γδ T cells contribute to the development of tolerance to renal allografts. For instance, it has been discovered that γδ T cells can secrete immunoregulatory cytokines like IL-10, which can inhibit the activation of conventional T cells and encourage tolerance (31). Furthermore, some research has indicated that, under specific conditions, γδ T cells might contribute to the induction of transplant tolerance. A specific γδ T cell agonist was reported to be able to prolong the survival of cardiac allografts in mice in one investigation, indicating the potential therapeutic role of γδ T cells in fostering transplant tolerance (32).

Overall, γδ T cells have a complex and context-specific role in renal transplantation. Although they have the potential to cause acute rejection and inflammation, they can also foster tolerance and long-term graft survival (Figure 1).

Allogeneic hematopoietic stem cell transplantation is a therapeutic approach that is increasingly being employed with individuals who have hematological malignancies. γδ T cells are a distinct subset of lymphocytes that play a key role in innate immunity against a range of illnesses and have strong anticancer activity (33). They quickly regenerate following bone marrow transplantation, in contrast to αβ T cells, which take longer to mend and lead to an immunological deficit in the months immediately following transplantation. It is highly debatable whether or not γδ T cells play a role in GVHD prevention or promotion, which is one of the most frequent causes of posttransplant mortality after bone marrow transplantation. This is because distinct subsets of γδ T cells may have conflicting effects. While some research suggests that having more γδ T cells is linked to an increased frequency of acute GVHD, other research contends that there is no link between having more γδ T cells and GVHD or that having fewer cells is linked to a greater incidence of condition (34). As a result of their involvement in leukemia and infection control, γδ T cells are also expected to contribute significantly to the efficacy and safety of bone marrow transplantation, increasing patient survival (35) (Figure 1).

Pulmonary transplantation is a treatment that can treat terminal lung disease and save lives. With a median life of only 6.5 years, pulmonary transplant recipients had a worse long-term survival rate than those of other solid organ transplant recipients. Meanwhile, research has demonstrated that interleukin (IL)-17+ γδ T cells during mouse pulmonary transplantation, after 21 days of transplantation, it has been noted that it makes up a sizable fraction of the infiltrating immune cells, and in small animal lung transplant models, the generation of IL-17 by γδ T cells also plays a role in acute and chronic allograft failure (36).

In accordance with findings from additional research, γδ T cells have a role in both the early and late stages of pulmonary allograft rejection. Additionally, their presence in lung tissue is linked to an increase in inflammation and tissue damage. According to one study, acute pulmonary allograft rejection resulted in a large increase in γδ T cells, and their activation was linked to an increase in the production of pro-inflammatory cytokines like TNF-α and IFN-γ (37).

γδ T cells have been linked to promoting tolerance to pulmonary allografts in addition to their pro-inflammatory function. These cells can release immunoregulatory cytokines including IL-10 and transforming growth factor beta (TGF-β), and studies have linked their presence to lower rates of acute rejection and better long-term graft survival (38) (Figure 1).

The effector mechanisms and γδ T cell subtypes involved in organ transplantation are intricate and varied overall. To clarify the functional functions of various γδ T-cell subsets in certain transplant situations and to identify the most effective methods for influencing γδ T-cell responses for therapeutic goals, more study is required.

CONCLUSION

In conclusion, γδ T cells represent a diverse population of lymphocytes with innate and adaptive immunological characteristics. They play a complex and multidimensional function in organ transplantation, with early investigations yielding contradictory findings. However, recent research

has indicated that strong γδ T-cell immune reconstitution following organ transplantation has an advantageous outcome. High γδ T-cell counts had a considerably greater survival rate and lesser acute GVHD cases. It is still unclear how effector mechanisms and different types of γδ T cells function after organ transplantation; some subsets play protective functions while others play cytotoxic roles during rejection. To completely comprehend the functional functions of various γδ T-cell subsets in certain transplant contexts and to identify the most effective methods for influencing γδ T-cell responses for therapeutic reasons in organ transplantation, more study is required. Overall, immunomodulatory medicines in organ transplantation may find success with targeting γδ T cells.

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