Study Of The Effect Of Pretransplant Dialysis Techniques and Complications On Post - Transplant Outcome

THESIS

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By

Dr . Amin Abdulla Awad

M. B. , B. Ch.

Supervised By

Prof. Dr. Wahid M. El-Said

Professor of Internal Medicine and Nephrology

Dr. Mahi M. Al Teheawy

Assistant professor of community Medicine

Dr. Mohamed Ali Ibrahim

Assistan professor of Internal Medicine and nephrology

Faculty of Medicine - Ain Shams University

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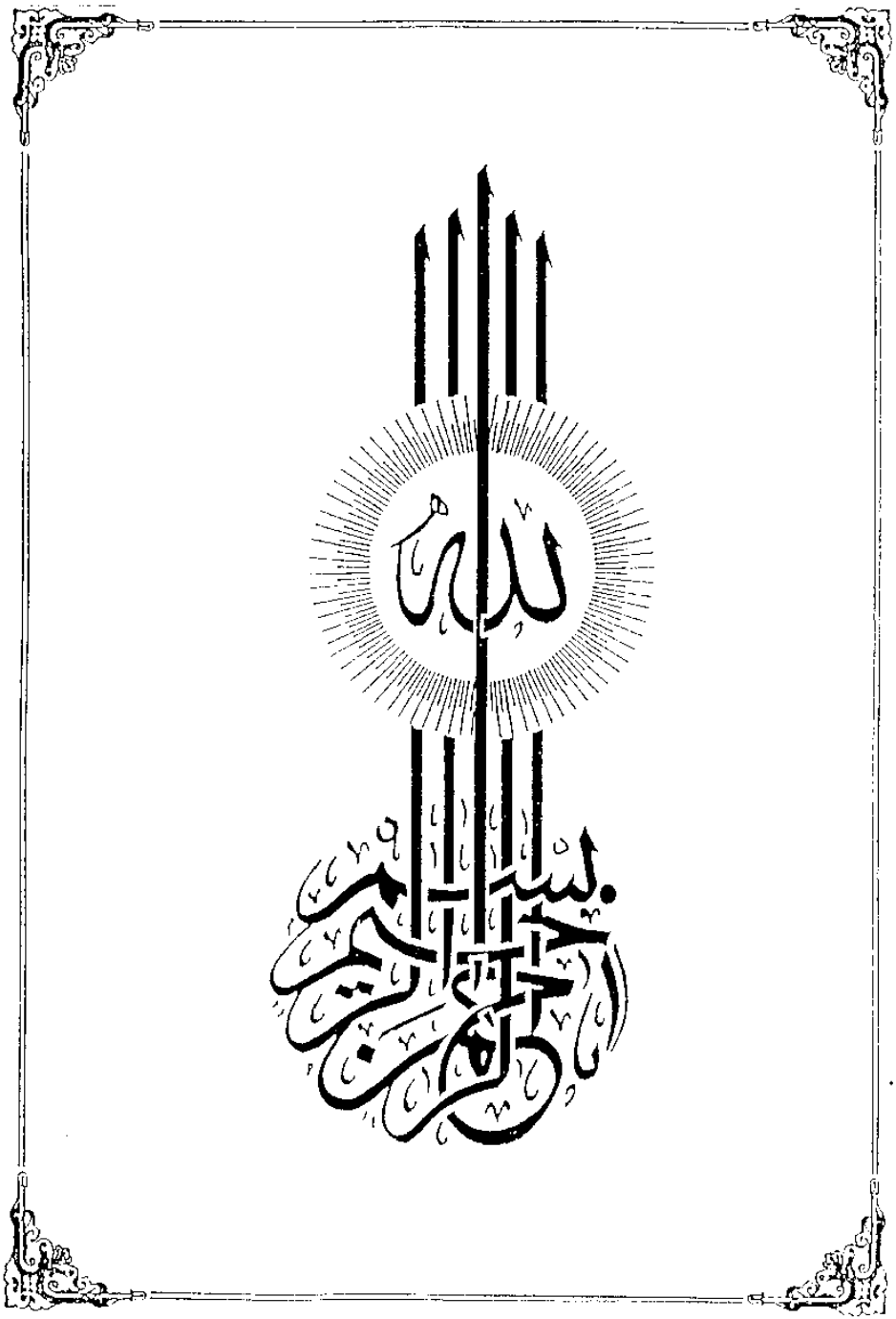

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INTRODUCTION AND AIM OF THE WORK

INTRODUCTION

Most renal transplant patients experience variable periods of dialysis treatment and are exposed to various complications in the dialysis period.

Among these infection, cardiovascular, gastrointestinal hepatic, Musclo-skeletal complications may affect the post-transplant course, and may even modify lines of antirejection therapy **(Baile et al., 1987)**.

The effect of dialysis technique (including membrane used, frequency, type of water treatment.... etc.) on the graft and patient morbidity and mortality is not well studied. **(Eli - Friedman, 1991).**

Also many of post-transplant complications may be predisposed to, or appear during the dialysis period. **(Rao, and Anderson, 1988).**

Chronic dialysis and renal transplantation as therapeutic procedure has made it possible to extend the lives of many patients with renal disease after nephron population has been reduced below a critical level **(Sladen, et al. 1987)**.

Although dialysis improves the function of some organ system, it can not reverse many of the adaptive and maladaptive changes induced by renal failure. (**Michael, Lazarus 1991).**

Renal transplantation is now commonly performed as treatment for chronic renal failure. Nonetheless graft failure remains a substantial problem, particularly in the first few months after transplantation (**Honto, et al. 1987**).

Haemodialysis is the common renal replacement therapy. The short duration of each treatment (Four hours three times weekly) allows time for work and leisure. Disadvantages are the complexity of the extracorporeal dialysis, system and the need for vascular access. Some older patients can not tolerate the rapid changes in fluid and solute balance and major logistic problems arise if hemodialysis is allowed to become the principle treatment for end stage renal failure. (**Marsh, 1985**).

The goal of renal transplantation is to achieve maximal rehabilitation of patients with end stage renal failure. This can be accomplished by prolonged patient and graft survival. Renal transplantation as currently practiced comes close to, but has not yet fully achieved this goal. (**Garovoy et al., 1986**).

Aim of the Study:

The aim of this study is to :

1. Study of the possible relation between dialysis technique and duration and the post-transplant graft and patient survival.
2. Study the possible relation between the pretransplant dialysis complications and post-transplant complications.

CHAPTER I :
OUTCOME OF RENAL TRANSPLANTATION

The goal of renal transplantation is to achieve maximal rehabilitation of patients with end stage renal failure. This can be accomplished by prolonged patient and graft survival with relative freedom from complications related to immuno suppression and minimal risk of morbidity or mortality from surgically related events. Renal transplantation as currently practiced comes close to, but has not yet fully achieved, this goal. Yet for all but a small number of patients with end stage renal failure, renal transplantation remains the treatment of choice. This is especially true for children and middle-aged adults, but it is also true to some extent for individuals of more advanced age, in the absence of extrarenal disease that limits survival **(Garovoy and Guttman, 1986).**

The outcome of renal transplantation, both short-and long-term is affected by a large numbers of factors. Each of these factors. Contributes to some extent to the ultimate outcome of renal transplantation as assessed by the survival of both the patients and the functioning graft.

The outcome of renal transplantation may be measured in terms of the duration of renal allograft functional survival at particular points in time. The course of renal transplantation can be described in terms of two periods, each with differing risks of graft failure and factors that influence graft survival. The early period up to one year is characterized by a greater fractional graft loss due to acute rejection, infections and surgical complications; the late period from one to twenty years or more, is characterized by Lower fractional graft loss. **(Garovay and et al. 1986).**

The short term outcome may not always consistently and reliably predict long-term outcome, because of the late emergence of chronic rejection, nephrotoxicity, and extrarenal complications especially opportunistic infection, chronic liver disease, malignancy, and significant extra-renal disease such as coronary artery disease. Some factors, for example pretransplant blood transfusion have their major effect on short term outcome (First year) whereas other factors exert their influence predominantly on long term results (one to ten years).

In the final analysis, the outcome of renal transplantation must be assessed at several levels. Survival and rehabilitation of the patient and survival of a functioning allograft. Patient mortality can be the direct result of a surgical complication, the consequence of a comorbid events (e.g. myocardial infarction due to coronary astherosclerosis) or the result of a complication arising from immunosuppression (bacterial or viral pneumonia). Graft failure in the absence of extra-renal complications seldom leads to patient mortality since patients can readily return to regular maintenance dialysis and hence become candidates for second or multiple renal transplants. **(Garovoy, and et al. 1986).**

Nonetheless, graft failure, particularly when associated with complications of excessive immunosuppression, influences the subsequent rehabilitation and overall mortality of patients who have returned to dialysis following an unsuccessful transplant. Conversely the clinical course during dialysis therapy of a patient with end stage renal failure has an influence on the outcome of renal transplantation. For example, uncooperative patients developing multiple complications of dialysis therapy tend also to have poor outcome of renal transplantation, not infrequently due to noncompliance or to the cumulative adverse effects of extrarenal complications such as hypertensive cardio-vascular disease. **(Garovoy, and et al. 1986).**

*** Factors affecting outcome of renal transplantation:**

1. Age of recipient and donor
2. Sex of recipient and donor.
3. Race of recipient and donor.
4. Underlying renal disease in recipient and its propensity to recure in the graft.
5. Concomitant extrarenal disease. e.g. Liver disease.
6. Prior blood transfusions (random or donor specific).
7. Prior sensitization to transplantation antigens including pregnancy, previous renal allografts or blood transfusions.
8. Tissue compatability between donor and recipient.
9. Experience of the center in renal transplantation and the skill of surgeon.
10. Duration of cold ischemia.
11. Nature and extent of immuno suppression used to prevent and/or treat rejection.
12. Intrinsic immune responsiveness of the recipient.
13. Long-term compliance of the recipient.
14. Retransplantation.

*** Age of recipient and donor:**

Recipient age has a major effect on patient survival. Transplant recipients between the ages of 6 and 15 years show the best long-term patient survival. Patients over the age of 45 years at the time of transplantation show the greatest mortality. Because of techniqual difficulties, very young patients may experience a somewhat increased mortality and patients over the age of 60 may experience high mortality largely due to the existance of comorbid events such as coronary or cerebral vascular disease and colonic disease.

Better preoperative assessment and management of these comorbid factors reduce the risk of complications or death in this group of patients. Long-term graft survival varies directly with age of the recipient. Thus the graft rejection process may be less severe in older patients, enhancing graft survival rates despite an increased risk of mortality.

The age of the donor has a significant effect on short-term graft survival. Poorest graft survival is seen with donors below 10 or over 55 years of age **(Richard Glassok 1989).**

*** Sex of recipient and donor :**

For at first renal transplant recipient sex has no significant influence on patient or graft survival. In fact male donor kidneys transplanted into female recipients have the highest graft survival rates, indicating that sex-associated H.Y antigens have little effect on transplant outcome. On the other hand. For reasons that are not fully understood, female donor kidneys have an inferior outcome whether transplanted into female or male recipients. This is particularly evident in regrafts with female donors in the face of HLA incompatability. **(Richard Glassok 1989).**

*** Race of recipient and donor :**

Overall patient survival is not greatly influenced by the various combinations of donor and recipient race. On the other hand, graft survival is significantly affected, with 5 year graft survival rates highest for Caucasian-to-Caucasian transplants and lowest in black recipients of kidneys from either Caucasian transplants and lowest in black recipients of kidneys from either Caucasian or black donors. This effect of racial origin of the recipient could be due to genetically determined tissue compatability factors: Concomitant

hypertension and poor patient compliance have been suggested to participate in the diminished kidney survival rates in black recipients. **(Richard Glassok 1989).**

*** Original renal disease**

Of the diseases causing end-stage renal failure, diabetes mellitus is the major one that influences patient survival following transplantation. Lower patient survival is consistently observed in diabetic recipients than in recipients with other diseases causing end-stage renal failure. This lower survival is due to concomitant vascular disease, particularly coronary artery disease. Coronary artery disease may be silent in patients with diabetes mellitus requiring extensive evaluation, possible even coronary angiography prior to transplantation to define the presence of surgically correctable coronary artery lesion that may adversely affect survival. After taking into account the adverse effect of diabetes mellitus on patient survival, actual graft survival is not greatly different than for other kidney diseases, at least among cyclosporin treated recipients. **(Bohman, et al 1987).**

(Recurance of the original kidney disease wherether systemic disease or a primary renal disease is one of the important factors affecting renal transplantation outcome.

*** Concomitent Extrarenal Disease:**

The effect of concomitant extrarenal disease on patient survival is generally quite obvious. For example longstanding hypertension in the recipient leading to premature coronary astherosclerosis, and/or cerebral vascular disease may have a significant effect on mortality risk. These effects, are augmented in the patient with diabetes mellitus. In addition other factors such as peptic ulcer disease with GI bleeding, chronic active granulomatous

disease (Tuberclosis, histoplasmosis, Coccidiodomy cosis) colonic diverticular disease, pancreatitis, lower urinary tract obustruction, previous urinary tract infections, bleeding disorders, and major psychatric illness all may adversely affect patient survival and theraby overall graft survival. Chronic Liver disease is an important cause of late mortality as is de-novo malignant disease. (Richard, J. Glassok 1989).

*** Prior blood transfursions:**

With the advent of cyclosporine the transfusion effect has decreased or entirely disappeared to the point that many renal transplant centers have abandoned programs of prospective intentional transfusion of potential allograft recipients, particularly when well-matched donors are used. Nonetheless, at least for poorly matched donor and recipient combinations, a modest "transfusion effect" persists in some group data analyzed retrospectively. This effect can be seen with as few as one pretransplant transfusion, and the risk of sensitization increase with the number of transfusions. Thus if such transfusions are given, the number should be limited, and routine pretransplant transfusions should be avoided in parous female recipients. For living related donors, even including HLA. identical siblings a policy of intentional donor-specific transfusions continues to be employed. There is a significant enhancement of short and long-term allograft survival when a policy of donor-specific transfusions is pursued. The combination of transfusions with concomitant azathioprine therapy, and the avoidance of random donor, blood transfusions in patients selected for donor-specific transfusions protocols, has reduced the risk of sensetization of the recipient to approximately five to ten percent. Even those recipients who are sensitized as a result of donor-specific transfusions may successfully receive a cadaveric donor kidney with no appreciable decrease in the likelihood of a