IMPROVING QUALITY OF LIFE, EMOTIONAL STATES AND MEDICAL COMPLIANCE IN RECIPIENTS OF KIDNEY TRANSPLANTS

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Abbreviations:
AR: Acute rejection
BDI: Beck Depression Inventory
BSI: Brief Symptom Inventory
CyA: Cyclosporine
ESRD-SC: End Stage Renal Disease Symptom Checklist
HQOL: Health-related Quality Of Life
ISSB: Inventory of Social Supportive Behaviours
LTMBS-scale: Long-term Medication Behaviour Scale
LAR: Late acute rejection
MHLC: Multidimensional Health Locus of Control
MMPI: Minnesota Multi-phasic Personality Inventory
NAR: No acute rejection
PACT: Psychosocial Assessment of Candidates for Transplantation
PLS: Psychosocial Levels System
QOL: Quality Of Life
QALY: Quality Adjusted Life Years
SF-36: 36-item Short Form Health Survey
SPK: Simultaneous Pancreas-Kidney
SCL-90-R: Symptom Checklist
SIP: Systemic Integrative Psychotherapy
TERS: Transplant Evaluating Rating Scale
UNOS: United Network for Organ Sharing

CONTENTS

ABSTRACT

Quality of Life (QOL) amongst transplant patients has become an issue as a means to optimize the use of scarce resources and improve outcome. The relationship between QOL, medical compliance, psychosocial states and QOL is presented as follows:

Patient empowerment: Patient empowerment and compliance with medications in patients who experienced late acute rejection, was assessed using the Long-term Medication Behaviour Scale (LTMBS-scale). We demonstrated a relationship between late acute rejection and low confidence in taking medication and items relating to physical and psychological symptoms.

Effect of psychotherapeutic program on emotional states after kidney transplantation: Recurring emotional states as recalled by patients during psychotherapy sessions (e.g. loss of QOL) were analysed and used to formulate effective group and individual psychotherapy intervention. The Beck Depression Inventory (BDI) was utilised as a measure of change before, during and after treatment. There was significant improvement in psychological states after therapy contemplated as follows, (i) fear of rejection, (ii) feelings of paradoxical loss (iii) psychological integration of the transplant.

Randomised controlled study to determine the efficacy of individual or group psychotherapy amongst kidney transplant patients: Analysis of group and individual psychotherapy in recipients of kidney transplants versus control patients was conducted. Improvement appeared to be more significant in the individual therapy compared to group therapy (p= 0.01). In both the individual and group therapy arm, lowering of scores was progressive and sustained (p=0.01). However, individual therapy resulted in the lowest BDI scores at the end of treatment period.

Coming to terms with the 'imagined past': After a successful transplant, patients may present with feelings of paradoxical loss (e.g. grief or low mood). We propose that paradoxical loss should be considered in terms of an *imagined past* (loss of life goals which have never been actualised as a result of chronic illness). Feelings of loss present an obstacle to a good QOL after transplantation as low mood may lead to ambivalence and subsequently to non-compliance.

INTRODUCTION

This context statement summarises the claim for which PhD equivalence is being claimed for work undertaken at the University of Glasgow, UK, and Avera Mckennan University Hospital, Sioux Falls, South Dakota, USA, as the Principal Investigator.

A standardised definition of QOL remains illusive along with the factors that actually constitute QOL. However, it is fair to say that academics that have been involved in the development of QOL have been concerned to evolve an instrument that is essentially a standard verifiable measurement tool. Schipper, Clinch and Olweny (1996) have arbitrarily divided QOL into the following components: physical performance and occupational function, psychological state, social interaction and somatic sensation. Whiting (2001) has succinctly defined QOL as the measurement and quantification of the patient's subjective perspective of various health-related concepts. Whiting went on to identify three basic elements of QOL instruments; health preferences, health values and utilities, however, in practice these are grouped under the term 'utility measure'. Both definitions are particularly apt for a research thesis concerned to determine the patient's experiences of kidney transplantation. Defining QOL and continues to be an area of intense research, while a universally accepted instrument to measure QOL remains elusive (Guggenmoos-Holzman, Bloomfield, Brenner and Flick 1995). In defining QOL, there is also a conflict between choosing criteria based on societal values versus criteria based on the values of the individual and population groups and across different countries or across different ethnic groups within the same country (Patrick and Bergner 1990). Attempts are being made to create a culturally sensitive QOL instrument that may be applicable to different ethnic groups and in different countries, which will capture subtle ethnic and linguistic differences in QOL studies (World Health Organization QOL group

1993). It must, however, be realised that some persons living in social isolation, unemployment, poverty or adverse living conditions may still report a positive life satisfaction. This probably reflects their accommodation to adverse conditions and does not imply that they would not wish to improve their life circumstances should the opportunity arise in the form of better medications, rehabilitation of job opportunities. Occasionally, some patients when exposed to a positive intervention may give decreased QOL from the baseline. This may suggest that the patients are now more aware of the opportunities and are eager to improve their lives even more (Lehman, Postrado and Rachuba 1993).

To measure QOL, the most widely used generic questionnaires are the Sickness Impact Profile [SIP] (Bergner, Bobbit, Carter and Gilson 1981), Nottingham Health Profile (Hunt, McKenna, McEwen and Papp 1981) and the SF-36 (36-item Short Form Health Survey) [Ware Jr and Sherborne 1992], the latter instrument has been condensed to SF-12, a measure validated in numerous disease states and in many countries (Ware Jr and Sherborne 1992). The disease-specific questionnaires in transplantation, which have been validated, are the Kidney Transplant Questionnaire (Laupacis et al. 1996) and the End Stage Renal Disease Symptom Checklist [ESRD-SC] (Franke et al. 1999). SF-36 is a global QOL instrument looking at eight scales - physical function, physical role, pain, and perception of general health, vitality, social function, emotional role and mental health. Other instruments in use are the disease-specific QOL instrument such as the Karnofsky Index, Activities of Daily Living, Brief Symptom Inventory (BSI) [Derogatis 1993] and Mini Mental State Examination.

There is reported confusion between health-related quality of life (HQOL) and the broader topic of QOL and the components of measurement (Bowling 1995; Levine

1995; Albrecht and Devlieger, 1999). "Quality of Life is an evaluation of the condition of the external environment in part by observing the impact on individuals, while HQOL is an evaluation of the condition of the individual as influenced by his or her own bodily state as well as external antecedent and intervening factors such as medical care, health policy, and social settings and conditions" (Lerner and Levine 1994). In other words, QOL is a more general concept and includes various life issues such as income, standard of living, work conditions, marriage, family and friends, neighbourhood, system of government and even public safety. The term QOL is more readily understood by the general public; "QOL" is used in every day conversation and is the preferred term in transplant literature. HQOL on the other had is a more restricted term, which is defined by Patrick and Erickson (1993) as "HQOL is the value assigned to the duration of life as modified by the impairments, functional states, perceptions, and social opportunities, that are influenced by disease, injury, treatment or policy". Therefore, HQOL is more influenced by the physical health status and the person's ability to perform the social roles in his/her life and his/her satisfaction with these roles. Furthermore, HQOL is also dependent was is also dependent upon a person's social environment such as his/her friends, confidants and a supportive community environment to which he/she can turn for help and guidance (Patrick and Erickson 1993).

A study of QOL is important as it measures the effect of treatment or procedure on a person's 'goodness of life', a person's happiness and the ability to function independently and to enjoy life (Parmet 2002). It has been speculated that the definition of QOL may have been inspired by the World Health Organization's constitution in 1948 that stated that health is not just the absence of disease, but "a state of complete physical, mental and social well-being". Information obtained by

QOL studies can be integrated into economic outcomes to evaluate the performance of individual centres (Keown 2001). Transplant centres will be able to compare their outcomes with other programs and to monitor quality and implement appropriate changes, justifying the added administrative cost of this exercise. Data obtained from QOL studies can also be used to compare different medications (Hilbrands, Hoitsma and Koene 1995; Dew et al. 1997; Shield, McGrath and Goss 1997).

As there is a far greater demand for kidney transplants than the supply, it is important that we measure the QOL after the transplant to ensure that the patients benefit from a complex procedure and will comply with the rigorous demands of follow-up and life-long anti-rejection therapy (Keown 2001; Matas et al. 2002a). The need for such instruments has expanded in recent times because comparisons must be made between smaller differences in the outcomes and the effect of treatment. More importantly, there is a greater understanding and emphasis on the quality rather than merely the quantity or length of life preserved by medical technology. Furthermore, the development of QOL instruments has been facilitated by improved coding and computerisation of medical records, better understanding of social-role functioning, understanding of cultural and linguistic differences between races and peoples and the widespread implementation of statistical methodology and Diagnosis Related Groups (DRG) in hospital care.

There are only a few studies that have explored the link between QOL and morbidity after kidney transplantation. German investigators used the BSI and a German Social Support Questionnaire, SF-36, End-Stage Renal Disease Symptom Checklist-Transplantation Module to two group of patients; Group A consisted of 80 patients treated by dialysis while on the waiting list for transplantation when investigated at baseline and was followed after successful transplantation. Group B

consisted of 222 patients investigated twice after successful kidney transplant. Group A demonstrated a statistically significant increased satisfaction with social support after kidney transplantation while group B patients reported a decrease. The psychological distress at baseline predicted QOL at later time point in both groups (Franke, Reimer, Philipp and Heemann 2003). In another European study, the elimination of cyclosporine (CyA) from sirolimus, steroids and CyA combination anti-rejection therapy resulted in improved QOL. QOL was measured using the Kidney Transplant Questionnaire and the SF-36 at month three (time of randomization) and months 12 and 24 after transplantation. Statistically significant difference favoring sirolimus and steroid group were found on fatigue, vitality and appearance scores. No treatment differences were observed in physical symptom, uncertainty-fear, and emotion scores (Oberbauer et al. 2003). Siegal, Halbert and McGuire (2002) examined the associations between the Life Satisfaction Index and demographic factors, co-morbid condition; adverse effects of immunosuppressants, and medication compliance in 3676 kidney transplant recipients in the USA. Mean satisfaction scores were highest in persons who were older than 64 years, men, and those who were married. Satisfaction scores were positively correlated with education and income; scores was significantly lower among persons with medical co-morbidities, persons who reported that adverse effects of medications were more frequent, and persons who reported non-compliance with their medication regimen.

To date, much of the research that has set out to determine QOL before and after renal transplant has focused upon the designated time point or static measurement of QOL, defined in terms of vocational, medical status and classifiable psychiatric disorders. However, little attention has been given to considering QOL as an interactive entity in relationship to medical compliance with the transplant process

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and subsequent emotional well-being. Further, there has been very little attempt to develop effective psychotherapeutic intervention as a means to address emotional, medical compliance issues and subsequently improve QOL. This is particularly worrying as dialysis patients diagnosed with of classifiable psychological disorders and a history of non-compliance are often excluded or denied access to organ transplant. Therefore, it was hypothesised that there is a direct relationship between QOL, emotional states and compliance with the medical regime. Further, that the determination of QOL before and after transplant is better utilised as an indication for and as a means to determine, efficacy of psychotherapeutic intervention with a view to improving emotional states and compliance behavior amongst renal patients. This is in direct contrast to the tradition of using QOL as a psychosocial measurement tool without any form of intervention. Such studies rely entirely upon the receipt of a successful transplant, or not, as the case may be, to enhance QOL. Further, such studies are not sensitive to the subtleties of emotional experiences that accompany the increase or decrease in a patient's QOL.

The findings of the research abstracts presented in the thesis are threefold as follows: firstly, that there is a relationship between QOL, emotional states and compliance with medical treatment; secondly, that the emotional experiences of transplant patients are much more complex than originally realized. Finally, individual psychotherapy is an effective means of intervention amongst patients in whom QOL is compromised by emotion issues. Therefore, QOL measurement should be conducted as a progressive tool to understand and develop effective intervention, as opposed to a static single measurement in time. This will improve patient compliance with the post-transplant regime and subsequently lead to increased longevity of the transplanted organ.

The achievement of such an ambitious hypothesis has necessitated a multi-disciplinary effort consisting of a transplant surgeon and psychotherapist. This collaboration has facilitated an insight into the work of mental health professionals along with the thought processes and clinical presentations of transplant patients. However, the reader should not assume that attending to the emotional needs of the patients is the sole prerogative of psychotherapists; any member of the transplant team can find themselves face-to-face with a distraught or agitated patient. However, in order to administer QOL assessments, detecting non-compliance or observing for previously identified emotional themes amongst the patients participating in the research presented, I underwent a three month period of in-house training by a qualified medical sociologist and psychotherapist. During this time I learnt to monitor the words spoken by the patients and the context in which they placed them. I also sat in therapy sessions and evaluated the variety of instruments completed by the patient. This was done with the permission of patients. This psycho-medical pairing has also resulted in an appreciation of a pattern in which the emotional and compliance behavior in patients tends to parallel the medical course of their illness. Dr L.S. Baines, PhD, who is a qualified Psychotherapist, conducted the therapy sessions. The Principal Investigator for all the projects described in thesis was Dr R.M. Jindal. The hypothesis, design of the studies, analysis of results, follow-up and writing of the manuscripts was done primarily by Dr R.M. Jindal with the assistance of Dr L.S. Baines and Dr J.T. Joseph.

Much of the research presented in the abstracts has necessitated the utilisation of a combined quantitative and qualitative methodology. From a quantitative perspective, we have drawn from the traditions of medical and psychological sciences and utilised the previously quantified SF-36, the LTMBS-scale and the BDI (Beck and Steer

1987). We considered the suggestion that these measurements rely on patient self-report and could be misleading. For example, the BDI looks from the outset as if it is just assessing depression, and may lead the patient to distort the results of the tests. However, the BDI does assess the potential for depressive symptoms across stable versus unstable situational contexts, as does the LTMBS-scale in their respective assessment areas. By virtue of their very nature of being self-report, they leave the interpretation of the questions/statements to the patient. This risk is minimised by the use of multiple-choice questions. While written input from the patient is kept to a minimum as the questions statements only require either ticking or circling to indicate the answer chosen, eliminating the opportunity for interviewer bias. Rather, patients are able to evaluate themselves at their own (thought/reflection) pace, as opposed to the pace dictated by the interviewer, far outweighs any potential problems.

In the studies presented here, we have combined quantitative with qualitative analysis to understand, identify and intervene in emotional states amongst this patient group. This has involved analysis of thematic, in-context, recurring states recalled by patients during psychotherapy sessions and semi-structured interviews. By utilisation of combined quantitative and qualitative methodology, we were able to understand the subtle nuances of our patient's experience. Our study is limited to adult recipients of kidney transplants as issues dealing with QOL in paediatric recipients of kidney transplants involves numerous other variables such as growth, child development, social and sexual issues.

THEORETICAL FRAMEWORK: SYSTEMIC INTEGRATIVE PSYCHOTHERAPY

The concept of 'systematic' psychotherapy within the context of this thesis refers to the manner in which patient's experiences infuse into different areas of their lives. Further, it refers to the need for some semblance of order or understanding of these issues if patients are to develop insight into their problems. The meaning of the term 'integrative' in the context of psychotherapy has been defined in a two fold manner by Erskine and Moursund (1988) working at the University of Illinois, USA, as follows: Firstly, it refers to the process of integrating maladaptive personality traits (e.g. defense mechanisms, ego structure, intra-psychic function) as a means to form a more cohesive self. Secondly, it refers to the integration of a number of theories, which in the context of the thesis are those of the psychodynamic, existential and transpersonal. Therefore, it should be clear to the reader that the 'systematic' and 'integrative' components of the therapeutic intervention need to be compatible. In the context of the work presented in the thesis, there is a common theme of 'heightened sensitivity to time' that informs; guides and subsequently validates the therapeutic process.

After the death of Freud in 1939, there was a broadening of the concept of psychoanalysis away from viewing individuals as just biological beings, whose personalities could be understood in terms of the psychosexual stages of development, towards an approach that viewed individuals as social beings. The concept of social beings incorporated the work of Kohut (1971, 1977), Mahler et al. (1975) and Kernberg (1976, 1984) and their theories of 'self', generically known as the psychodynamic approach. The psychodynamic approach views problems experienced by patients in the present as having their origins in childhood experiences. Therefore,

psychodynamic theorists believe that in adulthood, patients recreate adult relationships that mimic the problematic ones of their childhoods. This phenomena is termed 'projective identification' and is the pattern of interaction and behaviour that therapist identify and use to disentangle troubled relationships of the past in relationship to the present.

The Existential approach is based upon philosophers such as Heidegger (1927), Sartre (1943), May (1950) and Laing (1960). The existential philosopher is concerned to understand patient's problematic experiences of 'being in the world' in the present in terms of their relationship with self, others and the physical world. Existential therapists place ultimate responsibility for the creation and compilation of above-mentioned aspects of experience upon the patient. In so doing, they draw upon the self, within a broad context of individual-patient experience, such as decision-making and choice, identity, isolation and interaction, love, time, death and freedom.

The Transpersonal approach perceives the psychotherapy process as an opportunity to explore dimensions of all the above-mentioned experiences and phenomena beyond the lived personal experience, a spiritual exploration. Sutich (1986) described Transpersonal

Psychotherapy as being directed towards enabling the patient to achieve the 'realisation of an ultimate state' through a spiritual path. Transpersonal Psychotherapy draws upon psycho-synthesis and the Jungian approach and ideas and techniques from meditation, Chakras, dream-work, imagery, healing, Sufism, Buddhism and astrology.

The experience of ongoing chronic illness and major surgery causes these patients to develop a heightened sensitivity to time in terms of time lost to chronic illness, 'present time' focused upon survival and 'future time' remaining to them with or without a transplant. Clarkson and Lapworth (1996) were the first to integrate

psychodynamic, existential and transpersonal approaches, compiled to be sensitive to 'the evolution of time' and appears well suited to client groups suffering from chronic illness. Further, it is capable of reaching across time, by virtue of its' integration of existential (present), psychoanalytical (past) and transpersonal (future) perspectives, essential to emotional stability and personal development after transplant. The ability of this model to incorporate such an expanse of time offers continuity throughout both the psychotherapeutic and transplantation process, which are likely to run parallel to each other. The emphasis is upon 'framework' as opposed to 'theory' or 'model', to allow the therapist to accommodate patient needs. We have found that this form of therapy best accommodates the needs of patients and reflects their heightened sensitivity to time. Patients view their life through three time zones, namely the past (time lost to chronic illness), present (based upon daily survival) and the future (time remaining to them). During dialysis, the focus is very much on the present, which manifests during therapy as doing what they need to do in order to survive, there is little personal development during this time and they barely glance back (past) or forward (future). After transplantation, patients are concerned about reconciling the past lost to chronic illness. There is often much talk of 'getting back to normal' after transplantation. However, 'normal' is defined in time past and is often not a realistic baseline after transplantation, as time has moved on. Ordinarily, individuals develop, or change over time (defined in terms of attitude, behaviour, values and perspective), a phenomenon, which is often reflected in their interaction and the nature of their relationships with others. However, for patients receiving dialysis, time and personal development often stagnates, while family and friends continue to make progress in their lives. Therefore, after transplantation, patients often find themselves in a sort of 'developmental limbo' in which they can flounder. Much of the therapist's work after

transplantation involves helping the patient to redefine 'normality' based on their present physical ability and emotional availability and gently contemplates the future. Normality might be determined differently after transplantation but that does not necessarily mean that it was inferior or any less worthy before. We often suggest to patients that life might be *different* after transplantation, but not necessarily any less meaningful than their pre-morbid life.

The theoretical integration or 'theory mushing' of different theoretical orientations and techniques of psychotherapy came about in the hope that collectively they would be more effective than the individual theories. Systemic Integrative Psychotherapy integrates psychoanalysis (past), existential (present) and transpersonal (future) theoretical models. In other words, it is based upon the need to consider needs over a time span, which includes the past, the present and future perspectives. These are recalled during therapy sessions and give continuity over the transplant process over an uncertain period of time. This specific form of therapy places great emphasis upon the concept of 'time'. More specifically, movement through time, a common concern amongst kidney transplant patients. Time is described as spanning 'back' (downwards) to the past, 'through' the present and 'upwards' to the future. Time spent in therapy is considered to be a mere moment on the scale and the counselling relationship relates to a point 'in time' of the patient's life. It has been suggested that it exists existentially in the present as a working psychotherapeutic alliance in order to accommodate current life experiences within the family, friendships and practicalities which make up daily experiences which are often complicated by feelings of loss, conflict and confusion. In turn, the relationship is likely to regress to the past as the patient recalls early childhood and experiences of chronic illness which have led to current feelings of conflict, confusion and loss. In considering the past, counselling

relationship is subject to psychoanalytical concepts of transference and counter-transference. As the past is left behind, it is thought that the future comes to be contemplated as a more realistic option with emphasis upon the transpersonal. This is largely uncharted territory for most patients, but amongst transplant patients, this concept is particularly difficult to contemplate and is complicated by fear of rejection of their organ. However, it is important that this aspect of uncertainty is overcome so that the patient can begin to contemplate the future and the direction in which therapy is heading.

LITERATURE REVIEW

There are numerous studies examining QOL after kidney and pancreas transplantation. We performed MEDLINE, the Cochrane Library, EMBASE, Cinahl, PsycINFO, ASSIA, RCN journals, SERFILE 202 and World Information Nursing and the World Wide Web for search using the terms 'Quality of life and kidney transplants' and 'Quality of life and pancreas transplants'. Only articles in English were included. Priority was given to articles that were prospective and randomised and used controls and articles after 1995. We generally avoided case reports or papers, which were in abstract form or were incomplete or duplicate publications. The selected papers represent studies across the world.

Parameters used in these studies include physical and psychological well-being and sexual function as well as the job satisfaction, income and social functioning. One of the commonest questionnaire is the SF-36, which is a global QOL instrument looking at eight scales- physical function, physical role, pain, perception of general health, vitality, social function, emotional role and mental health. Other instruments in use are the disease-specific QOL instrument such as the End Stage Renal Disease Symptom Checklist, Karnofsky Index, Activities of Daily Living, Nottingham Health Profile, BSI, SIP and Mini Mental State Examination.

Dew et al. (1997) reported in a meta-analysis of 14,750 patients that there was clear evidence that QOL improved after transplantation, however, QOL of transplant recipients did not generally improve to the level of matched healthy population. More recently, it has been proposed that QOL questionnaires may be able to differentiate between various immunosuppressive regimens. Shield, McGrath and Goss (1997) evaluated QOL in recipients of kidney transplants who participated in the Phase III trial of CyA versus tacrolimus. They recruited 303 patients and used a variety of

instruments administered at week 6 and months 3, 6, and 12. They found that the baseline scores were similar between the groups, the mean scores for patients with rejection were lower versus patients not experiencing rejection; overall scores in the two study arms were similar. Hilbrands, Hoitsma and Koene (1995) administered QOL instruments to patients who were on standard immunosuppressive therapy (CyA and prednisone) and then at three months allocated to either withdrawal of prednisone or conversion of cyclosporine to azathioprine. They found that in both groups of patients, scores improved progressively after transplantation reaching levels of general population in Netherlands, acute or chronic rejection had a negative effect on scores, while patients who were on CyA monotherapy had the best outcomes in terms of psychosocial functioning. This positive effect was thought to be due to the withdrawal of prednisone.

Most studies have found that the QOL improves after transplantation, however, only few studies have undertaken the five-year surveys (Hilbrands, Hoitsmma and Koene 1995; Dew et al. 1997; Pisani et al. 1997; Franke et al. 1999; Gross et al. 2000; Fujisawa et al. 2000; Martin, Shireman, First and Whiting 2001; Christensen, Raichle, Ehlers and Bertolatus 2002; Griva et al. 2002; Matas et al. 1998 and 2002a). Matas et al. (1996) looked at the employment patterns of 822 kidney transplant recipients. They found that a significant proportion of patients who were working or attending school before transplant continued to do so afterwards, while the majority of those returning to work did so in the first year post-transplant. However, with longer follow-up, more patients returned to work, major factor for dropping out of full-time work was failure of the transplanted organ.

Unlike renal transplants, kidney-pancreas transplants carry significantly higher morbidity. With experience, technical complications have diminished, but

post-operative morbidity remains high. In a recent review, Sutherland et al. (2001) have recommended early pancreas transplantation for labile diabetes. Even though the transplant, as such contributes to morbidity and immunosuppressive medications cause many side-effects, QOL, post-transplant, has been found to improve significantly, especially in ameliorating the secondary complications of diabetes. The major surgical complications of kidney transplants include graft thrombosis, renal artery stenosis, wound infections, lymphoceles, side effects of anti-rejection therapy such as hypertension, hyperlipidaemia, post-transplant diabetes and increased susceptibility to infections and certain types of cancer. The overall incidence of complications after kidney transplantation has decreased dramatically with improved surgical techniques and patient-tailored anti-rejection therapy and prophylactic anti-infection therapy (Jindal and Hariharan 1999; Hariharan et al. 2000; Bennet 2003). In case of pancreas transplantation, there has also been dramatic improvement in both short- and long-term survival, however, immediate complications continue to be a major issue due to the very nature of the organ. In general, hospital stay and incidence of complications after a pancreas transplant is 30% greater then after kidney transplantation (Jindal, Revanur and Jardine 2002; Beneditti, Sileri, Gruessner and Cicalese 2002).

Griva et al. (2002) compared HQOL in 76 living related and 271 cadaver organ recipients, looking at the social, medical and psychological improvements after transplants. They observed improved emotional well-being in all the patients. However, living-related recipients expressed higher levels of feeling of guilt probably because they continue to see the donors. In another such study from Japan, Isotani et al. (2002) questioned 104 patients who underwent living donor nephrectomies, using SF-36 survey and the questionnaire about donor satisfaction. They reported that QOL

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of kidney donors was not affected by donor nephrectomy. Pace et al. (2002) compared open versus laparoscopic donor nephrectomy and found that laparoscopic donor nephrectomy gave a better QOL at marginally higher cost. It is clear that QOL in recipients of live kidneys will be better than of those receiving cadaver kidneys as these kidneys work straightaway and the long-term outcomes are better than cadaver kidney transplants (Hariharan et al. 2000). There may also be decreased incidence of acute rejection and therefore decreased burden of anti-rejection medications leading to a reduction of side-effects (Jindal and Hariharan 1999). We will see an increase in both live related and live unrelated transplants; however, we will have to be sensitive to the emotional problems of both donors and recipients.

The demand for kidney transplants across the world far outweighs availability. Advances in surgical techniques and in immunosuppressive therapy have made kidney transplantation a routine procedure in most countries (Jindal and Hariharan 1999). Acute rejections, which generally occur in the first three months after transplantation can be reversed in most cases, however, chronic rejection in the later stages is still a major problem. The incidence of chronic rejection is approximately 15% per year. The magnitude of the problem is enormous, as five-year survival of grafts is 31% for those with biopsy-proven chronic rejection versus 81% for those without rejection. One year graft survival after cadaver transplant is now approximately 88% (Jindal and Hariharan 1999); while the cumulative rate of graft loss after the first year following transplantation is reported to be about 3% a year (Jindal and Hariharan 1999). Therefore, there is ongoing demand for kidney transplants.

The situation in most Western countries suggests that the number of organ donors has plateaued; according to the UNOS [United Network for Organ Sharing] (the agency that regulates organ supply in the USA), there were 82,134 patients waiting on the list for organs but only 8,324 patients received a kidney transplant this year while there were 4,285 organ donors. Despite, extensive publicity and campaigns to increase the number of cadaver organ donors, there has been very little impact. The logical way to increase donor supply has been the increasing use of live donors for kidneys and to a lesser extent for livers (Jindal and Hariharan 1999; Hariharan et al. 2000). Despite extensive public education, the number of deceased donors in the US has essentially plateaued (3,714 in 2003, 6,183 in 2002, 6,082 in 2001 and 5,985 in 2000 according to UNOS statistics) while the number of live kidney transplants has steadily increased (4,002 in 2003, 6,618 in 2002, 6,557 in 2001 and 5,867 in 2000 according to UNOS statistics). The overall mortality is 0.03%, which is the same as getting killed in a random car accident on the highway. The donor of a kidney transplant is not denied life insurance and the incidence of renal failure, diabetes, hypertension of other medical issues are not increased as comprehensively shown by a landmark study by Najarian et al. (1992). Investigators at the University of Minnesota studied kidney donors and their siblings 20 years after donation by comparing renal function, blood pressure, and proteinuria. In 57 donors, mean serum creatinine, blood urea nitrogen, creatinine clearance, and blood pressure did not differ from siblings. They also surveyed all North American transplant centres and found that there were 17 peri-operative deaths after living donation, an estimate mortality to be 0.03%. Despite these reassuring statistics, donors should be warned of the risks associated with surgery and should be seen by a physician and mental health professional who is independent of the transplant team performing the surgery. Donors usually also

undergo a detailed physical examination and comprehensive battery of investigations to rule out any medical or psychological contraindication to surgery. Studies from both the US and UK have confirmed that altruism and a sense of moral obligation were the prime motivational influences with the spontaneity of decision-making, however all appropriate precautions should be taken to prevent commercialisation of organs and protect the interests of the donor (McMaster and Mirza 1995; Eggeling 1999; Adams et al. 2002).

It has also been shown that recipients of unrelated kidney transplants even without good tissue match do as well as fully matched cadaver organs (Hariharan et al.2000). Added to this is the fact that surgery, anaesthesia and postoperative care of live organ donors has improved dramatically, making this procedure fairly straightforward. There is also the introduction of laparoscopic technique for removing kidneys from live donors, the hospital stay is shortened as much as by 50% (average hospital stay three days versus 6 - 7 days for the open procedure) and patients require less analgesia and return to work sooner (Pace et al. 2002). Therefore, live kidney donation, both from related and unrelated has appeared as a major advance in kidney transplantation. Living donation eliminates the recipient's need for placement on the national waiting list. Transplant surgery can be scheduled at a mutually agreed upon time rather than performed as an emergency operation. Because the operation can be scheduled in advance, the recipient may begin taking anti-rejection medications two days before the operation. This decreases the risk of organ rejection. Transplants from living donors are more successful, because there is a better tissue match between the living donor and the recipient and the cold storage time is minimal (Jindal and Hariharan 1999; Hariharan et al. 2000). This higher rate of compatibility also

decreases the risk of organ rejection. Perhaps the most important aspect of living donation to the donor is the psychological benefit. The recipient can experience positive feelings knowing that the gift came from a loved one or a caring stranger, while the donor experiences the satisfaction of knowing that he or she has contributed to the improved health of the recipient.

In the United States, UNOS maintains the national list of patients waiting for deceased organ donor transplants. UNOS' computer matches patients to donor organs according to objective criteria such as blood and tissue type, immune status, medical urgency and time spent on the waiting list. The ranking system determines which patient is offered the available organ. In addition to deceased (person declared brain dead) donor transplants, patients may also receive organs from living donors. In 2001, there were 24,101 organ transplants performed in the United States. Of these 6,082 were living donor transplants. Living donation offers an alternative for individuals awaiting transplantation and increases the existing organ supply (www.unos.org). Other countries have organizations similar to UNOS to regulate the supply of organs; 'UK Transplant' is an example in the UK and 'Euro-Transplant' in some European countries.

In general, live kidneys work straight away and there is not need for dialysis after surgery (Joseph and Jindal 2002). In our own study, we had a 50% incidence of delayed graft function; these patients required dialysis and increased hospital stay (Joseph and Jindal 2002). But more important is the fact that live kidneys have a clear long-term advantage. Hariharan et al. (2000) analysed the influence of demographic characteristics (age, sex, and race), transplant-related variables (living or cadaver donor, panel-reactive antibody titer, extent of HLA matching, and cold-ischaemia

time), and post-transplantation variables (presence or absence of acute rejection, delayed graft function, and therapy with mycophenolate mofetil and tacrolimus) on graft survival for all 93,934 renal transplantations performed in the United States between 1988 and 1996. A regression analysis adjusted for these variables was used to estimate the risk of graft failure within the first year and more than one year after transplantation. From 1988 to 1996, the one-year survival rate for grafts from living donors increased from 88.8 to 93.9 percent, and the rate for cadaver grafts increased from 75.7 to 87.7 percent. But more dramatically, the half-life for grafts from living donors increased steadily from 12.7 to 21.6 years, and that for cadaver grafts increased from 7.9 to 13.8 years. After censoring of data for patients who died with functioning grafts, the half-life for grafts from living donors increased from 16.9 years to 35.9 years, and that for cadaver grafts increased from 11.0 years to 19.5 years.

Kahan (2000) recently summarised the selection criteria for transplantation as follows: 'accepted notion of benefit' (medical need, life remaining and post-transplant quality of life); 'patient's rights' (based upon the right of every patient to transplantation if they so wish); 'cost effectiveness' (on the basis of best economic outcome); and 'scientific progress' (whether the patient's treatment will advance the medical science). These concepts are designed to assist the physician in allocating scarce resource of organs amongst an increasing number of patients. In general, psychosocial assessments have centred upon compliance, family support and the existence of any psychiatric disorders. Primary psychiatric contraindications generally include history of substance abuse, psychosis, suicide attempts, and dementia and borderline personality.

The principal assessment tools include the Psychosocial Assessment of Candidates for Transplantation (PACT), the Psychosocial Levels System (PLS), and

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the Transplant Evaluating Rating Scale (TERS). The BDI (Beck and Steer 1987), the SCL-90-L (Derogatis 1992) and the shorter version BSI (Derogatis 1993) and Minnesota Multiphase Personality Inventory (MMPI) have also featured in a number of psychosocial studies amongst renal patients. PACT focuses upon psychological variables such as substance abuse, compliance, social support, psychopathology, lifestyle and knowledge of the transplant process. However, PACT does not predict transplant outcomes as such, rather it highlights the correlation between decisions to accept or exclude the view of different assessors between recipients.

The PLS evaluates the correlation of decisions to include or exclude patients, based upon past coping skills, psychiatric history, affect, mental health status, support and susceptibility to anxiety. Patients are subsequently classified into three levels of suitability for transplantation. Level One patient is characterised by not having any psychiatric history, appropriate social responses and good social support. Level Two patients are likely to have a history of depression, agitation or dysphoria and only satisfactory levels of social support at diagnosis. While those patients classified at Level three are liable to have a significant psychiatric history of substance abuse or major depression and/or suicidal ideation.

The TERS evaluates ten psychosocial aspects of a patients functioning and is an expansion of the PLS. In addition to the above-mentioned TERS, PLS level-1 candidates may display cluster C traits (avoidant, dependent or obsessive-compulsive personality disorders). Level-2 patients may have cluster C traits or a combination of symptoms from clusters a (paranoid, schizoid, schizotypical personality disorders) and clusters B (anti-social, borderline, histrionic, narcissistic personality disorder). Level-3 candidates have cluster A and B diagnosis. The use of these have been aimed at the development a single or multiple measure of psychosocial suitability for

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transplantation, the underlining criteria being whether or not the patient would be likely or capable of complying with the medical regime. However, despite the use of rating tools, there is little consensus about the most effective method of predicting outcome.

To measure QOL, the most widely used generic questionnaires are the SIP (Bergner, Bobbit, Carter and Gilson 1981), Nottingham Health Profile (Hunt, McKenna, McEwen and Papp 1981) and the SF-36, the latter instrument has been condensed to SF-12, a measure validated in numerous disease states and in many countries (Ware Jr and Sherborne 1992). The disease-specific questionnaires in transplantation, which have been validated, are the Kidney Transplant Questionnaire (Laupacis et al. 1996) and the ESRD-SC (Franke et al. 1999). We have suggested that in addition to QOL, we should also measure compliance with medications and emotional well-being by LTMBS-scale (de Geest et al. 1995, Baines, Joseph and Jindal 2002a) and BDI respectively. Although other instruments may be used for this purpose, there are as yet no clear guidelines in this regard.

However, the validity (what the patient thinks in the here and now or concurrent validity) reliability (predictive validity, or whether the patient will do what they say they will) of the QOL tools utilised in the research abstracts themselves is likely to be high as they are composed of factual as opposed to non-factual questions. The questions also tend to flow in sets, or logical sequence, thereby reinforcing and re-testing for incongruence in or between themes being measured. The studies we have reviewed use a variety of questionnaires; the selection of QOL instrument was dependent on the bias of the investigators making it difficult to compare studies across centres. The majority of studies are retrospective and there is wide difference in the cultural patterns, sample size and duration of follow-up. Another problem with

the self-reported studies is the poor response from patients. None of the studies reported on the effect of self-reported questionnaires on the patient's ability to influence their physicians or indeed the physician's ability to better understand concerns of their patients. Transplant physicians and psychologists working in teams rather than in isolation may remedy the situation. There was also no information on the additional resources required to conduct these studies; and while these studies were found to be useful in clinical trials, there are no data on their usefulness in actual practice. Clearly, provision must be made for additional resources for the administration of instruments and appropriate psychological intervention. We are encouraged by the recent guidelines by the American Society of Transplantation (Kasiske et al. 2002) that psychosocial evaluation of transplant candidates should be done by a professional who understands that bias may be a factor in patients denied a chance to go on the waiting list. To avoid bias, the potential recipient should have adequate cognitive ability to understand the risk/benefit of transplantation, manage long-term anti-rejection therapy and the importance for life-long compliance. A Psychologist generally administers the questionnaires described above; however, in some centres, a qualified Social Worker with training in psychological methodologies can also do this work.

The studies we have reviewed are generally of small size with short-term follow-up and there is no consistency of the instrument used to evaluate QOL. There has been an exponential increase in the number of publications on QOL after solid organ transplants from zero in 1970 to 120 in 1992 (Joralemon and Fujinaga 1996), however, studies still do not include baseline assessment. Investigators used 159 different QOL instruments in 75 publications (Joralemon and Fujinaga 1996), while some investigators used multiple QOL instruments on the same group of patients,

making it impossible to find commonalities for inter-centre comparison. It is also hypothesized that negative results are omitted or explained away while the transplant patient's sense of indebtedness to the transplant surgeon and the collective experience of loyalty to the transplantation community is not taken into account as positive biases for QOL research (Joralemon and Fujinaga 1996).

CONTRIBUTION TO THE KNOWLEDGE BASE

I have co-authored a book and carried out original clinical studies in this field. I summarise these in the following pages:

<u>Book author:</u>

The struggle for life: A psychological perspective of kidney disease and transplantation, by Lyndsay S. Baines and Rahul M. Jindal. Publisher: Greenwood Publishing Group, Westport, CT, USA. Date for release: December 2003. ISBN: 0-86569-323-4 (www.greenwood.com)

<u>Manuscripts discussed in this thesis:</u>

Joseph JT, Baines, LS, Morris MC, Jindal RM. Quality of life after kidney and pancreas transplantation. American Journal of Kidney Diseases 2003; 42:431-445.

Baines LS, Jindal RM. Non-compliance in patients receiving haemodialysis: An in-dept review. Nephron 2000; 85:1-7.

Baines LS, Joseph JT, Jindal RM. Compliance and late acute rejection after kidney transplantation: A psycho-medical perspective. Clinical Transplantation 2002; 16:69-73.

Baines, LS, Joseph JT, Jindal RM. Emotional issues after kidney transplantation: A prospective psychotherapeutic study. Clinical Transplantation 2002; 16:455.

Baines LS, Jindal RM. Loss of the imagined past: an obstacle to emotional recovery to medical compliance. Progress in Transplantation 2002; 12:305-308.

Jindal RM, Joseph JT, Morris MC, Santella RN, Baines LS. Non-compliance after kidney transplantation: A systematic review. In Press: Clinical Transplantation Proceedings.

Baines LS, Joseph JT, Morris MC, Jindal RM. Group versus individual psychotherapy: Addressing emotional problems in recipients of kidney transplants. In Press: Kidney International.

My contribution to the state of knowledge:

The four unique contributions to the field detailed in this thesis are as follows:

(i) Patient empowerment: To determine the emotional impact of patient empowerment on compliance with medications in patients who had experienced late acute rejection, we requested that they complete a modified version of the LTMBS-scale, a self-report questionnaire; a 27-item instrument depicting a variety of social situations in which the patient might be required to take their medications. We identified 24 patients over a six-year period that suffered late acute rejection. It was seen that patients were only reasonably confident (mean score 2.17) in taking their medications. All patients demonstrated significantly lower self-efficacy in relationship to items relating to physical and psychological symptoms and psychological symptoms that affected their well-being.

(ii) Effect of psychotherapeutic program on emotional states after kidney transplantation: We designed a prospective study utilising the recurring emotional states as recalled by patients during psychotherapy sessions to understand and intervene in emotional issues in adult recipients of first cadaver kidney transplants. Forty-nine recipients of first cadaver kidney transplants were subjected to 12 sessions (at weekly intervals) of psychotherapy within three months of receiving their transplant. The BDI was utilised as a measure of change in emotional state, pre-therapy, at 3, 6, 9 and 12 months. A higher score on BDI was suggestive of psychological dysfunction. In the first instance, data was analysed within a quantitative framework, by virtue of the BDI. In the second instance, data was considered in terms of recurring themes described by patients during psychotherapy

and was analyzed qualitatively. In the third instance, both qualitative and qualitative data was considered in terms of individual patient's ability to achieve some feeling of having implemented some social, relational and vocational equilibrium into their everyday life. Recipients of live kidneys, pediatric transplants and patients who received more than one transplant were excluded, as emotional issues are different in this cohort of patients. All patients have completed one year of follow up. None of the patients were on antidepressant medication before or after therapy. The results reported in this paper form the 49 patients in the individual arm of the study. All the patients in our study happened to be Caucasians. There was significant improvement in the BDI scores following therapy. The mean score was 26.3 ± 7.9 before and 20.5 ± 8.8 after therapy ($p=0.001$); the lowering of the scores remained sustained at 12 months. Multivariate analysis of age, gender, employment status, duration of dialysis (if in dialysis for more than three years) and psychotherapy given before transplantation did not affect the results of our study. For the qualitative aspect of the study, we grouped the emotional problems as expressed by the patients into three recurring themes, (i) fear of rejection, (ii) feelings of paradoxical loss after a successful transplant despite having received a successful transplant (iii) the psychological integration of the newly acquired kidney. We found that psychotherapeutic intervention was an effective means of addressing emotional problems in recipients of kidney transplants. The recurring themes as identified above provided a baseline for psychotherapeutic exploration and resolution of these issues. Successful resolution of these issues was associated with lower BDI scores and the re-definition of normality in daily living.

<u>(iii) Randomised controlled study to determine the efficacy of individual or group psychotherapy amongst kidney transplant patients:</u> Recipients of kidney transplant have been shown to develop emotional problems. The research was founded upon the premise that by its' very nature group therapy might be more cost effective than individual therapy, as up to ten patients could be treated during one hour session, whereas it would take ten hours to treat ten patients in individual psychotherapy. While the small number of studies that have been carried out to determine the effectiveness of group psychotherapy amongst dialysis and transplant patients have suggested that group therapy is effective in alleviating emotional states and facilitating adjustment post-transplant (Freedman, 1983; Abbey et al. 1990), its' therapeutic effectiveness has not been compared to individual psychotherapy. We have compared the efficacy of two modalities of therapy in recipients of kidney transplants versus control patients who did not receive therapy. Recipients of first cadaver kidney transplants were randomised into two groups, to receive a 12-week course of group or individual psychotherapy. Control arm of the study comprised of 37 consecutive patients who had received a first cadaver kidney. Recipients of live kidney transplants and patients who received more than one kidney transplant were excluded as these patients have different emotional issues. We recruited 89 recipients of first cadaver kidney transplants into the study. They were randomly allocated in to the two study groups, 49 for individual therapy and 40 for group therapy. Of these, 82 patients completed 12 weeks of therapy (45 patients from the individual treatment arm and 37 from the group therapy arm). Fifty-five patients completed one-year follow-up (33 in individual therapy and 32 in the group therapy). Patients were required to complete the BDI before starting therapy and at 3, 6, 9, 12 months follow-up. The BDI is a questionnaire that can be completed by the patients. It presents patients with

a series of emotional scenarios that they have to rate according to their perceived severity. It is also quite quick to complete and therefore could be administered in outpatient clinics. The mean score was 26.3 ± 7.9 before and 20.5 ± 8.8 after therapy in the individual treatment group (p=0.001). This was in comparison with a mean score of 29.8 ± 3.9 before and 27.1 ± 3.9 after therapy for the group therapy arm (p= 0.01). Improvement appeared to be more significant in the individual therapy compared to group therapy (p= 0.01). Lowering of scores was progressive and sustained (p=0.01). In the control arm, mean score was 9.4 ± 5.4 before and 20.5 ± 5.5 at the end of the first year (p=0.005) suggesting a significant worsening of BDI scores. The control group's lower starting BDI scores were attributed to them not thinking about their psychological status too deeply as they were not expecting to receive therapy. This is contemplated in the corresponding abstract below in more depth and termed the 'barrier of gratefulness'. Another reason could be "paradoxical" effect seen in certain groups of people such as those living in social isolation; unemployment, poverty or adverse living conditions may still report a positive life satisfaction. This probably reflects their accommodation to adverse conditions and does not imply that they would not wish to improve their life circumstances should the opportunity arise in the form of better medications, rehabilitation of job opportunities. They have probably made peace with themselves and the world. Occasionally some patients when exposed to a positive intervention may give decreased QOL from the baseline. This simply means that the patients are now more aware of the opportunities and are eager to improve their lives even more (Lehman, Postrado and Rachuba 1993).

Multivariate analysis of age, gender, employment status, duration of dialysis and psychotherapy received at any time before transplantation did not affect results. We

concluded that both individual and group psychotherapy were beneficial to our patients, however, individual therapy was found to result in lower BDI scores versus group therapy at the end of treatment period.

(iv) Coming to terms with the 'imagined past': Our research has suggested that even after a successful kidney transplant, patients may present with feelings of bereavement, grief or low mood that might appear paradoxical to both patient and staff, given that they have just received a much desired kidney transplant. We propose that this sense of bereavement should be considered in terms of an *imagined past* which may help to understand the patient's current mood changes and medical non-compliance. We have used the concept of Systemic Integrative Psychotherapy in a case report to analyse change in a patient's life. Based on our research, we suggest that feelings of bereavement and grief are generated as patients come to terms with their past which has been irretrievably lost to chronic illness and contemplate their future. Feelings of grief and bereavement in the post-transplant period may be due to the loss of an *imagined past*, and must be differentiated from the bereavement the patient feels for the donor and the donor family. If these feeling of loss are not resolved it can lead to social isolation and medical non-compliance.

ANALYSIS AND CRITIQUE

These are divided into the following sections:

(i) Quality of life in relationship to medical compliance:

Psychosocial issues and compliance are increasingly discussed in relationship to QOL. Compliance is generally considered in terms of the physician's ability to influence the patient and the patient's willingness to respond. Compliance amongst patients undergoing dialysis and after transplantation has become an important issue as non-compliance with the primary treatment regime leads to complications and even death. The problem of non-compliance is thought to be particularly acute amongst the lower socio-economic groups (Leggat et al. 1998), in patients between 20-30 years of age, females (Alexander and Sehgal 1998) and in patients of minority race such as African-Americans in the USA (Alexander and Sehgal 1998; Baines and Jindal 2000; Baines, Hamilton and Jindal 2001). Furthermore, patients who do not adequately comply with dialysis are less likely to be placed on the waiting list for kidney transplants. This is particularly true in women from black or from lower socio-economic groups who are more likely not to complete the transplant selection process, and therefore, have higher rates of morbidity than those patients who do comply and receive a kidney transplant (Alexander and Sehgal 1998; Baines and Jindal 2000). It has also been shown that non-compliance continues to be a major factor resulting in graft loss in the 1990s (Matas et al. 2002).

Patients who do not comply with the medical regimen and lose their grafts may be denied a second transplant, an area of considerable controversy and debate. Furthermore, health care financing is assuming a central role in our society. Patients

who lose their transplants due to non-compliance will result in significant drain on finances as these patients are placed back on dialysis; a modality of treatment more expensive than a functioning transplant. It is estimated that over 25% of patients who enter into clinical trials of anti-rejection drugs may be non-compliant and hence influence the results of these trials (Leggat et al. 1998).

A variety of validated instruments have been described to assess and in some cases predict non-compliance after a kidney transplant. These methods include pill counts, clinic attendance, drug levels and self-administered questionnaires. Each of these methods has pitfalls and may not be equally applicable to all patients.

We have applied meta-analytic techniques to the literature on medical non-compliance after kidney transplantation to enable a consensus to be reached in this important area. The aim of this study was to identify patients at risk for non-compliance after kidney transplant. Further work is required to identify the best instrument to identify patients at risk of medical non-compliance after a kidney transplant. Our study is limited to patients receiving kidney transplants as this group form the largest cohort of patients receiving a solid organ transplant.

Two authors searched independently using the Medline followed by hand searching. The most recent search was done in June of 2001. The search included the terms: compliance, non-compliance, medical compliance and kidney transplants, transplantation, organ transplantation and medical compliance/non-compliance. Additional reports were identified from the reference lists of key manuscripts and review articles. For the analysis of data, only peer-reviewed articles in English language journals were considered. Only manuscripts in the CyA era and involving adult recipients of kidney transplants were included. Data was extracted by two authors and checked for accuracy by a third author. Tables of the collected data were

prepared for analysis. None of the papers reported a randomised trial; the majority of the studies were of a descriptive nature. The selected papers were prospective in which questionnaires were given to recipients who already had functioning kidney transplants.

Frazier, Davis-Ali and Dahl (1994) sent detailed questionnaires to 500 recipients of renal transplants at the University of Minnesota of which 49% were returned. They used a variety of standardised instruments such as the BDI, BSI, Inventory of Social Supportive Behaviours (ISSB) and Multidimensional Health Locus of Control (MHLC). They analysed their data using multiple regressions. Siegal and Greenstein (1999) prospectively sent questionnaires to 2500 patients in US transplant centres of which 1402 returned, of which 22.4% reported some level of non-compliance with their medications after renal transplant. These patients were over 18 years of age and were on CyA therapy and had a functioning transplant. In their study, non-compliance was scaled from 1 (never forgot) to 8 (forget every day). For each variable, they calculated the frequency, means, percentages and standard deviations and then logistic regression analyses were used to identify predictors of non-compliance. Cluster analysis was used to identify groups of noncompliant patients based on similarities with respect to variables identified by logistic regression.

Raiz, Kilty, Henry and Ferguson (1999) conducted a postal survey of 712 patients from the Ohio State University Medical Centre who were 18 years old and had a primary renal transplant for at least 12 months. They used the Dillman's method for mailed surveys with analysis by multiple regressions. Usable data was obtained from 50% of the patients. Didlake, Greyfus, Kerman, Van Buren and Kahan (1988) from the University of Texas Medical School at Houston, USA, performed a mail

survey of 295 patients who had received a kidney transplant between 1980 and 1986 and were compared with 70 patients who had a functioning transplant for at least 18 months. They defined non-compliance when the patients presented with rejection episodes and were interviewed by two members of the transplant team and the blood levels of CyA were sub-therapeutic. They analysed the mean values of population parameters using t-tests.

Schweizer et al. (1990) performed a combination of retrospective and prospective analysis of patients receiving kidney, liver and heart transplants at the Hartford Transplant Centre, Hartford, CT, USA. Their study was divided into retrospective chart review of 260 patients between 1971 and 1984 and a prospective study of 196 patients between 1984 and 1987. They excluded patients who lost their transplants in the first three months. The results were analysed descriptively. de Geest et al. (1995) performed a descriptive cross-sectional study from the Catholic University of Leuven, Belgium, on 150 recipients of kidney transplants who were at least 18 years old and one year after transplant. All but two patients were recruited and they were subjected to interviews and psychometric tests. These authors used a variety of statistical analyses, which included Wilcoxon rank sum test and Student's t test for independent variables. Logistic regression analysis was applied to determine which variables or combinations of variables best predicted whether a patient belonged to the compliant or non-compliant group.

The major difficulty faced in reviewing the selected papers was that no two papers presented data or analyses on the same outcomes in exactly the same manner. This made impossible the conduct of a formal meta-analysis. In its' place we have selected, as noted above, a list of potential correlates with non-compliance and have tabulated for each paper whether or not each potential variate was statistically

significantly related to non-compliance. Unfortunately some papers reported only univariate associations, some only multivariate associations and some both. The nature of these associations is indicated in the tabulations.

We identified 26 papers, which report on medical non-compliance after kidney transplantation. To analyse the different factors affecting medical non-compliance after kidney transplantation, we selected the manuscript by Frazier, Davis-Ali and Dahl (1994) as a template against which other studies were analysed. We selected this manuscript empirically as these authors analysed the majority of factors implicated in non-compliance. These factors were age, race, gender, martial status, and income, and employment, number of transplants, emotional and mental issues (anxiety, hostility, depression, distress, stress, chance, pain and coping). Other variables analysed were infection, type of transplant (cadaver or living), time since transplant, US born, education, diabetes, number of rejection episodes, dose of prednisone, tremor, clinic attendance, distance, dialysis compliance and treated rejection episodes. We also took into account the self-care agency score, self-efficacy score and situational operational knowledge.

Patients who were older, married, and male and had a higher income were significantly more compliant with medications in paper by Frazier et al. (1994). The numbers were too small for analysis in paper by Kiley, Lam and Pollak (1993), while in paper by Siegal and Greenstein (1999); younger patients and white-collar employment status were significant factors leading to non-compliance. Didlake et al. (1988) found that Caucasians and older age were associated with greater compliance. In paper by Schweizer et al. (1990), blacks and younger recipients of kidney transplants were more non-compliant, while De Geest et al. (1995) found that single or divorced patients were significantly more non-compliant versus the married.

In manuscript by Frazier et al. (1994), recipients with a history of previous transplant were less compliant and those who had been transplanted a longer time ago were less compliant with follow regimen than were recipients who were more recently transplanted. In manuscript by Siegal and Greenstein (1999), recipients who received a living transplant, had received a transplant long time ago, had no history of diabetes and had a history of infection and were born outside the US were more non-compliant. In manuscript by Raiz et al. (1999), transplant type and other transplant-related characteristics were not important. In manuscripts by Schweizer et al. (1990) and by De Geest et al. (1995), transplant characteristics were also not important. In manuscript by Didlake et al. (1988), no difference was seen in the type of transplant, duration of pre-transplant dialysis, primary or re-transplant but the important differences in the non-compliant group were greater then one rejection episode, prednisone dose, presence of tremor, greater distance from the clinic, dialysis compliance and greater rejection episodes.

Non-compliant patients were associated with greater emotional distress, higher transplant-related stress and the belief that health outcomes were due to chance and the use of avoidant coping strategies. In manuscript by Raiz et al. (1999), non-compliant patients had greater anxiety. In manuscript by De Geest et al. (1995), compliant patients had a higher level of self-care agency, perceived self-efficacy of long-term medication and higher situational-operational knowledge.

The half-life of transplants has increased steadily, cadaver kidney transplants to 9-11 years and 15-17 years for living transplants. This has meant that each centre is following larger numbers of transplants; current restrictions of health care financing do not allow each patient to be seen by a qualified therapist to address psychosocial concerns. Some of these unresolved concerns may lead to non-compliance with

medications. It is estimated that 25% of this cohort of patients may be non-compliant with medications; one-to-one therapy with a qualified therapist would be prohibitively expensive. In this scenario, we suggest that specific groups of patients be given special attention to increase the level of compliance such as younger, female, and unmarried and non-Caucasians. Other specific patients groups who may require special attention are recipients of living transplants and were transplanted longer time ago with a history of previous transplant. In addition, patients displaying emotional problems such as anxiety, hostility, depression, distress, lack of coping and avoidant behaviours may be targeted for special attention by qualified therapists to increase medical compliance.

Another issue that needs to be considered is if addressing emotional problems leads to an increased compliance with medications. Although we have shown that there is an improvement in BDI scores after systematic integrative psychotherapy therapy, it is not known if this will lead to improved compliance with medications. The lack of a standardised instrument for predicting or measuring non-compliance will make it difficult to prove or disprove the latter point. A variety of self-assessment questionnaires have been devised to investigate patient compliance with medications, however, these are useful only after the patient has lost the transplant. In addition to group therapy, we plan to assess the questionnaire devised by de Geest et al. (1995) to profile patient concerns regarding the side effects of medications.

From our study, we concluded that patients who are at a higher risk of non-compliance after kidney transplants were younger, female, unmarried and non-Caucasians. Patients who were recipients of living transplants and were transplanted longer time ago with a history of previous transplant were also at risk of non-compliance. In general, all patients displaying emotional problems such as anxiety,

hostility, depression, distress, lack of coping and avoidant behaviours were also at risk of non-compliance after kidney transplantation.

(ii) Quality of life in relationship to psychosocial well being in recipients of kidney transplants:

Skotzko, Stove, Wright, Kendall and Dew (2001) carried out a survey to determine the views of the transplant community on psychosocial issues. They found that there was overwhelming support for providing psychosocial support both before and after transplant to increase rehabilitation of patients. There was also a broad support for substance abuse treatment programs for recipients of organ transplants; most respondents also acknowledged the impact of psychosocial factors on compliance, QOL and survival. Respondents to this survey also pointed to the need for formal studies of psychosocial intervention on cost and resource utilisation, which will convince health service planners to adequately fund such programs.

Research into psychosocial issues amongst this group of patients has tended to reflect the quantitative tradition of medicine (Baines and Jindal 2000). However, the subtleties of psychosocial intervention and subsequent change in behaviour and emotional states are more difficult to measure. This leaves the transplant team unable to translate medical or psychosocial research findings into practice, or to determine what might be the best intervention for an emotionally distressed patient at a particular point in time. There has also been a concerted effort to utilise these findings in the construction of 'scales' and 'assessments' to identify emotional distress, or predict post-transplant compliance and subsequently exclude such patients from the transplant process. However, such scales and assessments typify patients emotionally at the point of implementation and do not allow for the process of individual change

and intervention. Also, often they do not accommodate the unpredictable manner in which ongoing chronic illness compromises patients socially, politically and economically. Despite these shortcomings, there is a clear need to devise an instrument to capture psychological issues at a particular time point and to identify groups of patients who need early intervention. There are specific instruments, which can be used to identify groups of patients who need early intervention such as the BDI, the SCL-90-R or the BSI.

(iii) Strategies to enhance QOL after kidney transplantation:

(a) Patient empowerment: There is an increasing trend to involve patients directly in treatment planning which in turn may lead to increased compliance. However, there has been little legislative support for this position. Empowerment does not come about by some miraculous process of osmosis, but through the acquisition of communicative and behavioural competence on the part of both the staff and the patient. Skills, which may well, be lacking amongst patients from lower socio-economic groups who might be easily overwhelmed by the professional classes and/or whose confidence and self-esteem have been eroded by chronic illness. These patients will need to be presented with empowerment as a multi-component educational package that may utilise modelling, coaching, feedback and homework assignments, all conducted within a supportive and developmental framework. Patient empowerment is an approach to health care that advocates for the active involvement of patients in their treatment. This involves educating patients about their care options, the decision making process, treatment goals, and administering and controlling care input, with the aim of achieving optimal outcomes in terms of

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treatment and patient satisfaction (Brennan and Saffran, 2003). Research conducted by Roberts (1998) at North-Eastern University, Boston, studied the active promotion of patient empowerment through 'liberating education' and referred to patients as being 'oppressed' as a result of 'medical domination'. Recognition of these issues is all very helpful but it is difficult to put into practice. To date the implementation of patient empowerment has taken a number of formats. These may be combining treatment goals with treatment options (McHale and Seidman 2002), patients participating in their own assessment (Mitcheson and Cowley 2003), giving patients an active role in the treatment (Salmon and Hall 2003), educational programmes (Roberts 1998) and through the empowerment of nursing staff (Kuokkanen and Katajisto 2003).

McHale and Seidman (2002) combined treatment goals with treatment options in metastatic breast cancer. They found that through acknowledging and incorporating patient-led treatment goals into their therapeutic program, patients were more likely to comply with treatment. Mitcheson and Cowley (2003) in their study of the relationship between health visitors and their patients developed this concept a stage further by involving patients in the assessment stage of their health needs and subsequent health visitor intervention. However, their findings suggested that while health visitors were well motivated towards patient empowerment, they were hampered by the nature of the assessment tool that assumed that a families health needs could be predicted in advance as opposed to being responsive to patient's changing needs.

Empowerment has also become an issue amongst the nursing profession and linked to job satisfaction, further training and commitment. In particular, empowerment has been seen as an essential pre-requisite for leadership and the

profession of collegial support (Kuokkanen and Katajisto 2003). Patient empowerment has developed alongside medical accountability in the form of 'informed consent', or the need for doctors to obtain patient's consent before medical procedures and to inform patients of any risks. This has developed partly as a response to judicial edits and partly as a result of the recognition of the need to be pro-active in obtaining consent and informing patients of the treatment process. Luderitz and Wolpert (2003) developed informed consent guidelines for patients undergoing implantation of pacemakers. They pointed to the need for comprehensiveness in terms how consent is delivered, in simple easily understood language, the form of delivery, written as opposed to verbal, and detail of complication rates and post-treatment QOL. In a study amongst dermatology patients who were exposed to informed consent procedures, Fleischman and Garcia (2003) found that less than a mere 26.5% of patients recalled being informed of ten possible complications twenty minutes after being informed. Therefore, patient empowerment has to be incorporated as part of the philosophy of an entire hospital as well as individual services within the hospital.

Baines, Joseph and Jindal (2002a) retrospectively analysed the case records of patients who had their first cadaver renal transplantation at our centre during a six-year period from January 1991 to December 1996. We identified 26 patients who had late acute rejection (LAR). The Medication Behaviour self-efficacy Scale is a 27-item instrument depicting a variety of situations in which the patient might be required to take their medication. The self-efficacy score was calculated by summing the scores of all items divided by 27. Thus the self-efficacy scores range between 1 and 3; higher score indicates greater self-efficacy. We modified the original scale to a 3-point questionnaire as our pilot study showed that patients found it difficult to discriminate

between 5 options. The LTMBS-scale was initially used to determine self-efficacy and non-compliance with immunosuppressive medication in a group of 150 renal transplant recipients (De Geest et al.1995). The study hypothesized that there might be a relationship between low rates of self-efficacy, knowledge of medication regime, non-compliance and subsequent graft loss. Non-compliance with medication was calculated at 22% with perceived lower scores of self-efficacy associated with items 8, 9 and 14 relating to physical (sexual impotence, brittle bones, facial spots and excessive hair growth) side effects of immunosuppressive medications.

The LTMBS-scale has also been utilised in conjunction with electronic tagging in a longitudinal study of 101 heart transplant recipients to evaluate sub-clinical non-compliance with CyA over a three-month period. Patients were at an average of three years after a kidney transplant (De Geest et al.1998). The findings of this study suggested that overall compliance was high, with a median medication compliance of 99.4%. However, on a micro level, they identified three clusters of patients as follows: excellent compliers (84%), minor sub-clinical non-compliers (7%) and moderate sub-clinical non-compliers (9%) and showed a 1.19%, 14.28% and 22.22% incidence of LAR respectively in these three groups of patients. There was a clear association between higher degree of non-compliance and LAR. A larger multi-centre study is in progress to validate the LTMBS-scale as a predictive measurement is indicated. We have recently initiated such a study in the US.

Our study is a variation on the above-mentioned studies, in that it was conducted retrospectively amongst patients who had already undergone LAR after successful cadaver kidney transplantation. This is in direct contrast to the prospective studies described above and thereby contributes to the validity of the LTBMS-scale. Further, our findings were utilised not only as a means to identify non-compliance,

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but also as a preface to supportive psychotherapeutic intervention amongst no compliers. It was hoped that such intervention might serve to prevent graft loss or as a means to detect and address non-compliance before receiving a further transplant should these patients loose their transplant.

Acute rejection after renal transplantation results in reduced graft survival and it is known that LAR is even more detrimental to graft survival. In our own study (Joseph et al. 2001), we determined the impact of LAR by analysing 687 consecutive adult renal transplant recipients. All received CyA-based immunosuppression, from 1984-1996, with a median follow-up of 6.9 years. Details were abstracted from clinical records, with emphasis on age, sex, co-morbid conditions, HLA matching, rejection episodes and patient and graft survival. Patients were classified by the presence and time to AR from the date of transplantation. Using those patients who had no AR episodes (NAR) as a baseline, we determined the relative risk of graft failure by time to rejection. The characteristics of patients who had no rejection, EAR and LAR were compared. Compared to NAR, the risk of graft failure was higher for those patients who suffered a rejection episode. A much higher risk of graft failure was seen when the first rejection episode occurred after 90 days. Thus a period of 90 days was taken to separate EAR and LAR (relative risk of 3.06 and 5.27 compared to NAR as baseline, p<0.001). Seventy-eight patients (11.4%) had LAR, 271 (39.4%) had EAR and 338 (49.2%) had NAR. The mean age for each of these groups differed (LAR 39.6 years, EAR 40.8 years compared to NAR 44 years, p<0.003). The 5-year graft survival for those who had LAR was 45% and 10-year survival was 28%. HLA mismatches were more frequent in those with EAR versus NAR (zero mismatches in A: 36% vs. 24%, B: 35% vs. 23% and DR: 63% vs. 41%, p<0.003). There was no difference in mismatching frequency between NAR and LAR. AR had a deleterious

impact on graft survival, particularly if occurring after 90 days. AR episodes should therefore be divided into early and late phases. In view of the very poor graft survival associated with LAR, it is important to gain further insight in to the main etiological factors. Those such as sub-optimal CyA blood levels and non-compliance with medication should be further investigated with the aim of developing more effective immunosuppressive regimens in order to reduce the incidence of LAR.

LTMBS questionnaire was mailed to 24 patients (14 women and 10 men), with an explanatory letter; patients were requested to complete the questionnaire anonymously (Baines, Joseph and Jindal 2002a). After two weeks, we telephoned each patient to inquire whether he or she had completed the questionnaire. If the response was negative, she encouraged patients to complete and return the questionnaire. Summing up all the responses and dividing by 27 computed confidence of each patient. The values range from 1 (least confident) to 3 (most confident). When a comparison of clinical data was needed, t-test was used. Statistical significance was assumed at a p value of 0.05. The mean values are expressed as mean +/- standard deviation. For statistical analysis and construction of the graph, a software package (SPSS 9, SPSS inc. Chicago) was used. Our results showed a definitive correlation between LAR, and individual patient's perceived low rate of self-efficacy across a variety of contextual or environmental situations. It was seen that patients were only reasonably confident (mean score 2.17) in taking their medication in the above-mentioned contexts. All patients demonstrated significantly lower self-efficacy in relationship to items 14, 20 and 21 (mean score 1.0), the items relating to physical and psychological symptoms (brittle bones and generally feeling 'very ill') and psychological symptoms (feeling 'sad') that affected their well-being. These

symptoms were considered to be side effects of either the medications or a response to the experience of chronic illness.

The majority of patients (10 women, 5 men) returned their completed questionnaires before the two-week telephone reminder. However, the seven questionnaires (4 women, 3 men) that were returned after the telephone reminder demonstrated an even lower self-efficacy score (mean score 1.2). The second group of patients demonstrated the same trends as with the first group of patient (who returned their questionnaire without prompting).

Potential drawbacks of this study is the reliance of the LTMBS-scale on patient self-report and the absence of controls, as means to rule out the influence of the above-mentioned environmental, or situational variables and increase internal and construct validity. However, it was our intention to develop this tool as a means of identifying the presence, as opposed to the degree of, non-compliance amongst patients who might benefit from supportive psychotherapeutic intervention. Therefore, the disadvantages of self-report (potential for distortion in the patients favour) and the use of the control group (as a baseline for intervention) in the traditional sense might be of little use. This is particularly valid in the present climate as heightened patient awareness and independent help seeking behaviour is making it increasingly difficult to maintain a sterile control group in both the medical and social sciences. In developing this work further, we propose to extend supportive psychotherapeutic intervention to vulnerable patients. This strategy will enable us to address inconsistent answers or contradictory responses in completing the questionnaire. Responses to the questionnaire could be further analysed and modified by cognitive behavioural therapy.

(b) Formal counselling: A common means to address depression and anxiety in this group of patients is to implement counselling and psychotherapy programs. The renal and transplant centre at the University of Toronto, Canada, has successfully implemented a comprehensive counselling and psychotherapy program aimed at facilitating the adjustment of organ (liver, kidney, heart and lung) transplant patients, while supporting them through psychosocial and psychiatric support. To support, patients on dialysis and awaiting kidney transplants the 'While you are waiting' psycho-educational group was formed which comprised of a support and educational program. Group discussions involved living with a life threatening illness, preparing to live versus preparing to die, and preparing for transplantation (Abbey and Farrow 1998). This program was aimed at relatively emotionally stable patients placing emphasis upon education and support as opposed to systematic psychological intervention.

(c) Effect of psychotherapy on emotional states after kidney transplantation: We designed a prospective study using psychotherapeutic principles to understand and intervene in emotional issues in adult recipients of first cadaver kidney transplants. Forty-nine recipients of first cadaver kidney transplants were subjected to 12 sessions (at weekly intervals) of psychotherapy within three months of receiving their transplant. The BDI was utilised as a measure of change in emotional state, pre-therapy, at 3, 6, 9 and 12 months. We used the BDI to study the efficacy of our trial by an objective method (Baines, Joseph and Jindal 2002b).

Of the many instruments available, we choose the BDI; we were however, concerned that this instrument might be considered overly simplistic. We found that references to BDI during treatment sessions were much more positive as patients

appeared to find regular completion of the questionnaire therapeutic in terms of contemplating the cause behind any regression, stagnation, or progress and helping them to focus on specific problems and solutions and encouraging.

A higher score on BDI was suggestive of psychological dysfunction. In the first instance, data was analysed within a quantitative framework, by virtue of the BDI. In the second instance, data was considered in terms of recurring themes described by patients during psychotherapy and was analysed qualitatively. In the third instance, both qualitative and qualitative data was considered in terms of individual patient's ability to achieve some feeling of having implemented some social, relational and vocational equilibrium into their everyday life. Recipients of live kidneys, paediatric transplants and patients who received more than one transplant were excluded, as emotional issues are different in this cohort of patients. All patients have completed one year of follow up. There was significant improvement in the BDI scores following therapy. The mean score was 26.3 ± 7.9 before and 20.5 ± 8.8 after therapy ($p=0.001$); lowering of scores remained sustained at 12 months. Multivariate analysis of age, gender, employment status, duration of dialysis and psychotherapy given before transplantation did not affect the results of our study. Successful resolution of these issues was associated with lower BDI scores and the re-definition of normality in daily living after the transplant.

(d): Group versus individual psychotherapy: In general, group psychotherapy is more cost effective than individual therapy. In this study, we have prospectively, in a randomised trial, compared the efficacy of group versus individual psychotherapy in recipients of first cadaver kidney transplants versus age and gender matched control patients who did not receive therapy. Both individual and group psychotherapy aim to

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benefit the patient emotionally, socially and relationally to promote the understanding of them. The therapist aims to facilitate personal growth through interpretation, intervention and reflection in response to the stories, thoughts, hopes, and ambitions, fears that patients bring to sessions. In both contexts, a satisfactory psychotherapeutic alliance is an essential pre-requisite to effective outcome. In addition, in a group situation, they will be expected to interact with other group members.

In the group situation, as opposed to individual psychotherapy, the therapist needs to pay attention to both individual and group interaction. It is through group and individual interaction that themes emerge which in turn facilitate progress of the group. However, too much or indeed too little intervention on part of the therapist can hinder or totally suppress progress of the group. During individual therapy, therapist will be concerned to contrast, invite comparison, or match stories and recollections in keeping with the patient's past or present experiences and hopes for the future. In the group situation, therapist might use one patient's experience to encourage other group members to contribute similar happenings or as an opportunity to compare or contrast experiences between group members. Similarly, if members ignore, deviate, act in a dismissive manner, fail to give proper consideration or avoid particular themes, therapist will need to decide whether to draw this to the group's attention immediately, in the future, or not at all (Abbey and Farrow 1998).

In our study, groups were member-led, while the therapist remained 'with' the group aiming to identify, understand, refine and develop, individual experiences and build group themes. Group members were encouraged to raise whatever issues they wished. In turn, we aimed to be responsive, interactive and emotionally supportive to facilitate individual and group goals. Primary problems associated with ongoing chronic illness such as low self-esteem, uncertainty regarding future, lost of time to

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chronic illness and re-defining normality were incorporated into the goals of the group. It soon became apparent that individual attempts to define normality in terms of the pre-morbid past meant that they had difficulty constructing a daily routine. Through sharing of common experiences we hoped to address interpersonal issues, which might be obstructing the formation of a more satisfying existence.

Recipients of first cadaver renal transplants within three months of surgery were randomised (using computer generated numbers to ensure even gender and age distribution) into two groups, to receive a 12-week course of group or individual psychotherapy. BDI was utilised as a measure of change in emotional state, pre-therapy, at 3, 6, 9 and 12 months. A higher score on BDI was suggestive of psychological dysfunction. Patients were treated using the same therapist and theoretical model (Systemic Integrative Psychotherapy) in both the groups. Study was based on the need for at least 80% statistical power to determine differences between success rates. Thirty-seven patients served as control group, however, it should be noted that these patients were recruited consequently after the first two groups were recruited for logistic reasons, to enable us to obtain adequate numbers for group arm. The study was done on the basis of an intention to treat principle. The data are expressed as mean ± standard deviation. The comparisons of the means of the scores at various time periods between the individual and group therapy groups were made by the use of Mann-Whitney U test and one-way ANOVA test as appropriate. The significance of the impact of therapy within each treatment arm was assessed by Wilcoxon rank sum test. The individual parameters were assessed for their effect on the final result with the help of multivariate analysis. All the significance was calculated as two tailed and was measured at a level of ≤ 0.05. A statistical software package was used for the computations (SPSS 9, SPSS Inc., Chicago).

Eighty-nine patients who had a cadaver kidney transplant were recruited in to the study. They were randomly allocated in to the two study groups, 49 for individual and 40 for group therapy. Of these, 82 patients completed 12 weeks of therapy (45 patients from the individual arm and 37 from the group therapy arm). Fifty-five patients have so far completed one-year follow-up (33 in individual and 32 in the group therapy); the rest did not complete one year as they moved away or did not return their questionnaires. Thirty-seven age and sex-matched patients were recruited as controls; two dropped out of the study at three months and four at six months respectively. A higher percentage of patients who had been on more than three years of dialysis were allocated for group therapy; otherwise, there was no significant difference between the characteristics of the study groups in the two arms. Our population in the West of Scotland is approximately 98% Caucasians; therefore all the patients in our study happened to be Caucasians. All patients had received their first cadaver transplant, as psychological issues with a second or third transplant are different than those receiving their first transplant. We also excluded paediatric recipients and those receiving living kidney transplants as emotional issues and graft outcomes are different to patients receiving a cadaver kidney.

In both the treatment groups, there was significant improvement in the scores following therapy. The mean score was 26.3 ± 7.9 before and 20.5 ± 8.8 after therapy in the individual group (p=0.001). This was in comparison with a mean score of 29.8 ± 3.9 before and 27.1 ± 3.9 after therapy for the group arm of the study (p=0.01). Improvement was more significant in the individual therapy arm compared to group arm (p= 0.01). Lowering of scores remained sustained in both therapy arms. In the control arm, mean score was 9.4 ± 5.4 before and 20.5 ± 5.5 at the end of first year (p=0.005) suggesting significant worsening of BDI scores. Multivariate analysis of

age of the population, gender, employment status, duration of dialysis (if in dialysis for more than three years) and psychotherapy given before transplantation did not affect the results.

The BDI has generally been considered as crude measurement that does not do justice to the idiosyncrasies of treatment or of the patient. However, we wanted to produce objective data, which could encourage other centers to embark on similar projects using the BDI or other instruments, or even devise a specific instrument for this purpose. Our study clearly shows that psychotherapy was effective in lowering BDI score; this presumably will lead to improved QOL and adherence to medications. The fact that patients in the control group started with a lower BDI score is an interesting finding; it is known that patients not expecting to receive therapy will not think too deeply into psychological issues that affect their lives.

Methodology using patient self-report has also been criticised as liable to exaggeration and underplaying of problems in an attempt to please the therapist. A scenario commonly referred to as the *'hello-goodbye'* effect or socially desirable responding. We concluded that both individual and group psychotherapy were beneficial to recipients of first cadaver kidney transplants, however, individual therapy was found to result in lower BDI scores versus group therapy; while patients in the control group had significant worsening of scores.

(e) Reconciling bereavement and loss of the imagined past: Loss has been used interchangeably with bereavement and grief and is generally associated with death or feelings of total desolation. These concepts have generally been considered within a recognized time frame of social withdrawal and resolution (Kubler-Ross 1978; Arieti and Bemporad 1978; Parkes 1996). Kubler-Ross (1978) interviewed over two

hundred patients with terminal illness during her work on bereavement. She divided

bereavement into a five stage recognized time frame as follows: denial and isolation,

anger, bargaining, depression and finally acceptance. Arieti and Bemporad (1978)

referred to bereavement and grief as a form of 'unbearable sadness' in response to the

death of another person. They viewed bereavement as a series of 'sad reactions', which

involved 'searching' and 'impressioning' of the person that had been lost. The length of

the bereavement process was thought to vary with each individual, but resolution was

considered in keeping with adjustment or acceptance that the person was dead. Parkes

(1996) studied the bereavement process of sixty-six widows. Arieti and Bemporad

(1978) described the notion of 'searching' for the dead person as a direct response to

the death of their husbands. The gradual realisation of the futility of the search was

equated with detachment from the dead person and the resolution of grief.

Amongst kidney transplant patient's loss, grief and bereavement have been

associated with graft rejection (Streltzer, Moe, Yanagida and Siemsen 1983; Alleman

et al. 1994), the death of relatives (Alleman et al. 1994), the death of fellow patients

(Vamos 1997), the fear of death amongst renal transplant patients (Eisendrath 1969),

and the death of the unknown donor (Kemph 1967). Graft rejection and the resolution

of grief and rejection of a kidney have been considered in terms of facilitating the

grieving process to resolution, measured in terms of re-adjustment to dialysis

(Streltzer et al. 1983-1984). The death of relatives from kidney failure has prompted

the use of unit-based support groups to treat bereaved families after transplant

(Alleman et al. 1994). The impact of death of a fellow patient within a treatment unit

has been described by some studies in keeping with pathological grief reactions. The

findings have considered grief in relationship to psychosomatic symptoms, which in

turn were thought to be complicated by the existence of 'survivor guilt' (Vamos 1997).

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The fear of death amongst renal patients as a result of post-operative complications has been equated with fear, anxiety, depression, and deterioration in the quality of inter-personal relationships (Eisendrath 1969). Donor family support programs have gained momentum in recent years and have not only offered support to families upon the death of their relatives (Kemph 1967; Alexander and Sehgal 1998), but also helped relieve the burden of survivor guilt upon recipients.

We propose that grief and bereavement in the post-transplant period needs to be considered within a wider context of an *imagined past* and as an entity independent of the other causes of bereavement and grief. Loss of the *imagined past* refers to a past (complied of experiences, sensations and achievements) that patients consider that they might have had, if they had not developed renal failure. Loss in this context (post-transplant) is generated as individuals contemplate fantasies, aspirations and ambitions that were never realised. Clinically, this is expressed during psychotherapy as feelings of low self-esteem, indifference to peers, a life without purpose and hesitancy regarding the future. Unlike feeling of bereavement and grief, loss is not systematically resolved within a time frame and does not necessarily result in social withdrawal. However, in common with bereavement and grief, feelings of loss amongst post-transplant patients are in keeping with a change in identity and social status. A change of identity and social status serve to generate expectation with regards an improved quality of life amongst patients and their families. In turn, the pressure of expectation can serve to generate stress and anxiety, particularly when a kidney transplant was viewed by the family as a panacea for any negative or ambivalent emotional states evoked during dialysis. Our observations are that such clinical presentation may be best explored and resolved within a time sensitive

framework such as Systemic Integrative Psychotherapy (Clarkson and Lapworth 1996).

During psychotherapy sessions, patients on dialysis often perceive life as being medically, socially (relationships with family and friends), economically (curtailed employment and subsequent debt) unpredictable, unstable and centred upon survival and preservation of their family and self. Given these circumstances, patients may develop symptomatic psychopathology such as depression, stress and anxiety (Marrone 1998; Harris and Bifulco 1991). While pre-existing family relationships may be of help to patients in resolving their difficulties, prolonged dialysis can put relationships under enormous strain and affect their ability to provide ongoing support for the duration of dialysis. The tradition of psychotherapy provides a significant, supportive, unconditional attachment figure, within a responsive and secure environment. Within this relationship, post-transplant patients can explore and recover from emotional problems such as loss. As mentioned above, dialysis patients demonstrate an acute sensitivity to time. That is, time lost to dialysis and time that comprises their future. More specifically, Systemic Integrative Psychotherapy is based upon the psychotherapist's need to identify patient's experiences over a past, present and future time-span. Our findings suggest that this segmentation of time during psychotherapy sessions helps patients comprehend their feelings of *paradoxical loss* after kidney transplantation. Further, such philosophy lends itself well to the reconciliation of disappointments and fantasies that comprise the *imagined past*, sustenance of patients in the *present* and provides a baseline for future development.

Our observations amongst kidney transplant patients suggest that while grief and bereavement may be recalled amongst all three of the above-mentioned time-spans, it

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is most prominent in the patients (fantasy) *imagined past*. Therefore, patients become hesitant and pessimistic regarding the future and they consider that any future that they might have, will be conducted within an arena in which they are materialistically, socially and economically disadvantaged, despite their kidney transplant. In summary, the *imagined past* is an entity that was never actualised; the present struggles to be meaningful and needs to be re-defined; while the future can only be actualised in the face of seemingly insurmountable odds. This scenario manifests in the daily lives of patients as social disintegration, isolation and subsequent feelings of grief and bereavement.

We have proposed a new concept of loss of *imagined past*; this condition if unresolved can lead to medical non-compliance and social isolation. This condition must be differentiated from grief and bereavement that the patient may feel for the donor and donor-family. In addition, this condition should not be confused with the ongoing fear of graft rejection, graft loss, fear of death and side effects of drugs. In working with transplant patients whose gift of life is somewhat paradoxical, we need to identify the meaning and experience of loss of an *imagined past* for individual patients, before it can be resolved.

CONCLUSIONS

This thesis considers the concept of QOL within the context of patients on renal dialysis and kidney transplantation. We suggest that QOL measurement tools can be utilised to determine whether there is a relationship between QOL, medical non-compliance and emotional states amongst this patient group. The research is developed within a psycho-medical framework using Systemic Integrative Psychotherapy. This facilitates the analysis and quantification of results favoured by the medical profession while exploring the subtle nuances and emotional states recalled by patients during the transplant process. The findings suggested that there is a relationship between QOL, medical compliance and emotional states amongst transplant patients. It is also suggested that emotional states are much more complex than originally thought; psychotherapy can effectively treat these states and subsequently improve QOL. To improve compliance and emotional states and hence QOL after kidney transplantation, we have suggested a number of strategies based on our research. These are patient empowerment, by asking them to fill up a specific instrument (LTMBS), group or individual psychotherapy and helping them to come to terms with their *imagined past*.

We propose that all recipients of organ transplants should be routinely assessed for QOL by SF-36 or a disease-specific instrument, compliance by the LTMBS-scale and psychological status by the BDI, BSI or the SCL-90-R. Adequate funding should be provided for the additional expense in implementing a program of assessment and intervention in appropriate cases. Over time, we may be able to construct a universal instrument, which will capture these three components. The merits of one instrument over the others will have to validated and accepted by the transplant community.

The debate on the ideal instrument and whether if should be generic or disease-specific continues. The Medical Outcomes Trust Boston, (www.outcomes-trust.org) is a not for profit organisation dedicated to improving health and health care by promoting the science of outcomes measurement, and the development, evaluation and distribution of standardised, high quality instruments that measure health and the outcomes of medical care. I am hopeful that efforts by organizations such as the Medical Outcomes Trust, and the medical, sociology, psychology and behavioural communities will result in a universally accepted QOL instrument. However, we must bear in mind that measuring QOL will remain subjective and the development of objective QOL instrument will be difficult; deriving an overall QOL score based on different domains may be even more problematic.

The results of the questionnaires should be made available to the clinician before consultation and additional time provided to discuss issues raised by the patient. A recent study incorporating these instruments into outpatient consultation for patients undergoing palliative chemotherapy was found to be useful to facilitate discussion of QOL issues for both patients and their physicians (Detmar, Muller, Schornagel and Wever 2002). We believe there is a pressing need for a 'Consensus Conference' on QOL issues after organ transplantation. We hope to sensitise transplant physicians to the many factors that can influence the 'goodness of life', a person's happiness and the ability to function independently and to enjoy life (Parmet 2002).

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ABSTRACT

We performed a systematic review of the literature on medical noncompliance after kidney transplantation in the cyclosporine era. We wished to define commonalities that may help the clinician identify patients for early intervention. We found that patients who were at a higher risk of noncompliance after kidney transplants were younger, female, unmarried and non-Caucasians. Patients who were recipients of living transplants and were transplanted longer time ago with a history of previous transplant were also at risk of noncompliance. We also found that patients displaying emotional problems such as anxiety, hostility, depression, distress, lack of coping and avoidant behaviors were also at risk of noncompliance after kidney transplantation.

INTRODUCTION

Compliance with medications after organ transplantation is emerging as a major health care issue with implications for chronic rejection and graft loss. Patients who loose their grafts due to noncompliance may be denied a second transplant, an area of considerable controversy and debate. Furthermore, health care financing is assuming a central role in our society. Patients who lose their transplants due to noncompliance will result in a significant drain on finances as these patients are placed back on dialysis, a modality of treatment more expensive than a functioning transplant (1-3).

Medical noncompliance is also important as it is estimated that over 25% of patients who enter into clinical trials of immunosuppressive drugs may be noncompliant and hence influence the results of these studies negatively. Noncompliance will also negatively affect a patient's quality of life after transplantation and ultimately have detrimental results on society itself. Patients who are on dialysis may also suffer from a lack of full employment versus those patients with a functioning transplant. Patients with a functioning transplant also have a significantly longer life span versus patients who are on chronic dialysis (4-8).

A number of authors have studied various factors, which affect medical compliance after kidney transplantation. These include demographics, social and educational status, mental and behavioral patterns, pre- and posttransplant symptoms and beliefs, and the characteristics of the transplanted organ. A variety of validated instruments have been described to assess and in some cases predict medical noncompliance after a kidney transplant. These methods include pill counts, clinic attendance, drug levels and self-administered questionnaires. Each of these methods has pitfalls and may not be equally applicable to all patients. A gold standard of assessing patients at risk of noncompliance has not yet been validated.

Research to date concerning predictors and levels of medical noncompliance have been

difficult to interpret and the outcomes of center-specific studies may not be easy to apply in clinical practice. We have applied meta-analytic techniques to the literature on medical noncompliance after kidney transplantation to enable a consensus to be reached in this important area. The aim of this study was to identify patients at risk for noncompliance after kidney transplant. Further work is required to identify the best instrument to identify patients at risk of medical noncompliance after a kidney transplant.

Our study is limited to patients receiving kidney transplants as this group forms the largest cohort of patients receiving a solid organ transplant.

METHODS

Searching: Two authors searched independently using the Medline followed by hand searching. The most recent search was done in June of 2001. The search included the terms: compliance, non-compliance, medical compliance and kidney transplants, transplantation, organ transplantation and medical compliance/non-compliance. Additional reports were identified from the reference lists of key manuscripts and review articles. For the analysis of data, only peer-reviewed articles in English language journals were considered. Only manuscripts in the cyclosporine (CyA) era and involving adult recipients of kidney transplants were included (1-26).

Data extraction: This was done by two authors and checked for accuracy by a third author. Tables of the collected data were prepared for analysis.

Validity assessment: None of the papers reported a randomized trial, the majority of the studies were of a descriptive nature. The selected papers were prospective in which questionnaires were given to recipients who already had functioning kidney transplants.

Manuscripts selected for analysis: Frazier et al. (1) sent detailed questionnaires to 500 recipients of renal transplants at the University of Minnesota of which 49% were returned. They used a variety of standardized instruments such as the Beck Depression Inventory (BDI), Brief Symptom Inventory (BSI), Inventory of Social Supportive Behaviors (ISSB) and Multidimensional Health Locus of Control (MHLC). They analyzed their data using multiple regression. Siegal and Greenstein (3) prospectively sent questionnaires to 2500 patients in US transplant centers of which 1402 returned, of which 22.4% reported some level of

noncompliance with their medications after renal transplant. These patients were over 18 years of age and were on CyA therapy and had a functioning transplant. In their study, noncompliance was scaled from 1 (never forgot) to 8 (forget every day). For each variable, they calculated the frequency, means, percentages and standard deviations and then logistic regression analyses were used to identify predictors of noncompliance. Cluster analysis was used to identify groups of noncompliant patients based on similarities with respect to variables identified by logistic regression.

Raiz et al. (4) conducted a postal survey of 712 patients from the Ohio State University Medical Center who were 18 years old and had a primary renal transplant for at least 12 months. They used the Dillman's method for mailed surveys with analysis by multiple regression. Usable data was obtained from 50% of the patients. Didlake et al. (5) from the University of Texas Medical School at Houston, USA, performed a mail survey of 295 patients who had received a kidney transplant between 1980 and 1986 and were compared with 70 patients who had a functioning transplant for at least 18 months. They defined noncompliance when the patients presented with rejection episodes and were interviewed by 2 members of the transplant team and the blood levels of CyA were sub-therapeutic. They analyzed the mean values of population parameters using t-tests.

Schweizer et al. (6) performed a combination of retrospective and prospective analysis of patients receiving kidney, liver and heart transplants at the Hartford Transplant Center, Hartford, CT, USA. Their study was divided into retrospective chart review of 260 patients between 1971 and 1984 and a prospective study of 196 patients between 1984 and 1987. They excluded patients who lost their transplants in the first 3 months. The results were analyzed descriptively. de Geest et al. (7) performed a descriptive cross-sectional study from the Catholic University of Leuven, Belgium, on 150 recipients of kidney transplants who were at least 18 years old and one

year after transplant. All but 2 patients were recruited and they were subjected to interviews and psychometric tests. These authors used a variety of statistical analyses, which included Wilcoxon rank sum test and Student's t test for independent variables. Logistic regression analysis was applied to determine which variables or combinations of variables best predicted whether a patient belonged to the compliant or noncompliant group.

Statistical issues: The major difficulty faced in reviewing the selected papers was that no two manuscripts, presented data or analyses on the same outcomes in exactly the same manner. This made impossible the conduct of a formal meta-analysis. In its place we have selected, as noted above, a list of potential correlates with noncompliance and have tabulated for each manuscript whether or not each potential variate was statistically significantly related to noncompliance. Unfortunately some manuscripts reported only univariate associations, some only multivariate associations and some both. The nature of these associations is indicated in the tabulations.

RESULTS

We identified 26 manuscripts, which report on medical non-compliance after kidney transplantation. Manuscripts 1-7 were considered to be suitable for inclusion in a review. To analyze the different factors affecting medical noncompliance after kidney transplantation, we selected the manuscript by Frazier et al. (1) as a template against which other studies were analyzed. These factors were age, race, gender, martial status, income, employment, number of transplants, emotional and mental issues (anxiety, hostility, depression, distress, stress, chance, pain and coping). Other variables analyzed were infection, type of transplant (cadaver or living), time since transplant, US born, education, diabetes, number of rejection episodes, dose of prednisone, tremor, clinic attendance, distance, dialysis compliance and treated rejection episodes. We also took into account the self-care agency score, self-efficacy score and situational operational knowledge. The results of the analysis are given in the table.

Demographics: Patients who were older, married, male and had a higher income were significantly more compliance with posttransplant medications in paper 1. The numbers were too small for analysis in paper 2, while in paper 3; younger patients and white-collar employment status were significant factors leading to noncompliance. In paper 4, Caucasians were more compliant while in paper 5; race (Caucasians) and older age were associated with greater compliance. In paper 6, blacks and younger recipients of kidney transplants were more noncompliant. In paper 7, single or divorced patients were significantly more noncompliant versus the married.

Transplant characteristics: In manuscript 1, recipients with a history of previous transplant were less compliant and those who had been transplanted a longer time ago were less compliant with

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follow regimen than were recipients who were more recently transplanted. In manuscript 3, recipients who received a living transplant, had received a transplant long time ago, had no history of diabetes and had a history of infection and were born outside the US were more noncompliant. In manuscript 4, transplant type and other transplant related characteristics were not important. In manuscripts 6 and 7, transplant characteristics were also not important. In manuscript 5, no difference was seen in the type of transplant, duration of pre-transplant dialysis, primary or re-transplant but the important differences in the noncompliant group were greater then one rejection episode, prednisone dose, presence of tremor, greater distance from the clinic, dialysis compliance and greater rejection episodes.

Psychosocial variables: Noncompliant patients were associated with greater emotional distress, higher transplant-related stress and the belief that health outcomes were due to chance and the use of avoidant coping strategies. In manuscript 4, noncompliant patients had greater anxiety. In manuscript 7, compliant patients had a higher level of self-care agency, perceived self-efficacy of long-term medication and higher situational-operational knowledge.

DISCUSSION

The half-life of transplants has increased steadily, cadaver kidney transplants to 9-11 years and 15-17 years for living transplants. This has meant that each center is following larger numbers of transplants; current restrictions of health care financing does not allow each patient to be seen by a qualified therapist to address psychosocial concerns. Some of these unresolved concerns may lead to noncompliance with medications. It is estimated that 25% of this cohort of patients may be noncompliant with medications; one-to-one therapy with a qualified therapist would be prohibitively expensive. In this scenario, we suggest that specific groups of patients be given special attention to increase the level of compliance such as younger, female, unmarried and non-Caucasians. Other specific patients groups who may require special attention are recipients of living transplants and were transplanted longer time ago with a history of previous transplant. In addition, patients displaying emotional problems such as anxiety, hostility, depression, distress, lack of coping and avoidant behaviors may be targeted for special attention by qualified therapists to increase medical compliance.

Another approach to comprehending, and impacting upon compliance behaviors is through the provision of psychotherapy services for renal patients. Our results show that there was a significant improvement in BDI scores in patients who attended both group and individual psychotherapy. However, individual psychotherapy is emerging as the most effective intervention, particularly amongst patients who have been dialyzing for 3 years or more (27). Even a successful implementation of group therapy program is difficult logistically in all recipients of organ transplants. Perhaps, all patients may be included for a fixed period of time, (perhaps 6 months) in group therapy. Further therapy may be limited to patients who are at high risk of being noncompliant.

There are a large number of psychometric tests available for patients who are on long-

term medications, such as recipients of kidney transplants. Authors have described the use of the BDI, BSI, ISSB and MHLC to evaluate recipients of kidney transplants for assessment of emotional problems, which may perhaps lead to medical noncompliance after kidney transplants. These standardized instruments have been validated successfully in many psychological disorders. However, their use in recipients of kidney transplantation are few and it is difficult to recommend one test over others. Certainly, it is not possible to apply multiple instruments to all recipients of kidney transplants, except as part of a research protocol. Based on our current study and review of the literature, we are unable to recommend a single instrument, which may be applicable universally to recipients of kidney transplants. We have used the BDI to evaluate patients before and after therapy and found it to be useful in follow up (27). However, other instruments may be equally valid forms of assessment. Indeed, such instruments are limited in that they commonly measure emotional state at a given point in time, in other words, at the point of administration. Furthermore, their ability to predict compliance is questionable and does not further our understanding of noncompliant behaviors. Further research needs to be done in this area.

It is not proven that a successful implementation of psychotherapy will definitely lead to increased survival of a kidney transplant. However, the value of many forms of psychological therapies has been proven in numerous psychiatric disorders. It follows as a corollary that recipients of kidney transplants who suffer from emotional problems will benefit by the implementation of psychological services in a transplant unit.

Another issue that needs to be considered is if addressing emotional problems leads to an increased compliance with medications. Although we have shown that there is an improvement in BDI scores after systematic integrative psychotherapy therapy, it is not known if this will lead to improved compliance with medications. The lack of a standardized instrument for predicting

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or measuring noncompliance will make it difficult to prove or disprove the latter point. A variety of self-assessment questionnaires have been devised to investigate patient compliance with medications, however, these are useful only after the patient has lost the transplant. In addition to group therapy, we plan to assess the questionnaire devised by de Geest et al. (7) to profile patient concerns regarding the side effects of medications. We will then be able to improve patients understanding of medications and their potential side effects increasing patient empowerment and hence compliance with medications.

CONCLUSION

From our study, we conclude that patients who are at a higher risk of noncompliance after kidney transplants were younger, female, unmarried and non-Caucasians. Patients who were recipients of living transplants and were transplanted longer time ago with a history of previous transplant were also at risk of noncompliance. In general, all patients displaying emotional problems such as anxiety, hostility, depression, distress, lack of coping and avoidant behaviors were also at risk of noncompliance after kidney transplantation.

Pre-transplant screening should include psychosocial assessment using one or more of the standardized instruments to identify patients at risk of noncompliance after transplant. Although desirable, it is impossible to provide long-term counseling to all recipients of organ transplants. A focussed approach directed towards patients at high risk of noncompliance would be more cost effective. This strategy may decrease the number of kidney transplants lost due to noncompliance with resultant economic benefit to the society (28).

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TABLE

Papers	1	2	3	4	5	6	7
		Too small					
Age	+		+*	+**	+***	+	
Race	0				+***	+	
Gender	+*				+***		
Marital Status	+*						+
Income	+						
Employment	0		+*				
# of transplants	+						
Anxiety	+			+**			
Hostility	+						
Depression	+						
Distress	+						
Stress	+*						
HLOC (chance)	+			+**			
Coping (avoidance)	+						
Pain							
(others)							

Notes: * = also significant in multivariate analysis
** = only reported for multivariate analysis
*** = only those with non-compliance leading to rejection vs complaints

3. Infection[*]
Living related donor[*]
Time since transplant[*]
US born
Education
Diabetes[*]

5. >1 rejection episodes,
Prednisone dose
Tremor
Clinic compliance
Distance
Dialysis compliance
Treated rejection episodes

7. Self-cast agency score
Self-efficacy score
Situational-operational
knowledge

PROSPECTIVE RANDOMIZED STUDY OF INDIVIDUAL AND GROUP PSYCHOTHERAPY VERSUS CONTROLS IN RECIPIENTS OF RENAL TRANSPLANTS[1]

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ABSTRACT

Introduction: Recipients of kidney transplant have been shown to develop

emotional problems. These have been associated with medical non-compliance,

compromised quality of life and difficulty integrating the newly acquired

transplant into their sense of self. In general, group psychotherapy has been shown

to be more cost effective than individual therapy. We have compared the efficacy

of two modalities of therapy in recipients of kidney transplants versus control

patients who did not receive therapy.

Methodology: Recipients of first cadaver kidney transplants were randomized

into two groups, to receive a 12-week course of group or individual

psychotherapy. Control arm of the study comprised of 37 consecutive patients

who had received a first cadaver kidney. Recipients of live kidney transplants and

patients who received more than one kidney transplant were excluded as these

patients have different emotional issues. The Beck Depression Inventory (BDI)

was utilized as a measure of change in emotional state, pre-therapy, at 3, 6, 9 and

12 months. A higher score on BDI was suggestive of psychological dysfunction.

Results: We recruited 89 recipients of first cadaver kidney transplants into the

study. They were randomly allocated in to the two study groups, 49 for individual

therapy and 40 for group therapy. Of these, 82 patients completed 12 weeks of

therapy (45 patients from the individual treatment arm and 37 from the group

therapy arm). Fifty-five patients completed one-year follow-up (33 in individual

therapy and 32 in the group therapy). The mean score was 26.3 ± 7.9 before and 18.9 ± 9.0 after therapy in the individual treatment group (p=0.001). This was in comparison with a mean score of 30.2 ± 3.8 before and 26.0 ± 4.2 after therapy for the group therapy arm (p= 0.01). Improvement appeared to be more significant in the individual therapy compared to group therapy (p= 0.01). Lowering of scores was progressive and sustained (p=0.01). In the control arm, mean score was 9.4 ± 5.4 before and 20.5 ± 5.5 at the end of the first year (p=0.005) suggesting a significant worsening of BDI scores. Multivariate analysis of age, gender, employment status, duration of dialysis, etiology of kidney failure, diabetes mellitus and psychotherapy received at any time before transplantation did not affect results.

Conclusion: We conclude that both individual and group psychotherapy were beneficial to our patients, however, individual therapy was found to result in lower BDI scores versus group therapy at the end of treatment period.

INTRODUCTION

Recipients of renal transplants have been shown to develop emotional problems (1). Psychotherapy has been shown to be effective in addressing developmental delay, coming to terms with the past and can be a catalyst for change (2). In general, group psychotherapy is more cost effective than individual therapy (3). In this study, we have prospectively, in a randomized trial, compared the efficacy of group versus individual psychotherapy in recipients of first cadaver kidney transplants versus age and gender matched control patients who did not receive therapy.

We have described elsewhere along with step-by-step framework for individual and group intervention and how emotional issues are more complex and multi-faceted than previously suggested (4). We have shown that patients have paradoxical depression and feelings of loss despite having received a long - awaited kidney transplant. This loss has been considered in terms of time (along with experiences and expectations) lost to chronic illness, in short, what might have been. Therapeutically speaking, this loss is contemplated in terms of the 'imagined past'. The 'imagined past' does not exist beyond the bounds of the patient's imagination and has not withstood the test of reality. Anxiety associated with the uncertainty of renal failure and organ transplant often presents as panic attacks. Patients in renal failure and after transplantation also have heightened sense of their mortality, distorted body image and fear of rejection of the transplanted organ.

The manner in which emotional problems impact upon compliance

behavior, quality of life and the psychosocial integration of the newly acquired organ adversely effect medical management and progression of the illness, resulting in graft loss and even death has been well documented amongst transplant patients (4, 5). The common thread running throughout the treatment of these patients is the curtailment of lifestyle, pervasive sense of powerlessness and loss associated with depressed mood. However, in contrast to other chronic illnesses, little attempt has been made to mobilize psychosocial support for these patients. Where such intervention does exist; it has been fragmented and intermittent. However, our research suggests that individual and/or group psychotherapy provides a forum to effectively address emotional issues in patients receiving a kidney transplant which impacts positively upon compliance, quality of life and the integration of the new kidney (5).

Individual and group psychotherapy rely on the utilization of patient self-report, a methodology criticized as being liable to exaggeration and underplaying of problems in an attempt to please the therapist. A scenario commonly referred to as the *'hello-goodbye'* effect or socially desirable responding. We used the Beck Depression Inventory (BDI) [6] to study the efficacy of our trial by an objective method. Of the many instruments available, we choose the BDI; we were however, concerned that this instrument might be considered overly simplistic. We found that references to BDI during treatment sessions were considered positively by patients who appeared to find regular completion of the questionnaire therapeutic in terms of identifying milestones in treatment.

Our study showed that individual as opposed to group therapy was more

effective in the treatment of emotional problems amongst recipients of renal transplants. However, given the potential for bias pertaining to the single therapist and cultural drift associated with single center studies, our study would need to be repeated in a multi-center manner using a comparable theoretical orientation but with different therapists.

METHODS AND PATIENTS

Recipients of first cadaver renal transplants within 3 months of surgery were randomized (using computer generated numbers to ensure even gender and age distribution) into two groups, to receive a 12-week course of *Systemic Integrative* group or individual psychotherapy. BDI was utilized as a measure of change in emotional state, pre-therapy, at 3, 6, 9 and 12 months. A higher score on BDI was suggestive of psychological dysfunction. Study was approved by the local ethics committee. Patients were treated using the same therapist and theoretical model (*Systemic Integrative Psychotherapy*) in both the groups. Study was based on the need for at least 80% statistical power to determine differences between success rates. Thirty-seven patients served as control group, however, it should be noted that these patients were recruited consecutively after the first two groups were recruited for logistic reasons, to enable us to obtain adequate numbers for group arm. The BDI consists of 21 groups of graded statements (the higher the score the more negatively intense the feeling) relating to mood as follows:

Question One
    0   I do not feel sad.
    1   I feel sad.
    2   I am sad all the time and can't snap out of it.
    3   I am so sad and unhappy that I can't stand it.

Question Two
    0   I am not particularly encouraged about the future.
    1   I feel discouraged about the future
    2   I feel that I have nothing to look forward to.
    3   I feel that the future is hopeless and that things cannot improve.

BDI is a self-report questionnaire in which the patient has to read the statement and circle a statement most accurately represented their feelings at the point of assessment (before therapy began, at termination and 3, 6, 9, 12 months follow up).

Statistics: The data are expressed as mean ± standard deviation. The comparisons of the means of the scores at various time periods between the individual and group therapy groups were made by the use of Mann-Whitney U test and one-way ANOVA test as appropriate. The significance of the impact of therapy within each treatment arm was assessed by Wilcoxon rank sum test. The individual parameters were assessed for their effect on the final result with the help of multivariate analysis. All the significance was calculated as two tailed and is measured at a level of ≤ 0.05. A statistical software package was used for the computations (SPSS 9, SPSS Inc., Chicago).

RESULTS

Eighty-nine patients who had a cadaver kidney transplant were recruited in to the study. They were randomly allocated in to the two study groups, 49 for individual and 40 for group therapy. Of these, 82 patients have completed 12 weeks of therapy (45 patients from the individual arm and 37 from the group therapy arm). Fifty-five patients have completed one-year follow-up (33 in individual and 32 in the group therapy); the rest did not complete one year as they moved away or did not return their questionnaires. Thirty-seven, age and sex-matched patients were recruited as controls; two dropped out of the study at three months and four at six months respectively. Demographics of the study population are shown in Table 1. A higher percentage of patients who had been on more than three years of dialysis were allocated for group therapy; otherwise, there was no significant difference between the characteristics of the study groups in the two arms. Our population in the West of Scotland is approximately 98% Caucasians, therefore all the patients in our study happened to be Caucasians. All patients had received their first cadaver transplant as psychological issues with a second or third transplant are different than those receiving their first transplant. We also excluded pediatric recipients and those receiving living kidney transplants as emotional issues and graft outcomes are different to patients receiving a cadaver kidney.

Table 2 shows mean BDI scores in the three groups before treatment and at various time points after therapy. In both treatment groups, there was significant improvement in the scores following therapy. The mean score was 26.6 ± 7.9

before and 18.9 ± 9.0 after therapy in the individual group (p=0.001). This was in comparison with a mean score of 30.2 ± 3.8 before and 26.0 ± 4.2 after therapy for the group arm of the study (p=0.01). Improvement was more significant in the individual therapy arm compared to group arm (p= 0.01) [Table 1 and Figure 1]. Lowering of scores remained sustained (Table 2) in both therapy arms. In the control arm, mean score was 9.4 ± 5.4 before and 20.5 ± 5.5 at the end of first year (p=0.005) suggesting significant worsening of BDI scores (Figure 2). Multivariate analysis of age of the population, gender, employment status, duration of dialysis (if in dialysis for more than three years) and psychotherapy given before transplantation did not affect the results (Table 3).

We also sought a correlation between clinical course and posttransplant events in the three groups. There was no difference in the incidence of acute rejection, wound infections or delayed graft function. Donor variables (age, gender and cold ischemia time) did not differ between the groups. The meantime for the development of first acute rejection following renal transplant was 68.8 days. The number of patients who developed early acute rejection was 19.2% in individual, 18.6% in group therapy arm and 17% in control group. Delayed graft function was diagnosed if the patient needed dialysis in the first week after transplant. The incidence of delayed graft function was 30.6% in the individual arm, 34% in the group arm and 30% in the control patients, which was not significant.

Immunosuppression was similar in all the three groups. Patients received cyclosporine-based therapy, with CellCept and prednisone. No induction with

antibodies was carried out. Patients received 1 gram solumedrol in the OR, followed by tapering doses so that all patients were on 20 mg/day at the end of 6 days, 15 mg/day at the end of 3 months and 5 mg/day at he end of a year. Acute rejections were treated with pulsed steroids with a rapid taper.

DISCUSSION

Negative pre-morbid personality traits are amplified during renal disease and their relational aftermath is an issue amongst all patients. The development of individual therapy has taken a predominantly psychoanalytical perspective to address the transition from dialysis to transplantation and the subsequent adaptation from illness to normal health (7). Cognitive-behavioral therapy has been used to address stress, anxiety, depression and psychosocial adjustment to illness (8). The findings were analyzed within the context of two intervening variables, interpersonal support and control over their treatment to determine compliance with the medical regime. The results suggested that cognitive behavioral therapy had a positive effect on all patients for some of the above issues, in particular for anxiety.

Transplant patients and their families have viewed short-term group psychotherapy positively. Buchanan (9) described the primary benefits of group therapy as being the opportunity to observe and support coping strategies, mutual support and encouragement. However, short-term nature of the group and open membership (ongoing or changing membership from week to week) was not conducive to the exploration of relationship difficulties.

Group therapy amongst multi-organ transplant patients has been integrated into the transplant program at the University of Toronto, Canada, as it was shown to be cost effective in addressing emotional issues before and after transplantation (10). Common recurring themes were those of infection, rejection, body image changes and emotional problems such as delirium and depression. However, in

our own comparative study of group and individual psychotherapy amongst post-transplant patients, group therapy did not appear to be as effective as individual therapy.

'Modified' group therapy has been has been utilized amongst patients receiving dialysis (11). The group was initiated as a result of the recognition of the stresses of ongoing dialysis and the need to address such problems if they were not to become an obstacle to transplantation. The author commented on how he had witnessed the progression of hemodialysis from an experimental to a definitive treatment, which sustained life, but created emotional stresses regarding body image, dependency on dialysis, resentment and conflict within families. Other studies have attempted to utilize group therapy in dialysis units to combat isolation and psychological denial and have been utilized as an effective educational tool (12-14).

While individual and group therapy are different modalities, they have common goals, namely to benefit the patient. This was achieved by encouraging the patient to disclose his/her feelings and experiences and in conjunction with the rest of the group, reflect and address them. The role of the therapist was to facilitate such an exploration and assist in making sense of them. Patients tended to present their feelings and experiences using a 'story' format; every patient had a tale to tell and this was usually related in the group in terms of recalled interactions with their social networks out side of the group and often replayed between members of the group. Each member of the group brought with them a set of expectations, fears and hopes of what they might achieve from treatment

and how the therapist would facilitate such change. The most difficult dilemma for most patients was that of wanting to change and yet reluctant to relinquish familiar coping mechanisms, ways of thinking, behaving and their perception of themselves.

However, we need to better understand why the control group reported less emotional difficulties at the start of treatment, but were significantly more likely to deteriorate over time, present for emotional crisis intervention and be admitted for medical complications associated with non-compliance than their group or individually treated counterparts. In order to do this we need to better understand the psychological profile of the renal dialysis and transplant patient and to be receptive to the utilization of a more pluralistic, combined quantitative-quantitative methodological analysis of data. These findings appear to feed into the current trend in the psychological sciences as to the need to establish which patients benefit from which particular intervention over stipulated periods of time. We suggest that given the above findings, any future research question to determine the effectiveness of therapeutic intervention would need to be reframed. That is, we should not ask which particular treatment intervention is the most effective amongst this patient group, rather, *which intervention is most likely to* permeate the 'boundary of inadmissibility'. This scenario was interpreted qualitatively within the bounds of the study as the 'barrier of inadmissibility'. In short, most transplant patients feel obliged to appear grateful for their transplant and try to live up to the subsequent expectations that accompany it, while putting their fears and uncertainties behind them. However, the availability of emotional

intervention acts as a cue to patients to recognize emotional difficulties, in short, it permeates the 'barrier of inadmissibility'. In our study, individual psychotherapy appeared to be most effective at permeating the 'barrier of inadmissibility', while group psychotherapy was less effective and the control group had virtually no permeable qualities at all. However, for the control group patients, over time the 'barrier of inadmissibility' is permeated anyway by the difficulties of living the fickle, uncertain and high maintenance life of a post-transplant patient. Hence, there was deterioration in their emotional state over time.

Norms or expectations as to what constitutes acceptable and non-acceptable behavior amongst group members might differ. Their cultural or family background will largely reflect the manner in which many group members will behave. The use of sarcasm or ridicule which, might to acceptable to some patients, but not to others. Furthermore, there is always a danger in socially mixed groups that better educated and more articulate patients might articulate their thoughts, while the less educated feel intimidated. There is also a tendency amongst the better educated to intellectualize issues which in a group situation can lead to a 'debating style' being adopted. However, some members who might remain silent for the most part in one group might be much more articulate in another group where they feel either intellectually or socially superior or equal to other group members. However, such individual trends tend to emerge over time and are apparent during group interactions. The psychotherapist will become aware of repeated patterns of interactions or silences, which will alert him/her to alliances, allegiances and exclusion between group members. One way for a

therapist faced with a fragmented group is to introduce some cohesion to the group through the 'shared beliefs' or views, opinions, attitudes and shared reality of group members.

The BDI has generally been considered as crude measurement that does not do justice to the idiosyncrasies of the treatment process, the patient or therapist for that matter (14). However, we wanted to produce objective data, which could encourage other centers to embark on similar projects using the BDI or other instruments, or even devise a specific instrument for this purpose. Our study clearly shows that psychotherapy was effective in lowering BDI score; this presumably will lead to improved quality of life and adherence to medications. The fact that patients in the control group started with a lower BDI score is an interesting finding; it is known that patients not expecting to receive therapy will not think too deeply into psychological issues that affect their lives.

We conclude that both individual and group psychotherapy were beneficial to recipients of first cadaver kidney transplants, however, individual therapy was found to result in lower BDI scores versus group therapy; while patients in the control group had significant worsening of scores. Improving emotional states will lead to improved quality of life and medical compliance and hence longevity of the transplanted organ.

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LEGENDS

Table 1: Patient demographics

Table 2: Mean scores of BDI index at various time points (S.D. is given in brackets).

Table 3: Results of the multivariate analysis (P-values for each parameter is given).

Figure 1: Box plot showing the effect of therapy on actual BDI scores.

Fig 2: Box plot showing the difference in the BDI scores in the three groups (control, individual treatment arm and group therapy arm) at three, six, nine and twelve months following recruitment to the study compared to the BDI scores before the recruitment. Group 0 denotes the control group, group 1 individual therapy and group 2, group therapy. The values represent the difference from the initial score and hence the higher the difference, the higher the effectiveness of the therapy.

Table 1: Patient demographics

		Control group N = 37	Individual Therapy N = 49	Group Therapy N = 40	p-value
Age (years) Mean ± SD		36.6 (± 11.9)	36.2 (± 8.9)	39.1 (± 11.1)	0.19
Gender	Female	15 (40.5 %)	27 (55%)	17 (42%)	0.29
	Male	22 (59.5 %)	22 (45%)	23 (58%)	
Dialysis status	Less than 3 years	13 (35.1 %)	35 (71%)	18 (45%)	0.01
	More than 3 years	24 (64.9 %)	14 (29%)	22 (55%)	
Previous psychotherapy		7 (18.9%)	7 (14%)	7 (18%)	0.45
Employment status	Employed	12 (32.4 %)	9 (18%)	7 (17%)	0.57
	Unemployed	25 (67.6 %)	40 (82%)	33 (83%)	

Table 2: Mean scores of BDI index at various time points (SD is given in brackets)

		Control group (n = 37)	Individual Therapy (n = 49)	Group Therapy (n = 40)
		Mean score	Mean score	Mean score
Before therapy		9.4 (±5.4)	26.6 (±7.9)	30.2 (±3.8)
At completion of therapy	12 weeks	-	20.6 (±8.8)	27.4 (±3.9)
After therapy	3 months	11.1 (±4.9)	19.8 (±8.9)	27.2 (±4.1)
	6 months	14.1 (±6.0)	19.6 (±9.1)	26.8 (±3.9)
	9 months	17.3 (±3.7)	19.2 (±8.8)	26.5 (±4.0)
	12 months	20.5 (±5.5)	18.9 (±9.0)	26.0 (±4.2)
p-value #		0.005	0.001	0.01

#: One-way ANOVA

Table 3: Multivariate analysis of possible factors of influence on final results: p-values

	Individual therapy	Group therapy
Age	0.55	0.57
Gender	0.58	0.84
Employment status	0.13	0.38
Previous psycho therapy	0.30	0.84
Duration of dialysis	0.39	0.84

Figure 1: Box plot showing the effect of individual vs. group therapy on actual BDI scores
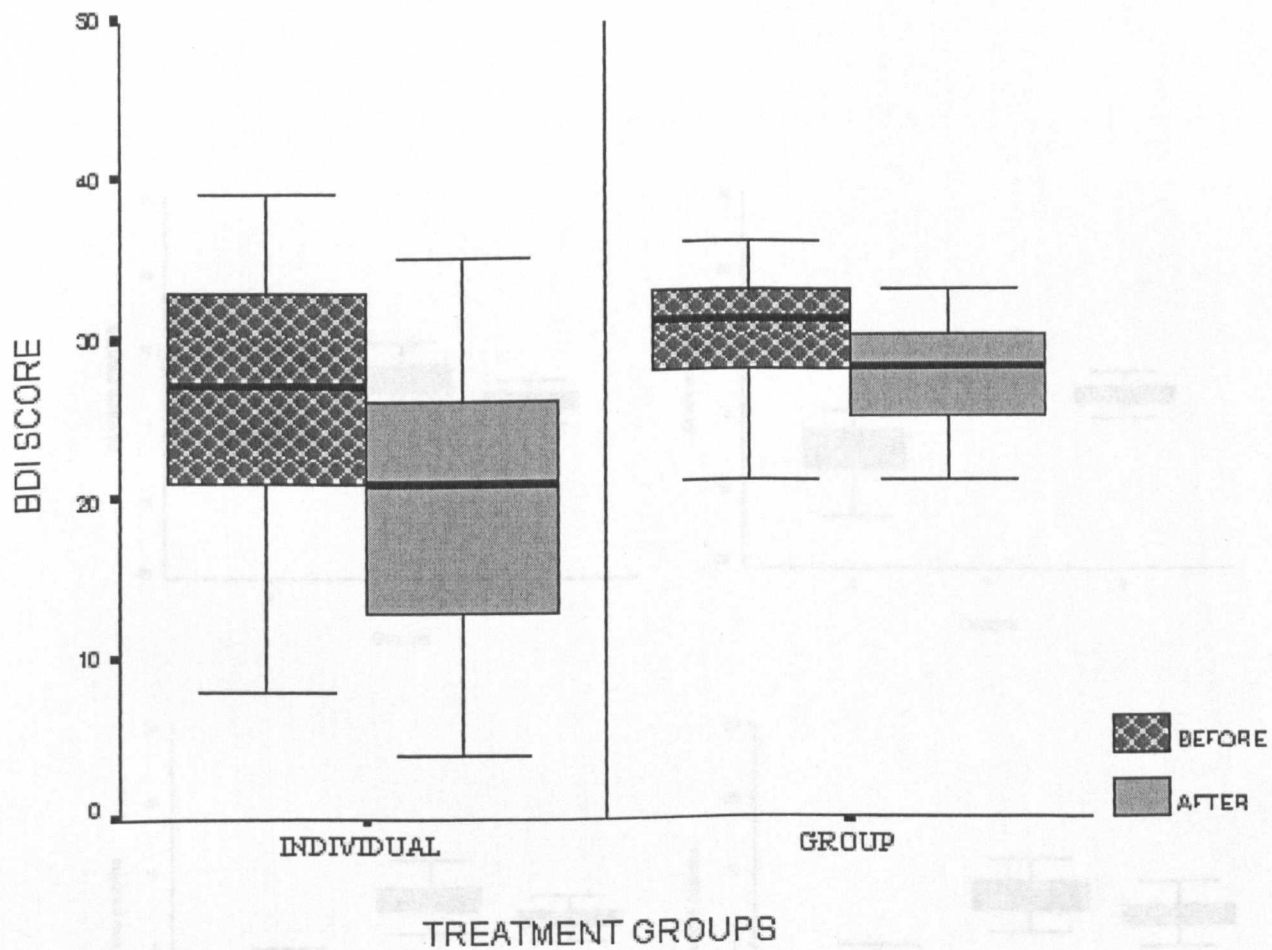
Fig 2: Box plot showing the difference in the BDI scores in the three groups (control, individual treatment arm and group therapy arm) at three, six, nine and twelve months following recruitment to the study compared to the BDI scores before the recruitment. Group 0 denotes the control group, group 1 individual therapy and group 2, the group therapy. The values represent the difference from the initial score and hence the higher the difference, the higher the effectiveness of the therapy.