

Methodological Considerations in Quality of Life Research in Renal Replacement Therapies

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Quality of life (QoL) of patients undergoing renal replacement therapies represents an important benchmark in the evaluation of different options that might be available to patients with end-stage renal failure. However, stringent and robust methodologies to study and evaluate QoL are not widely used, making the interpretation of findings of different stud-

ies difficult. In this paper, we attempt to focus on an evidence-based, balanced approach in order to better understand the impact of renal replacement therapies on the patients' lives. The need for QoL studies of specific patient populations, in different settings is emphasized.

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Research focusing on the *health related quality of life* (QoL) of patients undergoing renal replacement therapies (RRTs) is an essential component of the evaluation of the available treatment options for end-stage renal disease patients.

The term *Quality of Life* refers to a complex, multi-dimensional assessment of a spectrum of physical-functional, mental, social and other aspects of a person's everyday experiences. QoL represents a relatively recent concept used to evaluate, and potentially quantitate, the effects of different treatments, in different settings. The necessity for QoL research has been a result of the contemporary nosological patterns, which are marked by chronic, multi-factorial diseases and long-term treatments with significant side effects. In addition, financial as well as administrative considerations have combined to increase the pressure for more efficient use of available resources.

A *central assumption* of most of the literature on the QoL in RRTs, seems to be that the *psychosocial status of patients in RRTs tends to parallel the state of their 'renal function'* (i.e. the more, or the better a failing kidney is compensated for, the better the psychosocial QoL will be). In addition, on most occasions, *transplantation is being portrayed as offering a QoL that is superior to that of alternative RRTs*. In this paper, we attempt to critically evaluate the QoL in RRTs literature. More specifically, we empha-

size certain methodological issues that render the interpretation of the findings of many studies highly problematic.

Psychosocial QoL in RRTs

A Medline search¹ under the headings "quality of life, dialysis /renal transplantation" showed 1,539 papers including 338 review articles, 41 editorials and 3 meta-analyses.

Dew et al^{2,3}, in a meta-analysis of 144 (/218) studies of four domains of QoL (physical /functional, mental, social, and overall), found a general pre- to post-transplantation improvement in all four domains; however, studies that incorporated clinician-administered diagnostic assessments were less likely to report improvement in mental health than those that relied exclusively on self-report questionnaires. Studies that compared recipients to candidates did not find improvement in mental and social QoL. Additionally, no data were identified to confirm that QoL in transplant recipients is similar to, or better than QoL in healthy samples. Dew et al emphasize that "within any given patient sample, a significant subgroup will show little or no QoL gains, even though the average gain for the sample as a whole may be quite positive; specific patient characteristics seem to be the critical factor here, and we definitely need more work in order to be able to develop more effective interventions to improve QoL".

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Cameron et al⁴, in a meta-analysis of 49 studies, found differences in the emotional status of patients among groups undergoing different RRTs. They found that transplantation gave the most favorable results. However, validity was an important problem, possibly due to case-mix; results might have been explained by pre-existing differences. It should be emphasized, they had to exclude 85% of the studies that were initially selected (2,761 out of 3,267), because they had not looked into any psychosocial domain.

Cagney et al⁵, in a structured literature review, found that only 47 papers, out of a total of 436, contained evidence of reliability or validity testing of instruments used in QoL research in RRTs. Within these papers, there were 113 separate uses of 53 unique instruments. Only 32% of the articles defined the concept of QoL and only 6 instruments (*generic*: Sickness Impact Profile, Campbell Indices, Medical Outcome Study Short Form 36; *disease specific*: Kidney Disease Questionnaire, End Stage Renal Diseases Severity Index, Kidney Disease Quality of Life Questionnaire) are portrayed as having had fairly extensive testing. The numbers of times an instrument has been deployed, does not necessarily increase the likelihood that evidence for reliability or validity exists. In addition, domains very important to patients with ESRD (sexual functioning, body image, freedom /control) often were not included in the instruments. Of note, De Geest & Moons⁶ refer to patient's appraisal of side-effects (/body image concerns) as "the blind spot in QoL assessments in transplant recipients".

Work from the *transplantation psychiatry* has shown high levels of psychiatric morbidity in patients in RRTs. This conclusion is frequently overlooked in studies of psychosocial QoL, especially when it is thought that, patients referred for psychiatric evaluation are special samples and that information gathered from them is not generalizable². However, even large organizations openly talk about the possibility that transplant recipients might present psychiatric problems (the UNOS web-site⁷ for instance, begins its section of more common side-effects of anti-rejection drugs describing complaints such as anxiety, mood swings, trouble sleeping...).

In addition, non-compliance is another major issue, hinting at the possibility that reality for renal failure patients might be more wrinkled than the

reports finding "excellent QoL" would suggest. In a recent literature review, up to 20-50% of transplant patients were found to be non-compliant^{8,9}.

In conclusion, poorly defined concepts, weak research methods, and contradictory findings, suggest that the central assumptions underlying most of the literature lack the required scientific evidence, and that more, and better research is needed.

Methodological Problems

The very concept of QoL, being so complex and multi-dimensional, necessitates stringent, validated methodologies in order for any findings to be interpretable, meaningful, and, one would hope, reproducible. However, this is easier said than done; Joralemon & Fujinaga¹⁰, in a critical review of the literature found multiple methodological flaws, esp. positive biases.

It is not unusual to find small samples, not representative samples, case-mix, and drop out effect; unvalidated, author-constructed questionnaires, brief mailed questionnaires, as well as indiscriminate use of methodological instruments that have been designed to measure different contents and populations. Publication bias has also been reported^{10,11}.

QoL, as a state rather than a trait element, cannot be truly evaluated by cross-sectional studies; it requires longitudinal data (and qualitative research).

Not infrequently, one sees the answers given to questionnaires taken at face value, ignoring basic defense mechanisms (i.e. denial) or outright distortion (malingering, deception) on the part of the person answering the questions¹¹⁻¹³. Often times, researchers interpret patients' answers in a highly arbitrary way (i.e. body image concerns are handled in a linear-model and even Visual Analog Scales have been used^{14,15}; however other studies support a curvilinear-model¹⁶). Several clinical investigators have questioned the value of questionnaires, while results gathered from questionnaires are contradicted by data generated by alternative methods^{2,17}.

"Savior effect" (the tendency on the part of the patients to offer "idealized answers given their suffering and their sense of indebtedness to their 'saviors'"¹⁰) is a powerful, although neglected, source of positive bias.* Likewise, additional sources of positive biases stem from the novel social surroundings

* One might say that each therapy is accompanied by its own myth, and these are inseparable. We agree with that, but we must carry in mind that there is also the unpleasant side of the myth, although neglected by the medical community; "the very 'science-fiction' aura of transplantation"...¹⁸ Necessity to deny this dark side might have the same positive biased effects on QoL assessment.

(“transplant family”, “new socio-medical community”¹⁰) that the patients find themselves¹⁹.

Interpretation of the results constitutes another level of potential methodological issues. “Since QoL studies have more than purely scientific agendas, they can lead to premature and overly optimistic reading of actual data.”¹⁰ Problems related to such optimistic readings have been reported long ago²⁰.

A final note has to be made about the linguistic-conceptual gap in the field. When one thinks about complex and difficult to pin-down concepts, like QoL, it is obvious that they can be used to refer to different things [in the same way as well established (psychiatric) concepts, like depression, is used by different researchers to describe a whole spectrum of different things].

Historical Background

The first clinical studies of psychosocial domains of RRTs (mid-1960s to mid-1970s) were done mainly by psychiatrists who were working as *peripheral* members of renal units. Most of the time they were trying to understand the subjective personal experience and meaning, in what until then was an uncharted territory. Many issues that at the time were considered important, dropped out of sight in subsequent years^{18,21}. This initial period of *guarded optimism* was followed by a more or less *unchecked enthusiasm* for transplantation as a treatment inherently superior to any alternative. This is the period (mid-1970s to mid-1990s) that saw the widespread use of questionnaires, the mailed cross-sectional studies and the emergence of psychiatric morbidity as an undesirable, potentially dangerous complication. The conclusion from the well-known study of Simmons et al¹⁴ symbolizes that period: “[transplant patients are] *more happy than normal adults*, p.427”

[emphasis on the original]. A lot of studies^{2,22} seem to confirm that conclusion, although one must have in mind that a variety of positive biases suggest that studies were undertaken to support or advocate an already preferred type of treatment (Najam & Levine 1981)¹⁰. More recently (mid-1990s to today) we have been witnessing a more careful, *pragmatic, result-oriented approach*, focused on improving overall outcome¹⁸.

Clinical Implications

Research on psychosocial domains has an enormous clinical value; it can help us understand “what our patients *really* go through – not what they so often blandly present to us, their attending physicians”²³. Additionally, it might give us insights and one would

hope answers about major problems, such as non-compliance.

“Inadequate or fallacious results could potentially harm patients if treatment decisions are based on this research”⁵. The systematic bias in favor of a specific form of treatment correlates with the underestimation of alternative treatments, which may actually be more suitable and beneficial to specific groups of patients. Sometimes, in transplantation, this bias results in an inappropriate focus in the surgical procedure itself and in unrealistic expectations of a care-free post-operative course. Not infrequently, one of the major goals of pre-transplant psychiatric support is to provide a few reality-checks, so that patients may begin their adventure with a somewhat more realistic understanding about what renal transplantation entails.

If we are positively biased towards a form of treatment, how can we make sure that our patients are actually informed and truly consent to it? Have they understood that they have to exchange a set of problems with another, or are they waiting for *the cure*? Informed consent is not only an ethical obligation of the attending physician; it has also a serious impact on patient-physician relationship and on clinical course.

Unfortunately, sometimes positive QoL results are being presented in ways that seem to contradict established psychiatric observations, although the former may not be comparable to the latter. For example, some researchers^{14,24} are using their results of enhanced QoL to dispute Abram’s²⁵ findings. However the former refer to an overall evaluation of the QoL, while Abram is focusing on the rare event of suicide.

On the contrary, even when QoL research gives good reasons for optimism, almost always one finds significant subgroups of patients that will need specialized interventions. For instance, Simmons et al¹⁴ advocate psychiatric support specifically for adolescents and diabetics. However, although the literature supports the necessity of comprehensive psychiatric support (albeit with significant variations as to how many or which patients need to be offered this support), and very practical administrative (i.e. psychosocial evaluation) and financial issues seem to confirm the need for such a support as well, very few renal units offer routine psychiatric care to their patients.

[Of note, the same mechanisms that motivate positive biases (strong economic incentives, professional prestige, legitimation for a preferred type of treatment, psychological defenses that professional

develop to deal with the emotional demands of their work...) ^{10,20,26} prevent psychosocial interventions that might enhance patients' QoL.]

Although our current knowledge and understanding of QoL in RRTs leaves much to be desired, a critical evaluation of the available literature suggests a combination of positive biases. As clinicians, we need a more evidence-based, balanced approach in order to understand the full impact of RRTs on our patients' lives. In addition we are in need of better QoL-studies of specific subgroups and of studies of psychosocial interventions in order to improve the overall outcome of RRTs.

ΠΕΡΙΛΗΨΗ

Μ. Συγγελάκης, Μ. Παπαθανασίου. Μεθοδολογικές επιφυλάξεις για την έρευνα της ποιότητας ζωής ασθενών που υποβάλλονται σε θεραπεία υποκατάστασης της νεφρικής λειτουργίας. Ιπποκράτεια 2002, 6(2): 83-87.

Η ποιότητα ζωής των ασθενών που υποβάλλονται σε θεραπεία υποκατάστασης της νεφρικής λειτουργίας συνιστά σημαντικό παράγοντα για τη συγκριτική εκτίμηση των θεραπειών της χρόνιας νεφρικής ανεπάρκειας τελικού σταδίου. Τα υπάρχοντα βιβλιογραφικά δεδομένα, όμως, δε στηρίζονται σε αυστηρή μεθοδολογική προσέγγιση, καθιστώντας την ερμηνεία των αποτελεσμάτων ιδιαίτερος προβληματική. Η τεκμηριωμένη ιατρική προσέγγιση της ποιότητας ζωής των νεφροπαθών θα μας επιτρέψει να κατανοήσουμε τις επιπτώσεις της θεραπείας υποκατάστασης στη ζωή τους. Επισημαίνεται ιδιαίτερος το πρόβλημα της γενίκευσης των αποτελεσμάτων και η ανάγκη διεξαγωγής μελετών ποιότητας ζωής σε ειδικές ομάδες ασθενών.

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