Quality of life assessment and clinical decision-making*

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Summary

Survival and quality of life are the two end-points of cancer treatment. Recommendations are available as to how quality of life should be assessed in clinical studies in order for quantitative scores to be provided for it, along with survival data. The two measurements can be combined, and their total should yield a definition of the state of the art in cancer treatment with respect to both the quantity and the quality of life. However, at the individual level, quality of life can be traded off against survival only by taking into account the patient's attitude toward risk. More importantly, the quality of health status may be valued in a completely different way from patient to patient. Thus, when a clinical choice is to be made from among different treatment options, the ethical principle of respect for the patient's autonomy would require that the patient be informed of their possible respective outcomes, and allowed to provide his/her own assessment of the quality of life associated with these outcomes. This might have consequences for quality of life assessment in clinical studies, which should not only quantify average scores for treatment comparisons, but also provide a 'health state description' with respect to the aftermath of each of the treatment options. These data could be formalized in the already proposed decision instruments incorporating clinical scenarios for patient information. In any case, this should allow individualized clinical decisions incorporating each patient's preferences for the quality of his/her expected life span. Providing average quality of life scores may be useful, indeed, for population-based health decisions, as are those on resource allocation and those on registration of new drugs.

Key words: clinical decision making, outcome research, quality of life

Introduction

It is now acknowledged that survival and quality of life are the two end-points by which any cancer treatment should be evaluated [1]. Indeed, this represents an ongoing process, since only recently has quality of life begun to be incorporated into clinical trials [2]. It is, however, claimed that there are basic difficulties with the concept. A recent paper on 'the problem of quality of life' [3] recognizes that the notion "has created doubt, confusion, and misunderstanding among practitioners, researchers, policymakers, and patients. The principal reason for this state of affairs is that a clear conceptual basis for quality-of-life measures is lacking." It is suggested that the concept of 'subjective health status' be substituted for that of 'quality of life'. While formal quality of life instruments have been continuously validated over recent years, the impression is that some of the basic issues may have been overlooked.

It may be that the problem of the quality of life relates less to the concept itself and more to the way in which it is employed in clinical practice. Indeed, how often are results of formal quality-of-life assessments actually used in clinical practice? Survival has long dictated the choice of cancer treatment, but there is now very little doubt that quality of life should be given equal consideration. We, however, argue that the two end-points, survival and quality of life, should be approached differently in clinical decision-making, and if this is is a valid argument, it may be that the way in which they are assessed in clinical research also needs to be refined.

Quality of life viewed as a 'measurable' end-point

Rather restrictive recommendations are available for clinical researchers willing to assess quality of life in clinical studies [2, 4]. Standardized questionnaires for patient self-completion are administered, ideally covering all of the 'domains' of quality of life, i.e., physical, functional, psychological, social, and, possibly, spiritual. The score obtained from the patient's answers can then be

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used for numerical comparisons. For example, we may administer to the population entering a clinical trial a questionnaire comparing treatment A with treatment B, observe that treatment A scores better than treatment B, and thereby deduce that treatment A is superior to treatment B in terms of quality of life. If treatment A is also superior in terms of overall survival, the conclusion will be that treatment A is superior to treatment B and can enter the armory of the clinical oncologist as 'standard' treatment (assuming that one trial is enough to make this statement). Alternatively, treatment A and treatment B may prove equal in terms of survival, but the former may be better in terms of quality of life. Thus, treatment A will be deemed better than treatment B and can become 'standard' treatment.

Of course, survival and quality of life may also diverge. For example, treatment A may be better in terms of survival and treatment B in terms of quality of life. One must then make a 'trade-off' between survival and quality of life. Decision analysis [5] makes it possible to formally represent these choices. Figure 1 represents the formalization of a choice between treatment A, which, if cure is achieved, preserves full health, and treatment B, which, if cure is achieved, leads to an intermediate health state. On a 0 to 1 scale, full health by definition scores 1. The intermediate health state yielded by treatment B may score 0.9. If the probability of cure is 0.45 for treatment A and 0.5 for treatment B, the two options are equal, and vice versa. Of course, this is only a way to formalize, and even solve in a 'quantitative' fashion, a clinical problem. Although in a qualitative fashion, any clinician solves clinical problems every day which are strongly affected by patient preference. Formalization may help solve a clinical problem, but basically it does no more than help represent reality and render explicit the variables involved.

Thus, on the basis of this formalization, survival and quality of life may be combined into a unique outcome result. This is the theory of 'quality-adjusted life expectancy' [6], which 'discounts' life expectancy by quality of life. For example, if quality of life scores 0.9, on a 0 to 1 scale, and life expectancy is 10 years, 'quality-adjusted life expectancy' will be $10 \times 0.9 = 9$ 'quality-adjusted life years' (QALYs). A treatment allowing one to live nine years in full health would be equal to a treatment allowing one to live 10 years with a quality of life scoring 0.9, as formalized in Figure 2 (of course, the quality of a life may change over the years, and QALYs can sum up several intervals, each corrected by a different numerical value). The state of the art in medicine might be defined by comparing available treatment options in terms of QALYs, or similar outcome indicators [7]. If state of the art determines individual decisions, they are made on the basis of both survival and quality of life.

According to this paradigm, clinical research can basically approach survival and quality of life in the same way. Survival and quality of life are end-points for comparison in clinical trials, to make it possible to select the best treatment at the patient's bedside as well as to determine which treatment merits the label of 'standard'. Thus, clinical trials must make comparisons among treatments in light of both survival and quality of life. Theoretically at least, the difficulty of a divergence between survival and quality of life can also be accommodated by trading off between the two.

**Quality of life viewed as a 'subjective' end-point**

There may be theoretical problems with the concept of QALYs [8]. For the purposes of this discussion, we will point out two facts:

First, when choosing from among different options requiring a trade-off between survival and quality of life, survival should be corrected through a 'utility' value rather than a 'quality-of-life' value. In the language of decision theory, a utility is a value expressed in conditions of risk. For example, chemotherapy is not a pleasant experience, and an individual undergoing chemotherapy will say that his/her quality of life is not very high, certainly not close to the value of 1, i.e., to 'full well being' on a 0 to 1 numerical scale. However, in the decision tree represented in Figure 3, the utility he/she will attribute to undergoing chemotherapy for six

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**Figure 1.** The trade-off between quantity and quality of life.

**Figure 2.** Quality-adjusted life expectancy.

**Figure 3.** The utility value for chemotherapy.
months will actually be close to 1, if the risk entailed by avoiding chemotherapy is death. The issue goes beyond the limits of this discussion, but the concept is that, in order to be spared chemotherapy, the price in terms of a diminishment in the chance of cure that the individual is willing to pay will generally be quite low. In fact, chemotherapy is a treatment which may be more or less unpleasant, but which is, for instance, very unlikely to leave sequelae, etc. This is the reason why the utility of undergoing chemotherapy will always be quite high, quite close to 1 on a 0 to 1 scale. Quality of life instruments may at best provide us with health state values, not utilities. Utilities try to incorporate the attitude toward risk of the individual, in addition to the absolute values of health states. Of course, attitude toward risk is a subjective variable.

Secondly and most importantly, quality of life in itself is a subjective variable. This is not the case for survival. In fact, if one ignores the quality of the life to be expected, life is good and death is bad for everyone. (A person willing to commit suicide will attribute a value of 0 to the expected quality of life, not a value of 1 to death.) Therefore, survival in itself (i.e., independent of any consideration of quality of life) is not a subjectively evaluated end-point. If treatment A is superior to treatment B in terms of survival, it can reasonably be expected that it is superior for everyone, although it might prove equal or even inferior to treatment B with respect to quality of life. The opposite applies to quality of life. A health state may correspond to completely different values (and even more, to different utilities!) for different individuals.

Let us take a pianist and a runner, and consider the value (or utility) each would assign to losing a finger, or a foot. Preserving a finger could be worth a relatively high loss in terms of chances of cure for the pianist, but possibly not for the runner, and the opposite would apply to preserving a foot. As it is intuitive, any utility measurement would probably detect that the utility of living without a finger is lower for the pianist than for the runner, and that the utility of living without a foot is lower for the runner than for the pianist. The conclusion is that it is the pianist, or the runner, who must decide as to his/her quality of life. While survival will be better than death for both, quality of life may be evaluated differently by the two.

One may contend that we always measure variables with a wide individual deviation. The median survival assessed in a clinical trial corresponds to a distribution of many individual values of length of survival. Of course, the same variability affects quality of life assessment. However, if the above statement is true, a further variability affects quality of life. In addition to the random variability of health measures, there is something more. The quality of life score assessed in a trial reflects the variability of all of the subjective viewpoints of the enrolled patients. Every pianist and every runner would accept the random variability, affecting both survival and quality of life. On the other hand, they would not agree that the variability of the viewpoints of patients in a clinical trial has any relevance for their choices. They would accept the conclusions of the trial with regard to survival and would understand the variances they entail, but would prefer to give their own respective views on what losing a finger or a foot means to them.

Of course, before expressing their own utility, the pianist and the runner would wish to be informed of the objective consequences of losing a finger or a foot, i.e., of the health states of 'finger-loss' and 'foot-loss'. They would not be interested in a numerical 'score' attributed by other patients in a clinical trial to such health states, but would be very interested in a 'description' of those health states, in order to attribute a score in their own perspective.

Conclusions: Quality of life in the clinical decision-making process

This strongly corresponds to the needs of a decision-making procedure shared by the patient and the physician [9] whereby they should reach a clinical decision in which the patient's preferences are fully incorporated. The currently prevailing ethical principle of respect for the patient's autonomy [10] supports the concept of shared clinical decision-making. Its psychological counterpart is the 'adult' patient-physician relationship [11].

Objectively informing the patient is not necessarily an easy task, and instruments proposed in cancer literature [12, 13], like the 'decision boards', which incorporate the description of expected clinical scenarios, may be of assistance in the process. If one wishes to go further in the formalization of the decision-making process, tools to elicit patient utilities are available as well, such as the 'standard gamble' [5], for possible use in combination with clinical scenarios. In conceptual terms, what is important is that the patient be fully informed of the objective consequences of a given health state and thus be able to express his/her own evaluation of what the quality of his/her life would be in that health state.

In conclusion, quality of life can be incorporated into clinical decisions by two approaches, as outlined in Figure 4. The first approach moves from clinical studies, tries to assess average values for both survival and quality of life, perhaps combining them into a comprehensive value (e.g., a quality-adjusted life expectancy), to help the medical community establish the state of the art: the patient will be offered the 'standard' treatment, i.e., the best treatment available according to both survival and quality of life. A different approach would move from clinical studies, insofar as they quantitatively assess survival and are descriptive of quality of life, to let the medical community establish the state of the art basically on survival data, while leaving to the physician the task of properly informing the patient and sharing with him/her the final choice, which should be based both on state of the art and, at least conceptually, subjective
utility values for expected health states. Descriptive data on quality of life extracted from clinical studies could perhaps lead to the formalization of clinical scenarios as aids to the process of patient information about expected health states.

This would seem to have strong implications for quality-of-life assessment in clinical studies. Depending on which of the two approaches one chooses, assessment of the quality of life can follow one of two paradigms. The currently prevailing one can 'measure' population values for the quality of life related to different treatments and thereby provide an average score to correct life expectancy for a patient population undergoing a given treatment. The focus is on treatment comparisons rather than on descriptions of health state. Alternatively, quality of life assessment could try to objectively 'describe' health states, i.e., to provide a 'health state description' for each of the possible states following the treatments. The goal would be to let the physician properly inform the patient and arrive with him/her at a shared clinical decision on which treatment to select. This second paradigm might correspond to some change in the operational definition of quality of life. Even though the concept of quality of life should incorporate the physical, functional, psychological, social, and possibly spiritual domains, it might be wise, for example, just to study the physical and functional implications of health states, leaving it to the individual to evaluate how his/her psychological, social and spiritual attitudes could be affected thereby.

The second paradigm might correspond more closely to the ethical principle of respect for the patient's autonomy in the clinical decision-making process and render quality of life a subjective treatment end-point. Indeed, comprehensive quantitative scores would remain useful in other respects. In particular, health policy decisions, which deal with populations rather than individuals, may benefit from the incorporation of average quality of life data into comprehensive outcome indicators. Thus, 'cost-utility' analysis [6, 14], providing a ratio between costs and QALYs, may well be used by health administrators for population-based decisions incorporating quality of life in addition to survival. Of course, health policy decisions affect individuals insofar as they belong to a population. However, it may be acceptable that population values sometimes prevail over individual values in large-scale decisions. Likewise, registration of new drugs can well take into account average quality of life assessments, such as the scores provided by the currently used quality-of-life instruments. If a new drug is demonstrated to improve the average quality of life in a given patient population, this may well be enough for it to be registered. Our point is that the drug is registered, inasmuch as it 'can' be offered to the patient during a shared decision-making process. Nonetheless, because of patient-tailored quality of life considerations, it can well be that the individual decision will be not to use the drug.

In summary, it would probably be unacceptable to let the individual clinical decision-making depend entirely on population values for subjective variables. These values may differ from those of the actual patient, and the patient could well deduce them directly by him/herself. To do this, clinical studies would have to look for 'health state descriptions' in addition to average 'quality of life' scores (the latter to be used in other situations, e.g., for registrational evaluation). How to achieve rigorously formalized 'health state descriptions' within clinical studies and how to use them in clinical practice would be a good subject for methodological research.

References


Figure 4. The two pathways leading from clinical research to clinical decisions incorporating quality of life.


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