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Feature Articles

Offering Choice of Treatment to Patients With Cancers. A review based on a symposium held at the 10th Annual Conference of The British Psychosocial Oncology Group, December 1993

M.A. Richards, A.J. Ramirez, L.F. Degner, L.J. Fallowfield, E.J. Maher and J. Neuberger

INTRODUCTION

MARKED cultural changes have occurred in Europe and the U.S.A. over the past 30 years, with an increasing concern for individual autonomy and the rights of the consumer. Changes in medical practice have occurred which reflect these broader changes in society. Increasing emphasis is now placed on the provision of information to patients and on their participation in decision making about their management. Until the 1960s, it was rare even in the U.S.A. for patients to be told they had cancer [1]. By 1979 the reverse was true [2]. In Europe the pace of change has been variable, with use of the word "cancer" being considerably higher in Scandinavian than in Latin countries [3]. However, there is a widespread trend towards more open disclosure [3].

Involving patients in the decision making process (often abbreviated to "offering choice") could have both advantages and disadvantages for them. Proponents of offering choice may hope that this will lead to higher levels of patient satisfaction with care and improved acceptance of treatment [4]. It might also lessen psychological morbidity and improve quality of life. Against this, offering choice could place an undue burden of responsibility on patients [5]. Revealing uncertainty about the "best treatment" could lead to a loss of confidence in the doctor. Provision of the complex information required to make a valid choice may lead to confusion and could challenge a psychological response of denial/avoidance. Choice of a treatment which subsequently proves unsuccessful might induce feelings of self blame and regret in the patient.

In order to establish what constitutes good practice in this area, data and arguments presented at the 10th annual conference of the British Psychosocial Oncology Group have been summarised in this article, alongside evidence from published reports. In a symposium on "offering choice", there were presentations on patients' preferences for participation in decision making (Professor Lesley Degner) and on related clinical and psychosocial issues (Dr Jane Maher and Dr Lesley Fallowfield). Ethical issues surrounding "offering choice" were set in the context of four basic principles of medical ethics—beneficence, non-

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maleficence, autonomy and equity—by Rabbi Julia Neuberger. Choice should be available to patients if it can be shown to be of benefit and not to be harmful. Good practice should involve respect for a patient's autonomy. Equity/justice demands that, if offering choice is beneficial, it should be available to all patients.

Conflicts between the four ethical principles can, however, potentially arise. Offering choice could give rise to psychological distress, possibly in certain groups of patients and maybe only in the short term. Thus, in offering choice, respect for a patients' autonomy may be at the expense of non-maleficence. Many doctors were taught early in their careers "First do no harm". They may, therefore, take a paternalistic stance, giving greater emphasis to non-maleficence than to autonomy. An alternative, more rational approach is to evaluate the psychological impact of offering choice, and in particular to identify conditions in which it may be associated with increased distress. The information given to a patient who indicates a desire to participate in decisions about his/her clinical management should then include the risk of experiencing distress related to the process of participation.

WHAT DO CANCER PATIENTS WANT?

Information

If cancer patients are to be involved in decision-making, they require the necessary information on which to base judgements. Do they want such information? The literature from Europe is sparse, but studies in the U.S.A. have shown that the overwhelming majority of patients want detailed information not only about diagnosis, but also about treatment and outcome [6–8]. In a study of 256 patients with a variety of cancer types, surveyed on average 10 months post diagnosis, over 95% wanted to have information concerning "whether or not it is cancer", "what the treatment will accomplish", "what all possible side effects are" and "what the likelihood of cure is" [6]. Approximately 60% of patients believed they absolutely needed this information and 80% wanted "as much information as possible, good or bad". Seeking detailed information was significantly related to being young, caucasian, better educated and having been diagnosed recently [6]. A desire for detailed information has also been reported among Canadian and Australian cancer patients [9, 10]. Patients appear to rate effective communication with their doctor about their illness as being of equal importance to issues of technical competence related to their treatment.

Participation in decision making

A patient's desire for information about cancer does not necessarily mean that he or she will want to participate in decision making, although the two are correlated [6, 9]. In the study by Cassileth and coworkers, only approximately 60% of patients expressed a preference to participate in decisions regarding medical care and treatment, compared with more than 95% who wanted detailed information [6]. Similarly, Sutherland and associates noted that, although most of their patients sought information, a majority preferred the physician to assume the role of primary decision maker [9]. Thus, when they have the information, patients may express their autonomy by opting not to make decisions.

Professor Lesley Degner described how the extent to which patients wish to participate in decision making can be considered as a continuum. At one end, patients prefer to leave all decisions regarding treatment to their doctor (a passive role). In the middle, patients prefer to share responsibility with their doctor (a collaborative role). At the other end, patients prefer to make the final selection about treatment they will receive (an active role). Studies on the preferred roles of 436 cancer patients and 482 householders have been reported from Manitoba, Canada [11]. The procedure involved showing each individual five cards (two at a time) each of which described a possible role. An order of preference was thereby established. The results are summarised in Table 1, together with preliminary information using the same methodology on a second cohort of Canadian patients (limited to those with breast cancer) and patients studied in a breast unit in England (K. Luker and K. Beaver, University of Liverpool).

In keeping with the other Canadian reports [9], the majority of patients in Degner's first study (59%) preferred that physicians made treatment decisions on their behalf, but many expressed a desire for their opinions to be seriously considered in this process. Patients' preferences for participating in decision making were unrelated to their levels of distress or stage of their disease. Younger and more highly educated patients preferred more active participation, as did women (particularly those with reproductive cancers). However, these factors accounted for only 15% of the variance in patients' preference to participate.

This study also showed a marked difference between Canadian cancer patients and the general public, who showed a much higher level of preference for an active role. Similar proportions of British and Canadian breast cancer patients wished to adopt an active role (Table 1). A larger proportion of British women, however, preferred to adopt a passive rather than a collaborative role. Interestingly, patients with benign disease appeared to be intermediate between cancer patients and the general public in their role preferences. These data taken together suggest that the closer a person is to the diagnosis of a life threatening illness, the more inclined they are to delegate the decisional responsibility to the doctor.

WHAT FACTORS INFLUENCE A PATIENT'S CHOICE?

If patients are given the opportunity to choose between treatments, a number of factors are likely to affect their decision making. Patients' preferences may be influenced by their attitudes and beliefs based on previous experience, family, friends, the media and other health professionals. Their ability to avail themselves of treatment choices may be determined by their physical status and support network. For example, they may desire a particular treatment option, but be precluded from this because of difficulties in attending the hospital.

Dr Jane Maher highlighted the ways in which doctors attitudes influence the decision making process about treatment. She presented data from a study in which 600 oncologists from 21 countries were asked what treatment they would recommend for a patient with advanced non-small cell lung cancer [12]. The total dose and number of fractions of radiotherapy varied widely between respondents, with American oncologists generally recommending more intensive therapies than those in Europe or Canada. Oncologists who felt that the aim of treatment was to extend life, to prevent symptoms or to give hope were likely to give more treatment than those whose aim was to relieve symptoms. Economic factors and the availability of radiotherapy equipment may also influence treatment decisions, although these factors were not specifically examined in the study by Maher and coworkers [12].

The way in which information is presented may influence choices between alternative therapies. This has been evaluated for operable lung cancer (surgery or radiotherapy) using patients

Table 1. *Preferences for participation in decision-making*

	n	Active	Collaborative	Passive
Canadian cancer patients (1st cohort)*	428	12%	29%	59%
Canadian householders*	271	64%	27%	9%
Canadian breast cancer patients (2nd cohort)†	478	22%	40%	38%
British breast cancer patients†	150	20%	28%	52%
British benign breast disease patients†	200	24%	45%	31%

* Degner and Sloan [11].

† Data presented by Professor Degner at the 10th annual conference of the British Psychosocial Oncology Group, 1993 including data from the U.K. (K. Luker and K. Beaver, University of Liverpool).

with chronic medical conditions, graduate students and physicians as surrogates for cancer patients [13]. Choices varied significantly according to the way in which life expectancy was described, and according to whether the outcome was framed in terms of the probability of living or the probability of dying. The proportion of subjects choosing radiotherapy was lower when the two treatments were identified rather than being referred to as treatments A and B. However, in a study of patients making decisions about adjuvant therapy for breast cancer, the framing of treatment outcomes did not appear to influence the type of treatment chosen [14]. Patients generally followed the physician's recommendations, except when choosing whether to participate in a clinical trial [15, 16]. In another study, "trust in the physician" was cited most frequently by patients as their most important reason for accepting chemotherapy on an investigational protocol [17].

The nature of the risk and benefit involved in different treatment options may influence decision making. In some clinical situations, choice of treatment may influence overall survival (e.g. systemic adjuvant therapy for breast cancer), while in others outcome may vary in terms of local relapse (e.g. mastectomy versus breast conservation therapy). The cost in terms of toxicity may also differ between treatments (e.g. for tamoxifen or chemotherapy). The decision making process is also influenced by the extent of knowledge about the advantages and disadvantages of different options. For some clinical situations, there is an extensive knowledge base. In the choice between breast conservation and mastectomy, the equivalence of the two treatments in terms of survival and psychiatric morbidity has been demonstrated in randomised controlled trials. Patients may opt to undergo breast conserving therapy to preserve body image or may choose mastectomy to minimise the chance of local recurrence. Similarly, in considering the potential advantages and toxicities of adjuvant chemotherapy for breast cancer, hard data are available—although their interpretation may vary widely between physicians. However, in other clinical situations, such as the choice between palliative chemotherapy and supportive care for some advanced cancers, the relative value of the two treatments is less well documented. How can patients make choices without information—yet can doctors make any better decisions on their behalf?

WHAT DO PATIENTS CHOOSE?

There are still relatively few reports documenting which treatments patients select when provided with the opportunity to make a choice, the majority of these being related to early breast cancer. It should be noted that even in centres which offer choice, approximately half the patients presenting with breast cancer may be considered unsuitable for breast conserving therapy on clinical grounds [18, 19]. Among patients who are offered choice, the proportion opting for breast conserving therapy varies between 35 and 75% (Table 2) [18–24]. Without detailed knowledge of the way in which the information was presented to the patients, it is difficult to assess the reasons for this variation. However, the studies do show that a considerable proportion of women elect to have a mastectomy, and that this is not simply a function of age.

Patients with stage D prostate cancer have been offered the choice between orchiectomy and Zoladex, a depot luteinising hormone-releasing hormone (LHRH) analogue [25]. Of the 147 patients studied, 78% selected Zoladex and 22% selected orchiectomy. The primary reason given for selection Zoladex was to avoid surgery. Convenience was the most frequently cited reason for the selection of orchiectomy.

DO PATIENTS BENEFIT FROM BEING GIVEN CHOICE?

Again the evidence is currently limited and is mainly related to early breast cancer. Levy and coworkers have raised the possibility that offering choice may increase distress, at least in the short term [26]. Other reports have been more reassuring. In a small study, Morris and Royle [21] observed higher levels of anxiety and depression in 10 women who could not be offered choice because of centrally located tumours than in 20 women who were offered choice. Fallowfield and coworkers [18] have compared the psychological outcomes for 269 patients treated by three groups of surgeons: those who prefer mastectomy, those who prefer lumpectomy and those who prefer to offer choice. Patients managed by the third group of surgeons had the lowest incidence of psychiatric morbidity. However, among 118 of these patients, no differences in anxiety or depression were observed between women who had a choice ($n = 62$) and those whose treatment was determined by the surgeon based on technical considerations ($n = 56$). The communication style of the surgeon may thus be more important than whether choice is actually given.

For women who have chosen their own treatment for early breast cancer, no differences in quality of life or functional status 8 weeks after surgery were observed between those who opted for lumpectomy and those who chose mastectomy [27]. Both groups of patients experienced similar amounts of distress related to the diagnosis of cancer.

How easy or difficult do patients find it to select their own treatment? In the study by Cassileth and colleagues [25] more

Table 2. Proportion of women choosing breast conservation treatment in preference to mastectomy

First author/date [Ref.]	Proportion choosing breast conservation		Country	Period studied
Fallowfield 1990 [18]	43/62	(69%)	U.K.	1987–1989
Cotton 1991 [19]	41/91	(45%)	U.K.	1988
Wilson 1988 [20]	54/153	(35%)	U.K.	1979–1987
Morris 1987 [21]	13/20	(65%)	U.K.	1985–1986
Wolberg 1987 [22]	54/110	(49%)	U.S.A.	1981–1985
Sauer* 1992 [23]	773/1036	(75%)	Germany	1983–1989
Pozo 1992 [24]	15/39	(38%)	U.S.A.	Not stated

* 62 patients in this study were randomised between breast conserving therapy and mastectomy. Over 90% of patients were treated according to their own choice.

than 70% of prostate cancer patients indicated that the decision was "not too difficult", but approximately 10% found it "very" or "extremely" difficult. Consistent with this, approximately 70% of patients were able to make a choice right away rather than wavering backwards and forwards. Three months after starting treatment, almost all the patients stated that they would make the same decision again. Among the patients with early breast cancer studied by Fallowfield and coworkers, 8 of 62 (13%) who were offered choice could not make the decision and asked the surgeon to do so on their behalf. A further 15 patients (24%) experienced some or considerable difficulty [28]. Patients were asked 3 years after surgery how they felt about being asked to choose which operation they had. Almost half the women described positive reactions, while a fifth expressed quite definite reservations [28].

HOW SHOULD WE INVOLVE PATIENTS IN DECISION MAKING?

As patients differ in the amount and type of information they want, and in the degree to which they wish to participate in decision making, doctors need to be responsive to the wishes of individual patients [29]. Good communication skills are of paramount importance to ensure that patients' concerns and priorities are elicited, and that explanations about treatment have been understood.

Prior to a key interview, a patient may be assisted in deciding what questions he wishes to ask and what level of participation in decision making he wants by a nurse specialist [30]. After the consultation, the nurse can help to clarify any remaining questions, and can verify the patients' understanding of the information. Patients may find it helpful to be accompanied by a friend or relative.

Some patients may benefit from being given an audiotape of the interview [31], but the effects of audiotapes on recall and on psychological disorder need to be evaluated [32]. Written information can also be used as an adjunct to verbal communication, but is of secondary importance as a remembered source of information [17]. Visual displays of complex information are currently being evaluated as aids to decision making [33].

CONCLUSIONS

The study of patient participation in decision making is still in its infancy. More systematic enquiry is needed to evaluate the process of giving patients unbiased choice, and whether patients' preferences are influenced by the type of cancer, its stage or the nature of the risks involved in different treatment options. Most importantly, the long term consequences of involving patients in decision making need to be understood. Does "offering choice" confer benefit? Are there any circumstances in which it may be detrimental to the patient?

Patients' preferences for being involved in decision making are likely to change in parallel with the changing values in society. Currently, what many patients appear to want is adequate information as to why one treatment is being recommended as opposed to another, rather than necessarily wanting to take the ultimate decision. Patients who wish to be involved in decisions about their treatment should clearly be enabled to do so. Equally, it is the right of patients to choose to delegate that responsibility to their physicians. Doctors must attempt to tailor their approach to the wishes of the individual patient.

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Apoptosis in the Embryo and Tumorigenesis

G. Prindull

INTRODUCTION

PROGRAMMED CELL DEATH (apoptosis) as a targeted active metabolic process leading to the demise of individual cells is an inherent property of rapidly proliferating cell renewal systems. It does not require prior arrest of the mitotic cycle, but occurs during G_1 and/or S phases [1–3]. Several distinct "death pathways" appear to be available to physiological and neoplastic cell systems [4, 5]. Apoptosis is a response to environmental growth factors and antibodies. The propensity to apoptosis is counterbalanced continuously in the cell by genes stimulating cell survival and proliferation. Genes inducing apoptosis include *p53*. *BCL-2* counteracts apoptosis, and *C-MYC* can promote both cell proliferation and apoptosis.

Apoptosis is the terminal event in the natural history of cell differentiation. In segmented neutrophils, high levels of DNAse activity have been found [6–8]. Environmental factors may trigger apoptosis at earlier stages of cell differentiation. It then becomes a physiological means of eliminating "unwanted" cells, such as auto-reactive cells [9–12], "hyperactive" T-lymphocytes [13], and neoplastic cells [14–16]. Tumour suppressor genes inhibit malignant cell growth by inducing apoptosis. A marked inherent propensity to apoptosis is displayed by hyperdiploid leukaemias, and may account for their relatively good prognosis [17]. Apoptosis is also a key mechanism in antitumour therapy. A number of cytostatic drugs, including the anthracyclins and glucocorticoids [18–20], kill cells by activating apoptotic pathways [14, 16], a process that in some leukaemias can be influenced by cytokines [21]. It should be emphasised at this point that not all forms of individualised cell death necessarily are apoptotic: tumour associated CD8+ lymphocytes and NK cells predominantly induce neoplastic cell death directly by osmotic lysis of cell membranes and cytoplasm [22].

We have pointed out repeatedly that some paediatric neoplasms can be considered as resulting from abnormal processes during embryonal ontogeny [23, 24]. The embryo must develop protective mechanisms against the generation and expansion of neoplastic cell clones, similar to the elimination of auto-reactive lymphocytes. Apoptosis is a key mechanism of eliminating such

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