

COMMENTED SUMMARIES FROM CURRENT MEDICAL LITERATURE

COMPREHENSION DURING INFORMED CONSENT IN LESS-DEVELOPED COUNTRIES

Summary: Few practical guidelines exist on how to ensure that research participants in less-developed countries understand consent forms before enrollment. In a study of HIV-1 transmission in Haiti, participants were required to pass an oral examination on the contents of the consent form with a passing score of 12/15 (80%) before enrollment. Fifteen individuals were given information during a single meeting with a physician, and only three (20%) passed. Thirty subsequent volunteers were given information by a counselor during three meetings, and 24 (80%) passed. Formal assessment of research participants' comprehension of the consent form should be considered as a routine step in the informed consent process in less-developed countries.

Comment: Lack of information about safeguarding the interests of patients in biomedical research in developing countries is a major topic for ethical discussion. Unfortunately, neither medical ethics committees nor biomedical journal editors in Iran pay attention to this extremely crucial issue. No fully empowered organization exists in the country to supervise the process of obtaining consent from subjects entering into biomedical research studies and, in particular, clinical trials. Neither is there an authorized body at a high level of government checking the content of the consent forms. The figures presented in the above abstract simply mirror the level of public information about patients' rights in research in most parts of the world, particularly developing countries. The Ministry of Health and Medical Education has recently developed a 27-clause document with regard to respect for patients' rights in biomedical research. Although one can refer to it to find the most important points for developing an informed consent, the document does not meet all the researcher's needs in developing a consent form. The issues we refer to here are the paramount points about respecting the patients' rights in research. The following matters have been derived from reputable medical and bioethical resources including the Helsinki and Belmont declarations. For easy application, we present here the topics as a question-form checklist. The questions have been sorted by significance from top to bottom, with number 1 being most important:

1. Do investigators obtain written informed consent or oral consent that has been witnessed and verified by the subjects?
2. Do subjects have physical and mental capability of giving consent? If not, do investigators obtain consent from the legally authorized representatives for legally incompetent person?
3. Will subjects' physical and mental condition change in the period of study? If yes, do investigators obtain consent from them or the legally authorized representatives?
4. Does the informed consent form explain the nature and the purpose of the research?
5. Do subjects volunteer to participate in the study?
6. Is the volunteerism of the subject free of coercion and undue influence?
7. May subjects abstain from participation in the study or withdraw consent to participate at any time without penalty or reprisal?
8. Is the informed consent form copied for subjects to retain?
9. Is the informed consent form collected by a medically qualified person with responsibility for treating the patient?
10. Do investigators ascertain that the subject comprehends the information?
11. Do investigators focus on developmental factors, psychologic issues and illness-related considerations?
12. Is the source of funding clear?
13. Do investigators inform subjects about how long the trial will last and what will happen when it ends (for clinical trials)?

Commented Summaries

14. Do investigators inform subjects about their diagnosis, the nature of their condition and the treatment available?
15. Does the informed consent form have details about reimbursement and indemnity?
16. Do investigators respect subjects' privacy and confidentiality?
17. Do investigators inform subjects about serious risks that are rare, and about less serious events, which are expected to happen more often?
18. Do informed consent forms have the contact name and telephone number of the investigator when needed?
19. Does the investigator describe any benefits to the subject or to others which may reasonably be expected from the research?
20. Do investigators answer subjects' questions properly?
21. Does the investigator explain whom to contact for answers to subjects' question and whom to contact during the course of the research?
22. Do investigators use audio or videotapes to improve patients' understanding of the information?
23. Do the informed consent forms have names of project sponsors and director/coordinator?

We suggest that all research committees concentrate on these common implications when they evaluate research proposals, especially in the setting of clinical trials and other interventional studies. Also, journal editors should pay attention to a guideline in which the most fundamental implications are included regarding ethical standards of obtaining consent from human subjects before giving permission to the authors for publishing such works.

Saeed Shahraz MD, Academy of Medical Sciences,
Elnaz Jafarimehr MD, Research Center for Gastroenterology and Liver Diseases,
Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

Source: Fitzgerald DW, Marotte C, Irene Verdier C, et al. Comprehension during informed consent in a less-developed country. *Lancet*. 2002; **360**: 1301 – 2.

References:

1. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Protection of human subjects: Belmont Report—ethical principles and guidelines for the protection of human subjects of research. *Fed Regist*. 1979; **44**: 23192 – 7.
2. Sommerville A. Informed consent and human rights in medical research. In: Doyal L, Tabias JS, eds. *Informed Consent in Medical Research*. 1st ed. London. *BMJ*. 2001: 249 – 57.
3. Wager E, Tooley PJ, Emanuel MB, et al. How to do it. Get patients' consent to enter clinical trials. *BMJ*. 1995; **311**: 734 – 7.
4. Protection code of human subject. Booklet of Principles of Medical Ethics. Ministry of Health. 2001.
5. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. *J Postgrad Med*. 2002; **48**: 206 – 8.
6. Skene L, Smallwood R. Informed consent: lessons from Australia. *BMJ*. 2002; **234**: 39 – 41.
7. Roberts LW. Informed consent and the capacity for voluntarism. *Am J Psychiatr*. 2002; **159**: 705 – 12.
8. Meslin EM. A perspective from the USA and Canada. In: Doyal L, Tobius JS, eds. *Informed Consent in Medical Research*. 1st ed. London. *BMJ*; 2001: 148 – 55.
9. Bernard LO. Addressing ethical issues. In: Hully SB, Cummings SR, Warren S, et al, eds. *Designing Clinical Research*. 2nd ed. Philadelphia: Lippincott Williams and Wilkins; 2001: 215 – 20.
10. Alderson P. Will you help us with our research? *Arch Dis Child*. 1995; **72**: 541 – 2.
11. Macklin R. Informed consent for research: international perspectives. *J Am Med Womens Assoc*. 2000; **55**: 290 – 3.
12. Shapiro HT, Meslin EM. Ethical issues in design and conduct of clinical trials in developing countries. *N Engl J Med*. 2001; **345**: 139 – 42.
13. Zali MR, Shahraz S, Borzabadi S. Bioethics in Iran: legislation as the main problem. *Arch Iranian Med*. 2002; **5**: 136 – 40.

THE ROLE OF THE AUTOPSY IN MEDICAL MALPRACTICE CASES. II: CONTROVERSY RELATED TO AUTOPSY PERFORMANCE AND REPORTING

Summary: We studied 99 appellate court records in cases of alleged medical malpractice and found no relationship between discrepant clinical and autopsy findings and outcome of litigation. Standard-of-care issues and not diagnostic accuracy were at the heart of every case.

Our purpose was to characterize and discuss issues related to the autopsy and/or pathologist behavior that were raised in court records of medical malpractice litigation.

In 18 appellate court records, issues were raised about quality of autopsy performance and reporting, or about death certification. The details of these controversies are seriously reported here in a manner intended to be instructive to pathologists who perform autopsies in a hospital setting or on a private, fee-for-service basis.

Autopsy reports are intended to provide objective medical information in a coherent format to the patient's medical record, to the attending physician and other concerned staff physicians, to other healthcare professionals, and to the families of the deceased. Inevitably, occasions arise that require legal counsel to be added to this list of parties with a legitimate interest. Our findings emphasize that incomplete, incoherent, obfuscated, or delayed reporting of autopsy findings do not meet professional standards, are unethical if intentional, and may be counterproductive.

Comment: There are two reports in this issue dealing with the role of autopsy for malpractice cases. Along with this, I review the benefits of autopsy, both for clinicians and families of the deceased.

Historically, the postmortem examination was an indispensable diagnostic tool. No one should underestimate the importance of the clinical information, skills and imaging studies in medical practice, both in community and teaching hospitals. Nevertheless, it must be clear that these will have restrictive value to the medical students, practitioners and patient outcomes, unless it is confirmed by observational study of pathology procedures. Over time, by all clinical efforts, the frequency of major discrepancies between clinical diagnoses and diagnoses based on pathologic findings, including autopsy, has not changed. In the article by these authors, of 99 cases of autopsy, only 27 confirmed the clinical diagnosis. There were 54 cases with major discrepancies between the clinical diagnosis and autopsy findings, of which 40 cases were diseases that, if known, were deemed potentially treatable. Several reports from Iranian pathologists support this kind of discrepancy (Dr. Armin from Tehran and Dr. Dutz from Shiraz). Thus, autopsy is of critical importance in the evaluation of clinical practice. It has benefits in medical education, counseling, proof-findings, and as a source of tissue for studies of pathogenesis of disease and other research.

Despite these facts, autopsy rates are declining in many countries, particularly in Iran. The reason for this decline, in general, is different from one country to another. Of the many contributing factors to this decline are medical malpractice cases in western countries, and reluctance of physicians in the Eastern world, including Iran, for cultural and religious reasons. For Muslims, autopsy presents several ethical dilemmas, even though the advantages attributed to postmortem examination in modern medicine are also acknowledged by them. Koran, The Holy Book, places no restriction on autopsy, but because of Islamic respect for the dead they have to be handled with great caution. The Iranian way of dealing with such questions is via legal and religious opinion of high-ranking clergy (Ayatollah Ozma) through a contemporary opinion called Fatwa (religious-approved opinion). Today, according to religious and legal point of view, autopsy performed for medical research and training, and determination of cause of death is permissible. The Iranian Forensic Medicine Department has been performing autopsy according to law. They are not affiliated to universities, but rather are under the Jurisdiction Department.

Other reasons for this decline include: improvement in the medical diagnostic technology available; inadequate training of doctors as to the importance of autopsy; difficulties in obtaining consent from relatives; and certain legislative restrictions. There is another, less important, reason for the decline in autopsy performance: as there may be discrepancies between autopsy findings and clinical management, clinicians do not favor autopsy for their reputation and future career activity.

To maximize the benefits of autopsy for clinicians, medical students, residents, families and the community at large, the following steps must be taken: 1) change in the methods of obtaining consent (using trained autopsy advocates and enhancing awareness of cultural issues); 2) modification of autopsy procedures (the information obtained at autopsies is often unused or is unavailable to families and clinicians); 3) improvement in communications between clinicians and families (collecting clinicians' and

Commented Summaries

family contact information on autopsy permits; allowing students to attend and conduct postautopsy conferences); and 4) educating both medical professionals and public citizens about the value of autopsy.

Moslem Bahadori MD, FCCP. Professor and Consultant Pathologist, NRITLD.

Source: Bove KE, Lery C. The role of the autopsy in medical malpractice cases. II: controversy related to autopsy performance and reporting. *Arch Pathol Lab Med.* 2002; **126**: 1032 – 5.

TREATMENT OF BREAST CANCER: TO BE CONSERVATIVE OR INVASIVE

Summary: We conducted 20 years of follow-up of women enrolled in a randomized trial to compare the efficacy of radical (Halsted) mastectomy with that of breast-conserving surgery.

From 1973 to 1980, 701 women with breast cancers measuring no more than 2 cm in diameter were randomly assigned to undergo radical mastectomy (349 patients) or breast-conserving surgery (quadrantectomy) followed by radiotherapy to the ipsilateral mammary tissue (352 patients). After 1976, patients in both groups who had positive axillary nodes also received adjuvant chemotherapy with cyclophosphamide, methotrexate, and fluorouracil.

Thirty women in the group that underwent breast-conserving therapy had a recurrence of tumor in the same breast, whereas eight women in the radical-mastectomy group had local recurrences ($p < 0.001$). The crude cumulative incidence of these events was 8.8% and 2.3%, respectively, after 20 years. In contrast, there was no significant difference between the two groups in the rates of contralateral breast carcinomas, distant metastases, or second primary cancers. After a median follow-up of 20 years, the rate of death from all causes was 41.7% in the group that underwent breast-conserving surgery and 41.2% in the radical-mastectomy group ($p = 1.0$). The respective rates of death from breast cancer were 26.1 percent and 24.3% ($p = 0.8$).

The long-term survival rate among women who undergo breast-conserving surgery is the same as that among women who undergo radical mastectomy. Breast-conserving surgery is therefore the treatment of choice for women with relatively small breast cancers.

Source: Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* 2002; **347**: 1227 – 32.

Comment: In 1976, we initiated a randomized trial to determine whether lumpectomy with or without radiation therapy was as effective as total mastectomy for the treatment of invasive breast cancer.

A total of 1,851 women for whom follow-up data were available and nodal status was known underwent randomly assigned treatment consisting of total mastectomy, lumpectomy alone, or lumpectomy and breast irradiation. Kaplan-Meier and cumulative-incidence estimates of the outcome were obtained.

The cumulative incidence of recurrent tumor in the ipsilateral breast was 14.3% in the women who underwent lumpectomy and breast irradiation, as compared with 39.2% in the women who underwent lumpectomy without irradiation ($p < 0.001$). No significant differences were observed among the three groups of women with respect to disease-free survival, distant-disease-free survival, or overall survival. The hazard ratio for death among the women who underwent lumpectomy alone, as compared with those who underwent total mastectomy, was 1.05 (95% confidence interval (CI), 0.90 to 1.23; $p = 0.51$). The hazard ratio for death among the women who underwent lumpectomy followed by breast irradiation, as compared with those who underwent total mastectomy, was 0.97 (95% CI, 0.83 to 1.14; $p = 0.74$). Among the lumpectomy-treated women whose surgical specimens had tumor-free margins, the hazard ratio for death among the women who underwent postoperative breast irradiation, as compared with those who did not, was 0.91 (95% CI, 0.77 to 1.06; $p = 0.23$). Radiation therapy was associated with a marginally significant decrease in deaths due to breast cancer. This decrease was partially offset by an increase in deaths from other causes.

Lumpectomy followed by breast irradiation continues to be appropriate therapy for women with breast cancer, provided that the margins of resected specimens are free of tumor and an acceptable cosmetic result can be obtained.

Commented Summaries

Source: Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus Irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002; **347**: 1233 – 41.

Comment: Breast cancer is the most common cancer among women. Based on the published data, it seems that Iranian breast cancer patients are relatively younger than their western counterparts. Mastectomy for a young woman is frustrating and a more conservative treatment seems to be more appropriate. Furthermore, Iranian people usually would rather like to undergo much more conservative therapeutic modalities. As is shown in the above-mentioned studies, conservative treatments of breast cancer such as lumpectomy seem to be as good as mastectomy in certain cases in terms of survival and recurrence rate, provided that the tumor is not progressed substantially. Breast cancer comprises 12% of all female malignancies, and mostly present in advanced stages one. Consequently, early detection and screening programs should be emphasized.

M. Haghshenas MD, F. Habibzadeh MD, Shiraz University of Medical Sciences.

Source: Talei AR, Sadeghi-Hassanabadi A, Saalabian J, et al. A preliminary report on breast cancer screening program in Shiraz, southern Iran. *Iran J Med Sci.* 1997; **22**: 148.