Reflections on Controlled Clinical Trials in Surgery: A Plea for Clinical, Not Only for Statistical Criteria

Invited Comment

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Apart from the fact that controlled clinical trials are urgently required for developing clinical science, these middle-aged products [Hill, 1951] of medical methodology are highly fashionable – very similar to cimetidine, abortion, marihuana and the peace movement. Numerous articles (and very often very similar ones) are written and published every week on this particular subject. In the general public two kinds of emotional reaction to them are observed. Random and heartless assignment of individuals to rigid treatment groups, enslavement of uninformed patients to endure human experimentation, capital punishment for poor subjects in the control group of a trial (why only in the control group?): these are the nightmares of an emancipated, superficially informed society. Unfortunately, the cultivated anxieties of our patients are opposed to similarly dangerous ecstasies of our scientific community. Controlled clinical trials are demanded for any clinical problem (e.g. ‘randomization of the first patient’). A distinguished audience gets a gleam in their eyes if a ‘controlled clinical trials has shown that this completely new drug developed only yesterday

is superior to placebo treatment at a significance level of $p < 0.00001$.

However, more distinction is necessary, and this will help answer a simple surgeon’s philosophical and practical dilemma when he intends to conceive, to conduct or to participate in a controlled clinical trial.

Firstly, more time and intellectual effort should be devoted to the *clinical* aspects of a trial.

While statistical, legal, and ethical aspects now receive ample, if not undue, attention, clinical trials often fail because relevant existing information has been neglected, clinically unimportant end-points have been selected, known prognostic factors have been omitted, clinical pharmacology has been ignored, methods of assessment are imprecise, follow-up is incomplete and quality control is lacking.

Secondly, clinical trials fall into different categories, and the distinction is relevant to the question of informed consent: There is the comparison of two standard treatments, the comparison of an advanced new therapeutic or diagnostic regimen with routine management and the trial involving human experimentation (such as implantation of an

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artificial heart). The Workshop on Clinical Trials of the German Surgical Society [Lorenz et al., 1982] has recommended that only for trials of standard treatments which are administered

routinely and are expected to be equally effective, informed consent about randomization is *not* considered absolutely necessary. However, the term 'equally effective' needs a more ample definition in controlled clinical trials: 'effective' is not only pertinent to the physical but also to the psychological and social consequences of treatment. In comparative trials on standard operations for breast cancer 'equality' does not exist if in one of the surgical interventions the breast of the patient is completely removed, but not in the other.

As *G. Merlo* has stated in his article, 'the complicated organisation and undoubted practical difficulties of implementing a surgical trial make almost all that are undertaken rather expensive'. Indeed, more than any other criteria the clinical quality of a controlled trial can distinguish between research which aims at improving medical care or at establishing a medical career.

References

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