A Proposed Road Map for the Ethical Evaluation of Sham (Placebo) Surgery

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Objective: The study proposes a possible roadmap for the ethical assessment of sham surgery clinical trials (CTs), focusing on methodological aspects, as a result of the lack of this type of practical tool in the literature/practice.

Background: Surgical procedures are frequently conducted without closely controlled studies. For this reason, these procedures are less rigorous than those for drug/device clinical trials. The aim of a sham (placebo) surgery CT is to carry out a surgical CT with a legitimate control group. The use of sham surgery is controversial from an ethical point of view.

Methods: This evaluation system is set up according to ICH/GCP, World Medical Association Declaration of Helsinki, CONSORT 2010 standards. The proposed roadmap is based on the following 4 steps/levels: safety/clinical indications; adequacy of trial methodology/design adopted for a sham surgery CT; specific informed consent, and economic issues.

Results: A flowchart is proposed which can be used at two levels: as a basic guideline for the design of a surgical protocol representing a benchmark level of care; and a multiaxial assessment considering the first two sources of morality of human acts according to Aristotelian ethics: the object of the act (step 1) and some of its circumstances (steps 2–4).

Conclusions: The use of a placebo and of double-blind control groups in surgery CTs would improves the quality of results, providing that an accurate ethical assessment procedure is in place, firstly to ensure patient safety and secondly to prevent abuses/procedural biases. Future testing of the proposed flowchart is outlined.

Keywords: assessment, clinical experimentation, ethics, sham surgery

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Current surgical procedures are frequently based on uncontrolled studies: few controlled randomized surgical clinical trials (RCTs) are reported in the literature. Therefore, these procedures are less rigorous than those for drugs and/or devices. The standard of assessment for surgery is usually lower, because of the greater complexity of conducting surgical RCTs in terms of both scientific validity and ethical soundness. A double-blind/placebo-controlled RCT represents a benchmark standard in the evaluation of new procedures/drugs, ensuring avoidance of biases while monitoring the placebo effect. As regards clinical research, it is clear that the risk for the placebo group during surgical trials is higher than in pharmacological trials.

Sham surgery is "a treatment or procedure that is performed as a control and that is similar to, but omits a key therapeutic element of, the treatment or procedure under investigation."[1] The aim is to carry out a surgical RCT with a control group, thereby permitting comparison of a surgical technique with a sham (placebo) procedure and thus achieving a double-blind/placebo-controlled RCT.

According to Wartolowska et al, 53 clinical trials have been performed with a sham control group. The authors conclude that "the results provide evidence against continued use of the investigated surgical procedures. Without well-designed placebo controlled trials of surgery, ineffective treatment may continue unchallenged."[2] Despite this, "surgery of any form, including placebo surgery, is associated with some level of risk, whereas a placebo tablet or drug is not (...). Therefore, the balance between risks and benefits in placebo surgically controlled RCTs is different from that in drug trials."[2] Indeed, the use of sham surgery is much debated from the ethical point of view,[3–8] particularly regarding ethical issues, deception, and informed consent. According to Tenery et al,[6] "In addition however, the use of surgical placebo controls requires a careful assessment of the specific scientific benefits, and also surgical risks, such as anesthesia or infection, which should be as low as possible."

Already in 1961, Beecher[4] stated that researchers should investigate the extent of the placebo effect so that dangerous surgical procedures that were no more effective than placebos would not be performed. A report on internal mammary artery ligation in 1950s[3,6] for patients with myocardial ischemia proves the point. Consequently, strict requirements such as those proposed by the Council on Ethical and Judicial Affairs of the American Medical Association (2002) are needed for ensuring the ethical acceptability of sham surgery.[6]

Given the inherent conflict between observing the highest standards in both research design and ethics, our opinion is that neither should prevail, but that the highest level of research design should be combined with the highest ethical standards. In the meantime, we believe that the debate on the use of sham surgery is overly focused on specialist cases, whereas we need an affordable, and hopefully shared, framework for ethical assessment. Because, in general,[5–7] the literature includes few attempts at producing requirements for ethically sound sham surgery,[7] despite several surgical trials including sham surgery in their design are registered [648 ongoing or completed trials are listed in "clinicaltrial.gov" website (accessed May 26, 2016)], and also considering the not yet fully resolved ethical reflections on it, we believe it may be useful to propose a methodological road map for more detailed and accurate ethical assessment. This tool can be useful for both Independent Ethics Committees/Institutional Review Boards (IEC/IRB) and single researchers.

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