

# iVIEW

EDITOR'S PAGE

## The Ethics of Publishing Medical Imaging Research

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Although the editorial process is generally a placid activity, whereby the collective wisdom of the reviewers and editors provides a clear path, we are from time to time faced with issues that generate a lot of animated debate. This issue of *JACC* contains a report that triggered an important discussion among the Editorial Board. Yin et al. (1) compared 2 different image acquisition and reconstruction protocols for coronary computed tomography (CT) angiography for their diagnostic accuracy in 60 patients who underwent invasive catheter-based coronary angiography for clinical reasons. The investigators provide valuable insight into radiation dose reduction that is possible using a new iterative reconstruction algorithm in combination with modified image acquisition protocols. Clearly, this was an important clinical question, and the study was nicely done. However, all patients underwent 2 separate coronary CT angiographic acquisitions for research purposes, which of course immediately caught our attention and generated questions about the ethical implications of subjecting patients to 2 separate CT acquisitions, with the associated contrast injections and radiation exposure, purely for research purposes. Although the average overall effective dose per patient was about 2.5 mSv (substantially lower than the dose of a single coronary CT angiographic exam in numerous previous research protocols), we remain intrigued. What would we have done if the radiation dose were higher? Would the information in such a study justify the higher risk to its participants? What range of radiation would be unacceptable given that we are unaware of a threshold dose below which radiation is not harmful? Should such research have even been allowed by the ethics committee in the first place?

Should research be published just because the study has already been done?

Furthermore, although the investigators clearly indicated that institutional review board (IRB) approval had been obtained, how much more should the editors of a journal police for research ethics, when they perceive something as questionable? Although no concern remained regarding this particular report, this is not always the case. For example, in a previously submitted (and ultimately published) report, the researchers described coronary CT angiographic investigations performed before invasive workup of 87 patients admitted with ST-segment elevation myocardial infarctions (2). Although IRB approval had been obtained, the report was accepted only after the Editorial Board was convinced that patient treatment was not delayed by the research CT. As should have been the case, a discussion ensued after publication, with a letter to the editor questioning the research and publication ethics (3,4).

Because science is based on trust, journals usually take submitted manuscripts at face value, respecting the sanctity of IRB approval and the investigators' assurance that the study was conducted ethically. Clearly egregious cases are easily identified and denied entry to the publication domain. What about cases that are not so clear? Should editors question research ethics beyond the mere requirement that investigators obtain and indicate IRB approval, and if so, how much further delving is reasonable? A quick reflex answer would be in the affirmative; editors must police ethics. Such questions often do not have straightforward answers. While we at *JACC* tend to fall on the more rigorous side of this question (sometimes going beyond the investigators' declarations to ascertain that proper IRB approval was obtained and that all possible ethical rigor was maintained in the conduct of a study), we continually remain cognizant of the intricacies (and sensitivities) associated with such a question.

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Questioning research ethics, although a sensitive issue, could be regarded as an editors' right or as an obligation, and we endorse this position strongly. Clearly, the editors of a journal have the right to pose specific questions to manuscript authors and to require further explanation of critical aspects, including ethics. Their scientific expertise will typically go way beyond that of the members of an IRB, and they may be able to recognize problems where nonexperts would not. IRBs are chartered differently in each country, often without accreditation (5). Even regulatory agencies, let alone editors, often have no way of ascertaining the efficacy of an IRB (6) or that IRB approval means that the approved research followed the best ethical standards. Others have been even more dismissive about their performance (7). IRB expertise is highly variable, and this, coupled with high workloads, means that IRB approval is no guarantee that research has the best possible risk-benefit balance. A 2005 report showed that IRBs at major research universities in the United States had an average of 16 members, and together they reviewed hundreds of proposals; higher volume centers reviewed more than 1,000 proposals each year (8). These numbers have further increased. Clearly, journals and editors have a crucial role in making sure that research follows the best ethical practices throughout the study, in addition to whatever the IRB approved at the start of the study, but remembering that the process is often difficult to accomplish fairly. It could also be an obligation if a possible violation of basic ethical principles is suspected. The Declaration of Helsinki in its latest version, dating from 2008, clearly states, "Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports....Reports of research not in accordance with the principles of this Declaration should not be accepted for publication" (9).

Compliance with the rules of ethics in research and its publication remains the responsibility of study investigators, and the fact that a manuscript passes through peer review and the editorial process does not relieve the investigators of this responsibility. Journals should not publish research that does not comply, but they do not routinely require copies of IRB approval, IRB membership rosters (as contract research organizations seek during industry-sponsored clinical trials), or the applications that were submitted to obtain approval. Although that may be considered desirable by some, it clearly

would be impossible given the multitude of countries (with their local languages) represented by submissions to international journals. It is also important to note that the efficacy of IRBs has not been formally tested, and there is some argument regarding whether, in their present form, they effectively protect subjects (6). Not surprisingly, there have been multiple proposals to change the way human subjects are offered protection in research studies (10,11). Finally, the mere process of "obtaining IRB approval" (standard language in most submitted manuscripts) does not mean that a given research project is free of less obvious ethical problems. Power calculations in a submitted trial may have been way off, meaning that the performed research project fails to reject its hypothesis with the required level of significance, or data collection may have been performed in such a way as to lead to unacceptably high confidence limits. Even worse, a research project may be abandoned or finished but never written up, so that patients (or animals) were exposed to risk without benefit to the scientific community: the Declaration of Helsinki clearly states that investigators have a duty to publish their results. However, journals not infrequently receive manuscripts that may contain relevant results but are written so poorly that the true value of the content is impossible to assess. Some of the reports published in *JACC* have been substantially edited by the editors to make them comprehensible, but how much effort must a journal's reviewers and editors put into issues of language to make a manuscript "publishable" so that the results become widely available?

Finally, ethical requirements will not be absolutely equal in all cultures, countries, and institutions (12). The Declaration of Helsinki is the unifying standard, stating, "Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration."

However, interpretation of the Declaration of Helsinki may vary, and a very obvious example in imaging is the exposure to contrast agents and, especially, radiation, which requires specific approval from government authorities in some countries, while it is considered less problematic in others (13). Does a journal based, for example, in the United States (such as *JACC*) have the right to question IRB approval mandates from other countries with

different operating rules? When does this cross over into cultural snobbery and paternalistic attitudes? In the end, do the rules of the country where research was performed or the rules of the country where the results are to be published have superior reign? Although the Declaration of Helsinki provides excellent guidance regarding the ethics of performing and publishing medical research, there is clear potential for conflict and uncertainties. The editors of

*JACC* are committed to the highest standards in research ethics, but we also understand that there are shades of gray in this area. We look forward to hearing your thoughts.

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