

Reporting of Ethical Approval and Informed Consent in Clinical Research Published in Leading Anesthesia Journals

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Background: Ethical conduct in human research in anesthesia includes approval by an institutional review board (IRB) or ethics committee and informed consent. Evidence of these is sometimes lacking in journal publications.

Methods: The authors reviewed all publications involving human subjects in six leading anesthesia journals for the year 2001 (n = 1189). Rates of IRB approval and informed consent were examined and compared with potential predictors that included journal, type of publication, and patient demographics (age, sex, elective or emergency status). Rates were compared by use of chi-square and logistic regression.

Results: The authors found that IRB approval was documented in 71% of publications and consent was obtained in 66% of publications. Significant variation in IRB approval and consent was found among journals ($P < 0.0005$) and according to type of publication ($P < 0.0005$). Because publication type affected rates of IRB approval and consent (trials > mechanistic studies > observational studies > case reports), an analysis restricted to prospective studies also found a significant difference in IRB approval and consent among journals ($P < 0.0005$).

Conclusions: This study suggests that rates of IRB approval and informed consent vary among publications in anesthesia journals. Clearer guidelines (and author adherence) for all types of publication are needed, both as a protection for research subjects and to maintain public trust in the process.

CONTEMPORARY research standards mandate ethical approval of a study protocol by an institutional review board (IRB) or ethics committee and informed consent from the subjects.¹⁻⁴ These requirements are outlined by the World Medical Association's Declaration of Helsinki¹ and are included in good clinical research practice guidelines of most, if not all, medical research regulating bodies. Similarly, most medical journals require confir-

mation of IRB approval and patient consent before a manuscript is accepted for publication.^{2,3}

There have been some recent reports of low rates of ethical approval in major medical journals,⁵⁻¹² including research on at-risk groups, such as children,^{5,7} the elderly,⁶ and the critically ill.^{8,11} Patients about to undergo anesthesia and surgery are considered to be vulnerable and difficult to recruit into clinical studies and can also be considered at risk.^{10,13-16} Asai and Shingu¹⁰ found variations in instructions to authors regarding requirement for IRB approval and informed consent among 11 anesthesia journals. They reviewed 6 months of publications and found that more than 90% of human and animal research (673 publications) provided IRB approval and informed consent, but their analysis excluded many mechanistic studies, all case reports, and physician surveys.¹⁰

We therefore examined a selection of anesthesia journals and compared their rates of IRB approval and informed consent in all publications regarding human research.

Materials and Methods

We reviewed all publications of research in humans in six highly ranked anesthesia journals, according to the 1998 Journal Citation Reports¹⁷ impact factor, for the year 2001. We excluded journals dedicated to pain management, critical care, or emergency medicine. The journals were (in alphabetical order, with impact factor): *Acta Anaesthesiologica Scandinavica* (1.04), *Anesthesia* (2.34), *Anesthesia and Analgesia* (2.78), *Anesthesiology* (4.28), and *British Journal of Anesthesia* (1.83). These journals were chosen because of their relatively high impact factor ranking and because they report on anesthesia research from most regions of the world. Publications included in the analyses were all those that reported on original human studies (all or in part). We excluded animal and laboratory studies, equipment evaluations or reports (unless studied in humans), reviews, editorials, commentaries, and letters to the editor.

We collected data on study type (randomized controlled trials [RCTs], prospective observational studies [including audit and quality assurance activities and surveys], retrospective observational studies, case series/reports, and mechanistic studies that used human tissue

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Table 1. Frequency of Articles According to Type of Publication and Journal

Study Type	Journal											
	A		B		C		D		E		F	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Randomized trial	64	30	175	41	72	37	52	36	62	48	19	26
Nonrandomized trial	3	1.4	15	3.5	4	2.0	3	2.1	1	0.8		0
Prospective	39	18	104	24	41	21	52	36	31	24	14	19
observational study												
Retrospective	6	2.8	15	3.5	8	4.1	6	4.1	6	4.6	5	6.9
observational study												
Case report/series	62	29	95	22	44	22	22	15	19	15	30	42
Mechanistic study	43	20	23	5.4	28	14	11	7.5	11	8.5	4	5.6

or blood samples to ascertain anesthetic drug effect or other principles), sample size, and population (age group, sex, elective/emergency status). IRB approval and informed consent were recorded as being obtained if it was explicitly documented in the publication. Informed consent included that provided by the patient or subject, next of kin (including the parent in pediatric research), or a waiver given by the IRB.

Data extraction was performed by either of the authors. A random sample of approximately one third of the data set ($n = 359$) was used to confirm the accuracy of categorization and data entry. There was excellent agreement ($\kappa = 0.95$).

After the data retrieval and analysis, we contacted each of the relevant journal editors and asked them to provide some additional information as to why IRB approval or consent was not reported in the original publications.

Statistical Analysis

IRB approval and consent rates between journals were compared by use of chi-square analysis. Because it is known that variations in study type may confound this comparison,^{5,8} predetermined subgroup analyses were done on equivalent study types. Also, logistic regression analyses were used to identify predictors of IRB approval and consent (such as age group, sex, emergency/elective status) and to account for differences in study types when comparing journals. A value of $P < 0.05$ was considered significant.

Results

We retrieved 1,189 studies, of which 37% were classified as RCTs, 2% nonrandomized trials, 28% observational studies, 23% case reports/series, and 10% mechanistic studies (Table 1). There were 62 publications (5%) reporting on patients undergoing emergency treatment. Men were studied exclusively in 170 reports (14%), women in 240 reports (20%), and both sexes in 776 (65%); in 3 publications, sex could not be determined. Research on child subjects occurred in 162 publications (14%).

IRB approval was documented in 845 publications

(71%). Individual patient consent was documented in 660 (56%), next-of-kin consent was obtained in 114 (9.6%), and consent was waived in 34 (2.9%) publications. Thus, some form of consent was obtained in 787 publications (66%).

For all prospective studies (all trials and observational and mechanistic studies), IRB approval was documented in 94% and consent was documented in 87% of publications. IRB approval was obtained in most trials and mechanistic studies (each $>90\%$) but less often in prospective observational studies (85.1%), retrospective observational studies (52%), and case reports/series (2%). Similarly, informed consent was obtained most often with RCTs (97%) and less often with mechanistic studies (83%), nonrandomized trials (77%), prospective observational studies (75%), retrospective observational studies (41%), and case reports/series (3%).

We therefore restricted our analysis to a comparison of prospective studies (*i.e.*, excluding retrospective studies and case reports/series). There was a significant difference in rates of IRB approval and consent between journals (Table 2). Another analysis was restricted to RCTs ($n = 444$), in which we identified 12 publications without documentation of consent and 3 without IRB approval and found no difference in rates of consent or IRB approval (Table 2).

Logistic regression identified type of publication ($P < 0.0005$) and journal ($P < 0.0005$) but not age group ($P = 0.34$), patient sex ($P = 0.42$), or elective/emergency status ($P = 0.06$) as significant predictors of IRB approval. The predictors of informed consent were type of publication ($P < 0.0005$), journal ($P < 0.0005$), patient sex (if not recorded, $P = 0.002$), but not age group ($P = 0.63$) or elective/emergency status ($P = 0.23$). When the analysis was restricted to prospective and mechanistic studies ($n = 871$), the only significant predictors of IRB approval were journal ($P < 0.0005$) and elective/emergency status ($P = 0.001$). Similar results were obtained for informed consent, with predictors being journal ($P < 0.0005$) and elective/emergency status ($P < 0.0005$).

The subsequent correspondence with each of the journal editors responsible for publication of RCTs without

Table 2. IRB Approval and Informed Consent in All Prospective Studies (n = 871), or Limited to Randomized Trials (n = 444), in Six Leading Anesthesia Journals for 2001

Study Type	Journal												P Value
	A		B		C		D		E		F		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Any consent*													
All prospective studies	141	94.6	275	86.8	126	86.9	90	76.3	96	91.4	31	83.8	0.001
Randomized trials	64	100	165	94.9	70	97.2	51	98.1	61	98.4	19	100	0.30
IRB approval													
All prospective studies	144	96.6	311	98.1	134	92.4	98	83.1	94	89.5	34	91.9	<0.0005
Randomized trials	64	100	175	100	71	98.3	51	98.1	61	98.4	19	100	0.51

* Patient, next of kin, or IRB waiver.

IRB, Institutional Review Board.

documentation of IRB approval or consent, after they had contacted the authors responsible for the research, revealed that in all but one case, consent and IRB approval had been obtained.

Discussion

This is the largest study investigating rates of IRB approval and informed consent in the anesthetic literature. We found substantial variation in the reporting of IRB approval and informed consent between journals, even after accounting for type of publication. A significant difference persisted when the analysis was restricted to all prospective studies but not when restricted to RCTs alone. Significant predictors of IRB approval and consent were journal of publication and elective/emergency status. Patient age and sex did not significantly affect rates of IRB approval and consent.

The Declaration of Helsinki requires that IRB (or equivalent) approval and informed consent should be obtained.¹ The Declaration states in part: "The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence."¹ Standards of clinical research practice guide the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials. Although the process of informed consent has been criticized,^{3,18,19} it remains central to upholding patient autonomy, a key tenet of ethical practice. The basic elements of informed consent include an explanation of the purposes of the research, a description of the procedures to be followed, a description of risks and benefits, alternative treatments, and that participation is voluntary, that refusal to participate will not affect care to which the subject is otherwise entitled, and that the subject may discontinue his or her participation at any

time. Thus, IRB approval and informed consent protect human subjects participating in research.

Reported rates of IRB approval and informed consent in medical journals have improved over the past two decades.^{11,12,20} Instructions to authors widely published by all journals included in this study explicitly state that IRB approval must be obtained and documented in the submitted publication. Four of the six anesthesia journals studied had a similar statement regarding documentation of informed consent. Patient consent for use of an identifying photograph in a case report is widely accepted as requiring specific consent, but only two of the anesthesia journals included a statement concerning patient consent for case reports in general. These practices are less common in journals reporting many other specialty areas. A recent study found that only approximately 50% of journals mention IRB or ethics committee approval and approximately 10% mention informed consent in their instructions to authors.²¹ Some journals, including anesthesia journals, ask authors to provide a copy of the IRB approval letter or at least state that such a letter will be made available on request.

Most research-regulating bodies provide guidelines for research being conducted in special circumstances, such as use of discarded tissues, emergency care, audit or quality assurance activity, coma, dependent subjects, and the mentally ill. An IRB may allow research to proceed without patient consent, either by using a surrogate (parent or other next of kin, legal representative) or by waiving the requirement for consent. A waiver is more likely to be supported if there is probable therapeutic advantage to the patient, or at least minimal risk, and if adequate justification is presented and patient privacy protected. IRB-approved waived consent is common in critical care research.⁸ Updated guidelines for the waiver of informed consent and protection of subjects in emergency research should clarify this issue.²²

In our study, it was sometimes difficult to determine whether a publication was reporting a research project or the results of an audit or quality assurance activity. Some have argued that audit and quality assurance activ-

ities do not require IRB approval or consent because they represent routine clinical care, and advice to authors has been contradictory.²³ Some regulatory bodies take the view that if presentation or publication of such activities is planned, then approval and consent should be obtained. Surveys, although (apparently) noninvasive, also have specific considerations. In each of these circumstances, issues such as subject confidentiality, the likelihood of generating anxiety and other harm, and access to counseling, require deliberation.²⁴ Our opinion is that the best approach to dealing with uncertainty is to seek advice from a local IRB, and even the editor of the intended journal of publication, before commencement of the project.

In our study, it was clear that observational studies and case reports or series were less likely to include IRB approval and consent. This is consistent with other general medical and specialty journals.⁵⁻⁹ Some researchers may not believe that IRB approval or consent is necessary when standard treatments are being investigated, but this violates the principles of autonomy and may undermine the public's trust. Arguments have been made in favor of waiving IRB approval and need for informed consent in studies that will not alter patient management or outcome and have minimal risks. The alternative view is that this group of patients whose rights to privacy and confidentiality may potentially be violated in publications, without any direct benefit to them, are the ones most in need of protection.²⁵ Case reports are a case in point, and our study found very low rates of IRB approval and consent for these. These are often impossible in emergency situations, but retrospective approval can be sought. This goes beyond the approval for what is sometimes experimental treatment, to include consent for publication; despite not using patient names or initials, patient privacy is difficult to protect when the institution is readily identified and specific clinical details presented. Our belief is that all research ought to be submitted to an IRB (or equivalent body) unless an established policy exists in the particular institution; the IRB may waive the need for a formal application and/or patient consent. It is not appropriate for the researcher to make this decision without independent, expert advice.^{24,26}

We have found that rates of IRB approval and consent in anesthesia journals are at least as good as in other specialty or general medical journals.^{6,9,16,25} Weil *et al.*,⁷ in a study of general medical journals, found that 69% and 73% provided documented IRB approval and consent, respectively. Bauchner and Sharfstein⁵ found that 97% of RCTs in pediatric journals had ethics approval, defined as any statement about informed consent or IRB approval, with a variation in rates of 75–100% between journals. Obtaining consent in emergency and critical care research has been problematic, for various reasons.^{8,11,19,27} Matot *et al.*⁸ found that 58% of publications

in the critical care literature had evidence of IRB approval and consent, with apparently significant variations between journals (range, 23 to 86%; no *P* values presented). Asai and Shingu¹⁰ found that IRB approval and consent were reported in more than 90% of 673 publications in anesthesia journals in a 6-month period in 1996, but they did not compare anesthesia journals. They included animal research but excluded some surveys, mechanistic studies, and all case reports from their analysis.

Attempts to improve the consent process and reduce its "burden" on researchers and patients have been met with varying degrees of success.^{16,22,27,28} Obtaining informed consent for clinical trials in anesthesia has been studied previously, and patients accept recruitment on the day of surgery if approached appropriately (*i.e.*, private setting, adequate time to consider trial information).¹³⁻¹⁶

Limitations of this Study

Whether IRB approval and informed consent were obtained but not documented in the publications cannot be determined from this study. Our follow-up investigation of publications of RCTs suggests that at least for RCTs, IRB approval and consent were obtained but not reported. However, instructions to authors clearly state that such a declaration must be included, and the differential rate of RCTs compared with observational studies suggests that such approval was not obtained in many circumstances. We recognize that regulations may vary according to the nature of the research being undertaken, regions of the world, and individual institutions. These may partly explain some of the differences we have observed. Differences in rate or reporting of IRB approval and consent may not reflect the quality of a journal or the publications.

The Declaration of Helsinki states that reports of research in humans not in accordance with its principles should not be accepted for publication. Journal editors must make documentation of IRB approval and informed consent, unless specifically exempt by IRB deliberation, a requirement for publication. This is the final check in ensuring the highest scientific and ethical standards and a necessary step in protecting research subjects and maintaining public trust in the process.

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