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Review

Volume and methodological quality of randomized controlled trials in laparoscopic surgery: assessment over a 10-year period

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Laparoscopy;
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Abstract

BACKGROUND: Measures have been taken to improve methodological quality of randomized controlled trials (RCTs). This review systematically assessed the trends in volume and methodological quality of RCTs on minimally invasive surgery within a 10-year period.

DATA SOURCES: RCTs on minimally invasive surgery were searched in the 10 most cited general surgical journals and the 5 most cited journals of laparoscopic interest for the years 2002 and 2012. Bibliometric and methodological quality components were abstracted using the Scottish Intercollegiate Guidelines Network. The pooled number of RCTs from low-contribution regions demonstrated an increasing proportion of the total published RCTs, compensating for a concomitant decrease of the respective contributions from Europe and North America. International collaborations were more frequent in 2012. Acceptable or high quality RCTs accounted for 37.9% and 54.4% of RCTs published in 2002 and 2012, respectively. Components of external validity were poorly reported.

CONCLUSIONS: Both the volume and the reporting quality of laparoscopic RCTs have increased from 2002 to 2012, but there seems to be ample room for improvement of methodological quality.

There were no relevant financial relationships or any sources of support in the form of grants, equipment, or drugs.

The authors declare no conflicts of interest.

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Evidence-based medical practice entails that physicians make research-informed decisions. Meta-analyses and randomized controlled trials (RCTs) occupy the highest rank in the pyramid of evidence and are significant components of quality

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practice guidelines.[1] The medical community expects that measures are taken to minimize sources of bias in clinical research and to adequately report on methodological components.[2] Several assessment tools and algorithms have developed for this purpose. The Preferred Reporting Items in Systematic reviews and Meta-Analyses guidelines and the Consolidated Standards of Reporting Trials (CONSORT) initiative may be the most popular assessment tools for systematic reviews and RCTs, respectively.[3,4] A significant improvement in reporting quality has been observed among several disciplines, including general surgery, anesthesia, and intensive care medicine, although fields of further improvement have been identified.[5–7] Compliance with the CONSORT standards has been suggested as a factor of quality improvement in published RCTs.[8] A plethora of publications and an active endorsement of medical journal editors to comply with standards of reporting and methodological quality have contributed to a paradigm shift in medical publishing.

A systematic assessment of the trends of methodological quality of laparoscopic RCTs is lacking. Novel technological advances and the evolution of innovative techniques and approaches and the implementation of the findings of RCTs in clinical practice render such an approach essential. We hypothesized that the volume and methodological quality of RCRs in laparoscopic surgery would demonstrate an increasing trend through time, similar to other medical disciplines. This systematic review aims to evaluate the volume and methodological quality of RCTs in laparoscopic surgery within a 10-year period.

Methods

Study protocol

A protocol was established in a consensus meeting of members of the author team before initiation of the study. The primary author was responsible for the design of the study, and author team members proposed modifications, which were implemented when agreement was reached. This review conforms to the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement standards.[3]

Search of journal contents

Two independent investigators performed the literature search. For the purpose of the study, 10 journals with the highest impact factors according to the Thomson Reuters Journal Citation Report 2012 in the field of general surgery and the five highest impact factor minimally invasive surgery journals were selected: Annals of Surgery; The British Journal of Surgery; Journal of the American College of Surgeons; JAMA Surgery; Surgical Endoscopy; Surgery; Obesity Surgery; American Journal of Surgery; Journal of Gastrointestinal Surgery; International Journal of Colorectal Disease; World Journal of Surgery; Minimally Invasive Therapy & Allied Technologies; Journal of Laparoendoscopic & Advanced Surgical Techniques; Surgical Laparoscopy, Endoscopy & Percutaneous Techniques; and Journal of the Society of Laparoendoscopic Surgeons. The PubMed interface was used for the search of articles of interest because all journals were abstracted in MEDLINE. Relevant RCTs were searched using the filter "Randomized Controlled Trial" for the years 2002 and 2012.

Inclusion and exclusion criteria

As per protocol, RCTs on laparoscopic, robotic, transluminal endoscopic, minimally invasive thyroid and parathyroid surgery were included. Studies on colonoscopy, esophagogastroscopy, and endoscopic transurethral procedures were excluded. No further inclusion or exclusion criteria were applied.

Quality assessment

The Scottish Intercollegiate Guidelines Network (SIGN) checklist for controlled trials was used for quality assessment of the selected articles. This tool is organized into 13 components for evaluation of the internal and the external validity of the trial. Potential answers are "yes," "no," "can't say," and "does not apply." Based on this assessment, the study is characterized as "high quality," "acceptable," or "unacceptable–reject". Specific assessment of external validity was performed using five additional questions: (1) Does the study provide adequate details of the surgical intervention to allow reproducibility? (2) Does the study provide adequate details on preoperative care to allow reproducibility? (3) Does the study provide adequate details on postoperative care to allow reproducibility? (4) Does the study provide adequate information on the experience level of participating surgeons with the reported procedure? and (5) Does the study provide information on the case volume of the participating center(s)? Cohen's κ coefficient was used to evaluate inter-rater agreement of the two assessors for 15% of the RCTs. The assessment was planned to be undertaken by a single reviewer, if moderate or high level of agreement would be evident ($\kappa > .41$).

Data extraction and statistical analysis

The primary author's name, year of publication, journal of publication, bibliometric data, including title word count, number of authors, number of participating centers, country, and continent where the trial was conducted, interdisciplinarity, number of pages, and number of references; and study assessment data according to the SIGN checklist and the additional questions related to external validity were abstracted into an electronic datasheet using Microsoft Access. The spreadsheet was extracted to SPSS 18.0 (SPSS Inc, Chicago, IL), which was used for statistical analysis. Various RCT characteristics were summarized using descriptive statistics. Comparisons were made using the Pearson's

chi-square test or the two-sample Kolmogorov-Smirnov test for equality of distribution functions, as applicable. Data are presented as absolute numbers, proportions (%), median values, and 95% confidence intervals (CIs) for the median. Statistical significance was set at *P*-value .05.

Results

The database searches retrieved 422 results, and 180 RCTs were considered eligible; 66 articles were published in 2002, and 114 articles were published in 2012 (Fig. 1). The percentage of inter-rater agreement was 75%, with a κ value of .5 (95% CI: .30 to .70), suggesting moderate agreement. Further assessment of RCTs was undertaken by a single author. No statistically significant difference was noted with regard to the proportion of RCTs published from each journal between 2002 and 2012, although several journals of general surgery interest seemed to have undertaken a part of laparoscopic RCTs from traditional minimally invasive surgery journals (Fig. 2). The contribution of each continent was not statistically different; however, Asian countries demonstrated an increasing proportion of the total published RCTs (95% CI for the difference from .6% to 25.1%; $P = .065$). A concomitant, nonsignificant decrease in the proportion of published RCTs was noted for Europe, North America, and Oceania (Fig. 3). Comparison of the pooled number of RCTs conducted in high-contribution regions (Europe and North America) with the pooled number of RCTs conducted in low-contribution regions (Africa, Asia, Oceania, South America) demonstrated a decreasing trend for the former (74.2% vs 48.7%; 95% CI for the difference from 1.6% to 29.3%; $P = .037$). The absolute number of RCTs produced in Asian countries has increased by 66%, whereas the number of RCTs produced in Western countries has decreased by 27%. Comparison of the proportion of RCTs of acceptable quality between North America/Europe and Asia published in 2012 was in favor of the latter (46% vs 77%, 95% CI for the difference from −49.2% to −12.5%, $P = .003$), although this difference was not evident in 2002 (37% vs 42%, 95% CI for the difference from −21.8% to 39.8%; $P = .556$).

The subject domain did not differ significantly between RCTs published within the 10-year period. A decreasing trend for RCTs on biliary surgery was evident, although this was not statistically significant (Fig. 4). Funding was provided more frequently by national authorities in 2012 (30.4% vs 62.9% of RCTs which reported on the source of funding, $P = .060$). A decreasing trend of funding by scientific societies (39.1% vs 17.1% of RCTs which reported on the source of funding, $P = .06$) was marginally nonsignificant (Fig. 5).

Table 1 lists a summary of the comparisons of bibliometric and quality characteristics. International collaborations were more frequent in 2012 (1.5% vs 12.3%, odds ratio = .11, 95% CI for the difference from 4.1% to 17.5%, $P = .012$). Recent RCTs tended to enroll a larger sample size (median = 49, 95% CI: 40 to 60 vs median = 60, 95% CI: 57 to 80, $P = .045$), occupy more pages (median = 5, 95% CI: 5 to 6 vs median = 6, 95% CI: 6 to 7, $P < .0001$), cite more references (median = 20, 95% CI: 17 to 22 vs median = 26, 95% CI: 23 to 28, $P < .0001$).

Several SIGN domains related to methodology reporting demonstrated an improvement over time (Table 1). Acceptable or high quality RCTs accounted for 37.9% and 54.4% of the total number of 2002 and 2012, respectively (95% CI for the difference from 16.5% to 45.2%; $P = .033$). Applicability of results was considered more frequent in 2012 than in 2002 (72.7% vs 86%, 95% CI for the difference from 7.4% to 25.7%; $P = .029$). Among other factors of external validity, information on preoperative care was more frequently provided in recent RCTs (12.2% vs 39.5%, 95% CI for the difference from 4.9% to 31.6%; $P = .012$), otherwise no improvement was evident among articles published in 2002 and 2012.

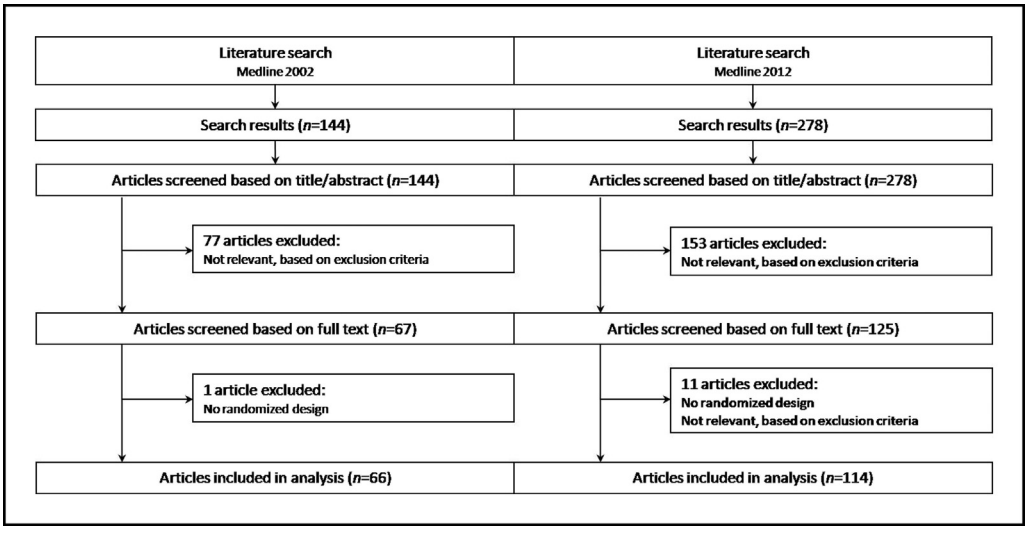

Figure 1 Flow chart of search history.

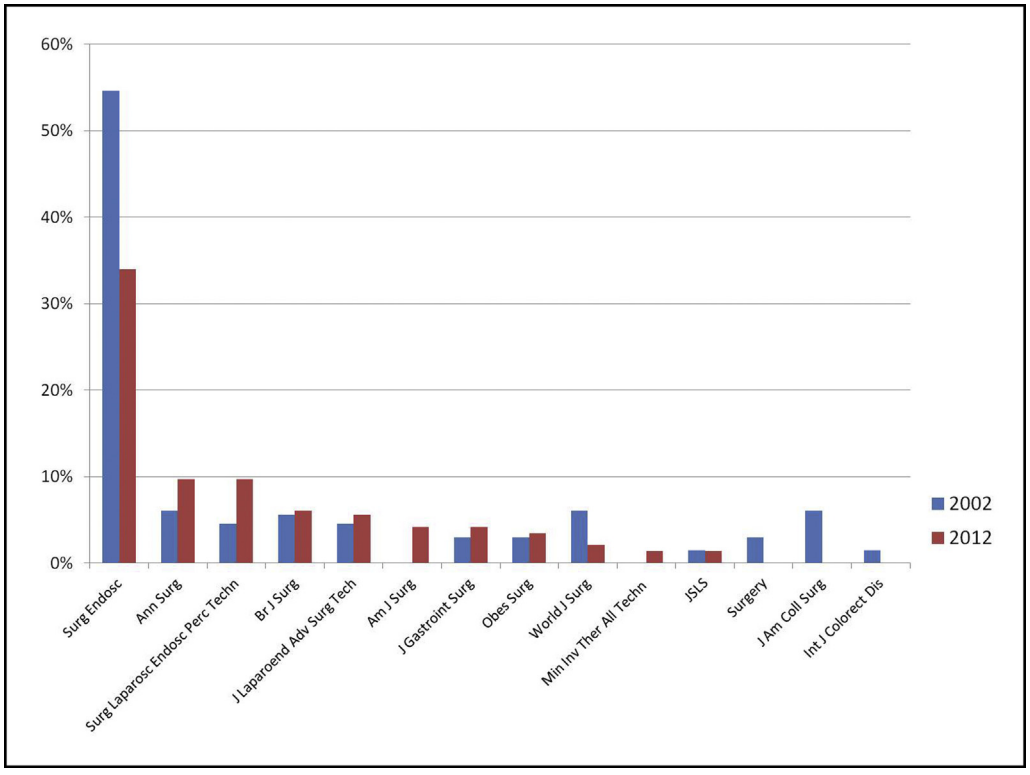

Figure 2 Distribution of RCTs by journal of publication in the years 2002 and 2012. All *P* values greater than .05. Statistical comparisons were made using the Pearson's chi-square test or the two-tailed Fisher exact probability test, as applicable.

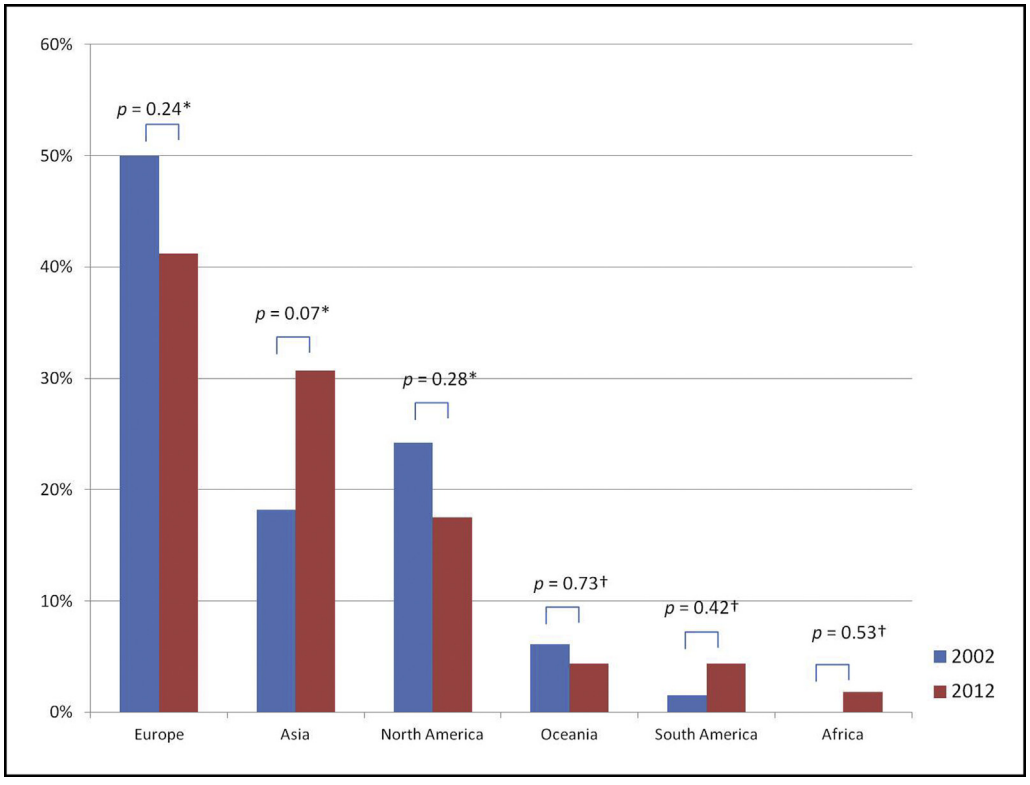

Figure 3 Distribution of RCTs by continent in the years 2002 and 2012. Statistical comparisons were made using the Pearson's chi-square test* or the two-tailed Fisher exact probability test†.

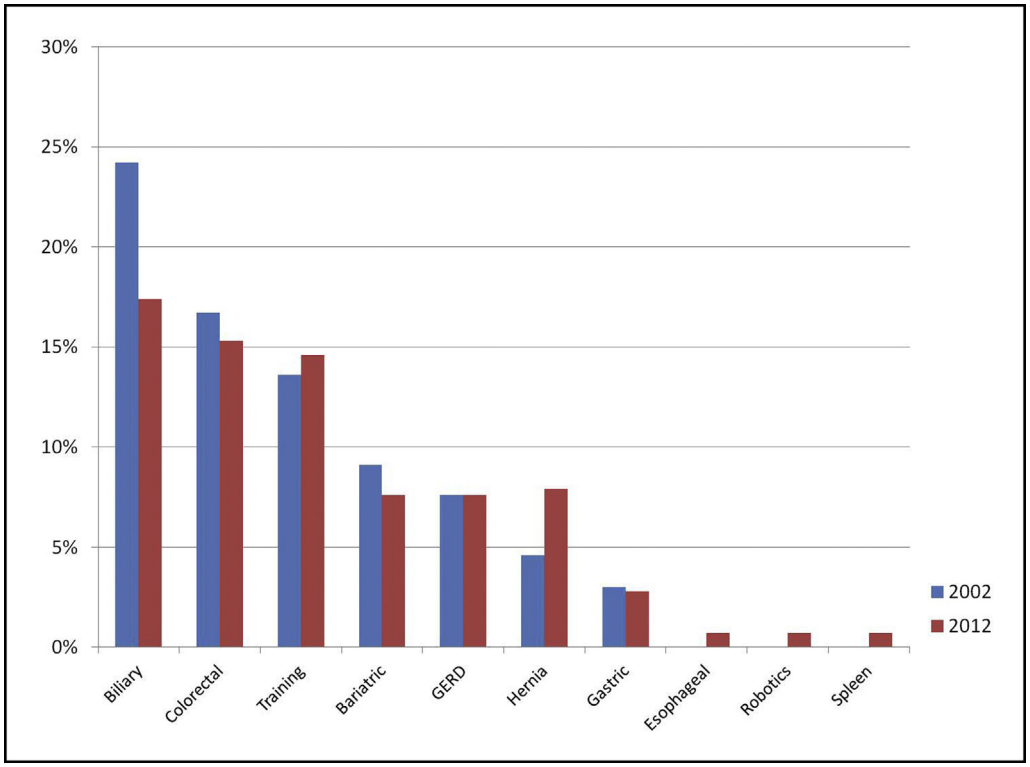

Figure 4 Distribution of RCTs by subject domain in the years 2002 and 2012. All *P* values greater than .05. Statistical comparisons were made using the Pearson's chi-square test or the two-tailed Fisher exact probability test, as applicable.

Comments

This review appraises the trend of published laparoscopic RCTs within a decade. Similar to other medical disciplines, a 40% rise in the number of published RCTs was evident. Furthermore, a significant improvement of the proportion of RCTs with acceptable methodological quality, from 38% in 2002 to 54% in 2012, was documented. Several factors for further improvement were identified; more specifically adequate reporting and items of external validity were associated with improved methodological quality.

A significant increase by 66% of the proportion of RCTs conducted in Asian countries is noteworthy, whereas the proportion of RCTs produced in Europe and in North America has decreased by 27%. Several reviews have implicated Asian countries in the production of low quality RCTs.[5] However, this analysis has demonstrated that laparoscopic RCTs produced by Asian countries were more frequently of acceptable quality than those produced in Western countries. This may reflect the evolution of minimally invasive surgery mainly in China, India, Japan, and South Korea and the enhanced exchange of information and the improved international collaboration promoted by scientific societies, such as the European Association for Endoscopic Surgery.[9]

Furthermore, a trend toward wider distribution of laparoscopic RCTs from traditional laparoscopic publications to journals of general surgery was noted, although it did not reach significance. This may be associated with the wider dissemination of both basic laparoscopic surgery and advanced minimally invasive techniques and the increasing spectrum of laparoscopic surgical procedures. Nevertheless, representation of advanced laparoscopic procedures in published RCTs was inadequate, with only 6% of trials in 2012 reporting on esophageal, gastric, robotic, and splenic surgery. Trials reporting on domains of basic laparoscopic surgery in 2012 figured a similar distribution to that of 2002. A nonsignificant trend for the decrease in the proportion of publications on biliary surgery was compensated by an increasing trend for RCTs on hernia surgery. This can be partly attributed to the specific interest of recent studies in noninvasive methods for mesh fixation in laparoscopic hernia repair. Furthermore, single-incision techniques, which revived the interest in biliary surgery, may be considered at their infancy, with only a few relevant RCTs having been published in 2012.

Assessment of the distribution of funding sources of laparoscopic RCTs has demonstrated a trend toward an increase of national authorities funding and decrease of sponsoring by scientific societies. Furthermore, only a subtle increase of industry-sponsored studies was documented. Nevertheless, variability in conflict disclosure policies among journals should be considered as a potential source of bias. Nevertheless, a significant proportion of trials not reporting on funding source has to be taken into account. Conflicting evidence from other disciplines suggests that the presence of conflicts of interests adversely

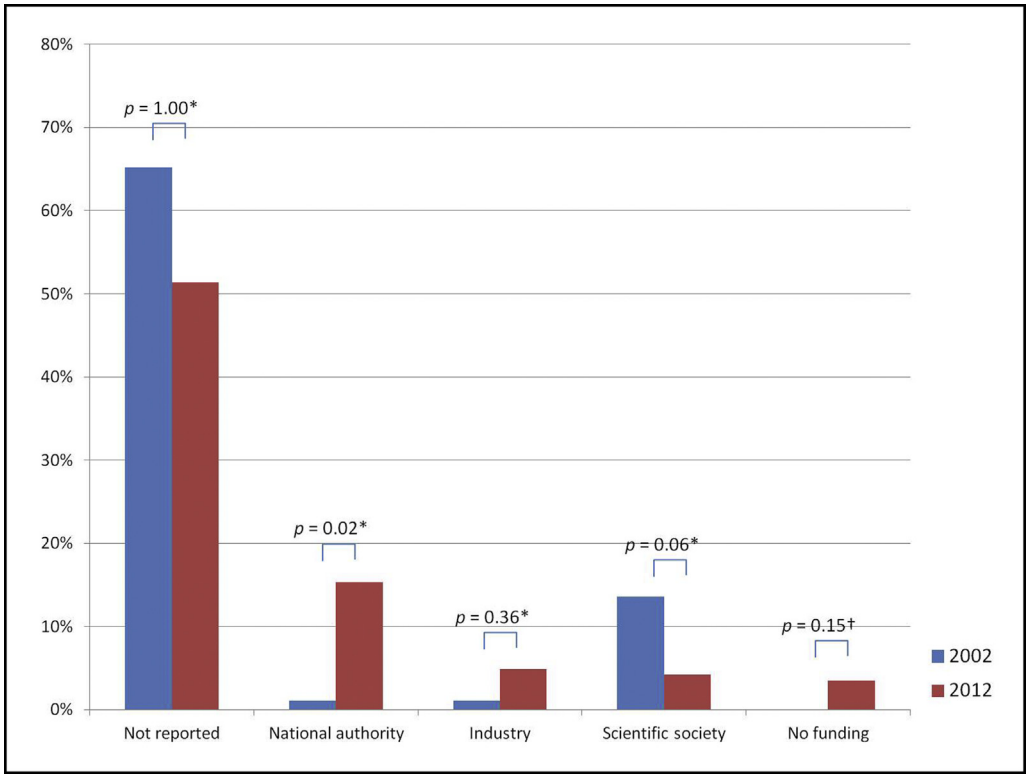

Figure 5 Source of funding of RCTs in the years 2002 and 2012. All *P* values less than .05. Statistical comparisons were made using the Pearson's chi-square test* or the two-tailed Fisher exact probability test†.

affects study quality.[10–12] The small number of industry-sponsored RCTs did not allow statistical assessment of such an association with a low risk of type II statistical error. Four of the 14 (28.6%) industry-funded RCTs in the years 2002 and 2012 were of acceptable quality compared with 83 of 166 (50%) of nonindustry-funded RCTs that were of acceptable quality. Clinicians should appraise the reliability of the provided information on the basis of potential conflicts. Medical journal editors have largely adopted mandatory conflict of interest statements; however, source of funding has been reported in less than half of RCTs published in the selected journals in 2012.

Several bibliometric characteristics presented with different trends within the 10-year period. The frequency of international initiatives has increased by 88% and the frequency of multicenter studies by 39%, although significance was reached only by the former. Such an association could not be demonstrated for RCTs published in the years 1999 and 2009 in the field of general surgery.[5] The relatively limited field of minimally invasive surgery as compared with general surgery, the effect of international laparoscopic congresses, bringing into communication specialists from different nations and continents, connecting multiple disciplines (surgery, gastroenterology, urology, gynecology), and the initiatives of international laparoscopic associations may account for this effect. The increased frequency of international and multicenter collaborations reflects on the increasing trend of sample size, which is associated to improved methodological quality (publication of data pending). Several other factors, such as word count, article length, and the number of references have also increased throughout the search period. This may be explained by the adherence to the CONSORT statement by a number of articles, which endorses reporting of PICOS domains (participants, interventions, comparators, outcomes, study design) in the title and analytical reporting of trial methodology. Indeed, length of the article and larger sample size have been associated with CONSORT score and increased number of citations.[13–15]

Only a few components of the SIGN questionnaire have been subject for improvement from 2002 to 2012. In a more detailed view of the analysis, these factors are associated more with reporting rather than methodological quality. For example, only a small improvement has been demonstrated in drop-out rates and the presence of similar baseline patient characteristics between study groups. However, relevant reporting has increased by 30% and 50%, respectively. Interestingly, reporting on the analysis method has decreased from 48% to 30%, although the intention-to-treat principle was respected by a larger proportion of trials, however, without reaching significance. Failure to report on the intention-to-treat concept cannot exclude selection bias and questions the adherence to randomization.[16]

External validity is a significant component of methodological quality and may be even more relevant in surgical RCTs. Several components of external validity have been reported by 17% to 78% of RCTs in general surgery.[13] Except for providing information on surgical interventions,

Table 1 Comparison of bibliometric, quality, and external validity characteristics of laparoscopic RCTs between 2002 and 2012

	2002	2012	*P* value	95% CI
Bibliometric characteristic				
International*	1.5%	12.3%	.012	4.1%–17.5%
Multicenter*	10.6%	17.5%	.209	−3.2% to 17.1%
Title word count†	13 (12–14)	15 (14–16)	.017	
No. of authors†	6 (5–6)	6 (6–7)	.220	
Interdisciplinarity*	50.0%	57.0%	.362	−8% to 22.1%
No. of pages†	5 (5–6)	7 (6–7)	<.0001	
No. of references†	20 (17–22)	26 (23–28)	<.0001	
Sample size†	49 (40–60)	60 (57–80)	.045	
Quality characteristics				
Appropriate and clearly focused question*	83.3%	85.8%	.651	−8.5% to 13.6%
Described as randomized*	100%	100%	1.000	NA
Adequate concealment method	36.4%	34.2%	.770	−16.7% to 12.3%
Blinding				
Reporting on blinding*	39.4%	38.6%	.916	−15.6% to 14.0%
Blinded (subjects, assessors, or both)†	31.8%	32.4%	.930	−13.5% to 14.8%
Groups similar at conception				
Comparison of patient characteristics reported†	34.9%	50.9%	.037	1.3%–41.7%
Patient demographics similar†,‡	85.2%	89.2%	.586	−11.3% to 19.4%
Lack of significant confounding bias*	60.6%	63.2%	.734	−12.2% to 54.3%
Lack of significant detection bias*	77.3%	86.0%	.136	−3.2% to 20.6%
Drop-out rate				
Reporting on dropout rate*	34.8%	60.5%	.001	11.1%–51.6%
<20%†,‡	85%	90.5%	.493	−11.8% to 22.7%
Intention-to-treat analysis				
Reporting on analysis method†	47.8%	29.9%	.045	−35.6% to .3%
Intention to treat†	66.7%	60.5%	.412	−20.6% to 8.3%
Results comparable for all sites				
Reporting on outcomes comparison†	.0%	11.1%	1.000	NA
Comparable outcomes for all sites†,‡	NA	11.1%	NA	NA
Acceptable quality†	37.9%	54.4%	.033	1.7%–31.3%
Results directly applicable to the study population*,§	72.7%	86%	.029	.7%–25.7%
Additional factors of external validity				
Details of surgical intervention*	59.1%	66.7%	.308	−7.1% to 22.2%
Reporting on preoperative care*,§	21.1%	39.5%	.012	4.9%–31.6%
Reporting on postoperative care*,§	25.8%	28.1%	.737	−11.1% to 15.7%
Reporting on surgeons' experience*	18.2%	25.4%	.264	−5.0% to 19.5%
Reporting on case volume†,§	3.0%	1.8%	.576	−6.1% to 3.5%

Data are presented as median (95% CI for the median).
CI = confidence interval; NA = not applicable; RCT = randomized controlled trial.
*Pearson's chi-square test with two-group proportion tests for the percentage difference.
†Two-sample Kolmogorov-Smirnov test for equality of distribution functions.
‡Proportion of the number of studies which reported on this outcome.
§RCTs of the domain "Training" excluded.

the remaining factors were reported by less than half of the RCTs, both in 2002 and 2012. Significant improvement in reporting was evident only for data on preoperative care. Both perioperative information and experience level of surgeons have been identified on multivariate analysis as independent factors predicting methodological quality in laparoscopic RCTs (publication of data pending). It is undisputable that information of perioperative care, the case volume of participating centers, and the available surgical expertise are of particular importance for appropriate interpretation and extrapolation of findings of laparoscopic RCTs.

The present analysis is limited by the selection RCTs published in a subset of surgical journals. An overview of the laparoscopic literature was not attempted for reasons of practicality and resources. Relevant selection bias is thus inherent to the study methodology. However, a selection based on the most cited journals and the disciplines of General and minimally invasive surgery aimed to identify the presumed best quality laparoscopic RCTs. Furthermore, there is no validated quality assessment tool for intervention studies, let alone for surgical RCTs. The SIGN assessment tool was preferred over the CONSORT checklist, as the latter is considered to have

directly influenced researchers and journal editors,[6] whereas the former may be used as an objective and independent assessment tool, although several crucial components are overlapping.

The volume of laparoscopic RCTs has increased from 2002 to 2012. Previously low-contribution countries have been actively involved in the production of RCTs with an increasing trend, suggesting a globalization of minimally invasive surgery, which is also endorsed by an increasing proportion of international collaborations. Although the proportion of quality RCTs has improved as well, inadequate methodology represents a field for further improvement.

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