

Assessing the Quality of Statistical Reports of Randomised Clinical Trials

تقييم نوعية التقارير الإحصائية إلى التجارب العشوائية التي تجرى على المرضى

Dr. Nazera Dakhil, PhD and M.sc. in Medical Statistics

Lecturer at Department of Mathematics, College of Mathematics and Computer Sciences, University of Kufa, Iraq

Abstract

Randomised clinical trials are the optimum way to compare effectiveness of different interventions. It is well known that randomised trials have the power promptly to influence patients care. In spite of that reviews of published trials have always found significant deficiencies in reporting [2][3]. It is therefore utterly realistic to call for higher standards for papers reporting randomised trials.

In this article we will report results of a systematic review examining the quality of statistical reports in randomised clinical trials in cancer radiotherapy. Checklists for statistical aspects of phase III randomised clinical trial were compiled from guidelines for the reporting of clinical outcome studies (Consolidated Standards of Reporting Trials) (CONSORT).

Keywords— CONSORT, Medline, randomised clinical trials, systematic review

ملخص البحث

في هذا البحث سوف نصف نتائج مراجعة منتظمة في فحص نوعية التقارير الإحصائية إلى التجارب العشوائية التي تجرى على المرضى السرطان والمنشورة في مجلات عالمية.

INTRODUCTION

In the mid-1990s, CONSORT (Consolidated Standards of Reporting Trials) introduced a set of guidelines aimed at improving the quality of reports of randomised clinical trials. These guidelines, in the form of a checklist relating to the content of the title, abstract, introduction, methods, results and discussion, have since been adopted by more than 100 biomedical journals.

We compiled a statistical checklist (61 questions) to evaluate statistical reports of phase III randomised trials. Some items appear on the checklist for controlled trials that has been used by the BMJ's statistical referees for over 10 years [1]. Other items on the checklist have benefit from greater explanation than is possible in the CONSORT statement. These are being used by two independent reviewers to check reports published in year 2000[4]

The statistical checklist consists of 61 questions ranging from general considerations such as whether the paper states the type of statistical software used to more specific questions relating to the statistical tests used.

A proportion of papers that a statistician was a co-author to the one without statistician, were compared on the quality of reporting and the quoting of confidence limits using the binomial probabilities that were obtainable from the actual binomial distribution formula or from a statistical table of binomial probabilities. SPSS for windows was used as statistical package to analyse the data, two-sided test was used with 5% level of significant.

MATERIAL

A Medline search for radiotherapy and cancer of year 2000 papers (limited to human randomised trials in English) yielded 155 papers.

Sixty-six of these papers were selected for this review after we rejected papers found to be reporting on benign disease, techniques other than randomised clinical trials, non-randomised studies and phase II trials. 27 papers (listed below) have been reviewed

Adelstein DJ, Cancer 88:876-883; Balzarini A, Br.Homeopath.J. 89:8-12; Bampoe J, J. Neurosurg. 93:917-926; Carvalho AL, Eur.Arch.Otorhinolaryngol. 257:164-167; Chang TC, J. Clin. Oncol. 18:1740-1747; Chella A, Lung Cancer 27:169-175; Creutzberg CL, Lancet 355:1404-1411; Dent SF, Ann. Oncol. 11:65-68; Duncan GG, Eur.J.Cancer 36:759-765; Etiz D, Oral Oncol. 36:116-120; Feng QF, Int.J.R.O.B.P. 47:925-929; Harima Y, Cancer 88:132-138; Jeremic B, J. Clin. Oncol. 18:1458-1464; Keller SM, New Eng. J. Med. 343:1217-1222; Khan AM, Am.J.Gastroent. 95:1961-1966; Kilic D, Rad.& Oncol. 57:125-129; Kirkbride P, J.Clin.Oncol. 18:1960-1966; Konigsrainer A, Hepatogastroenterology 47:724-727; Kortmann RD, Int.J.R.O.B.P. 46:269-279; Kwon HC, Rad.& Oncol. 56:175-179; Lajtman Z, Acta Med.Croatica 54:65-67; Martenson JA, J. Clin. Oncol. 18:1359-1370; Mead GM, Cancer 89:1359-1370; Onishi H, Cancer J. Sci. Am. 6:40-45; Petit JY, Plast. Reconstr. Surg.105:2544-2551; Pollack A, J. Clin. Oncol. 18:3904-3911; Postmus PE, J. Clin. Oncol. 18:3400-3408

RESULTS

A Medline search, for radiotherapy and cancer, of papers published in year 2000 (limited to human RCTs reported in English) yielded 155 abstracts. Of these 89 were found not to be reports of phase III RCTs in RT. The remaining 66 papers were selected for our review.

This article reports on results obtained from 27 of these 66 papers. The quality of reporting of statistics in randomised clinical trials.

Figure 1 shows the cumulative distribution of sample sizes of the studies survey. The non-linear upper axis indicates the minimum treatment effect needed for a trial of a given size to have a power of 90% assuming a 5% significance level.

Over 80% of the studies did not have adequate statistical power to resolve a 20% improvement in outcome with 90% probability.

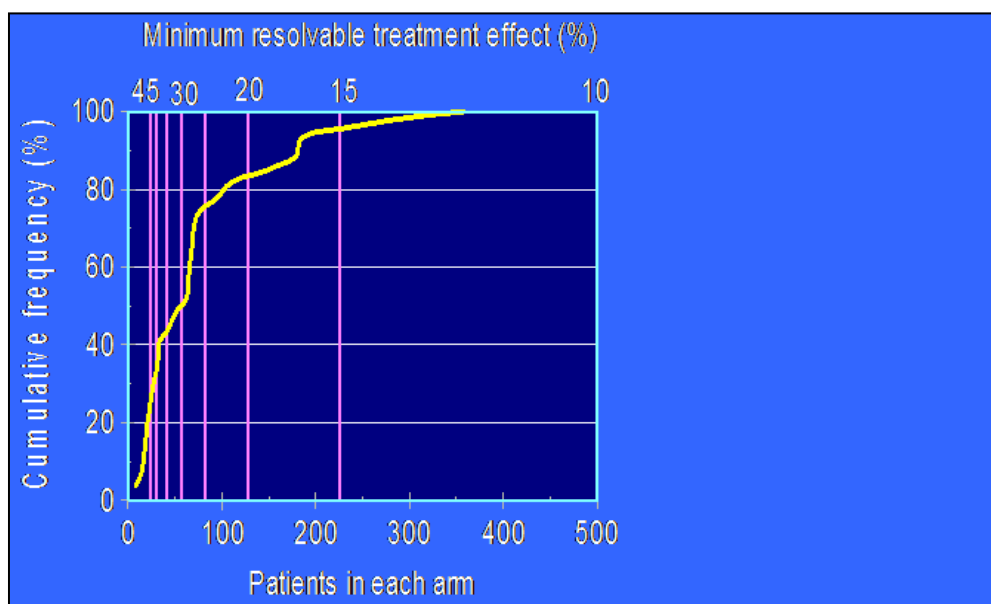


Figure (1): Cumulative distribution of sample sizes

Figure 2 shows the extent of piece of information in reporting survival statistic. About 50% of the papers defined censoring. Over 40% of the paper described patients at risk overtime and the mean or the median, on the other hand only 25% had stated type of the long rank test. It is fascinating to note that less the 20% of the studies provide details of the confidence limits.

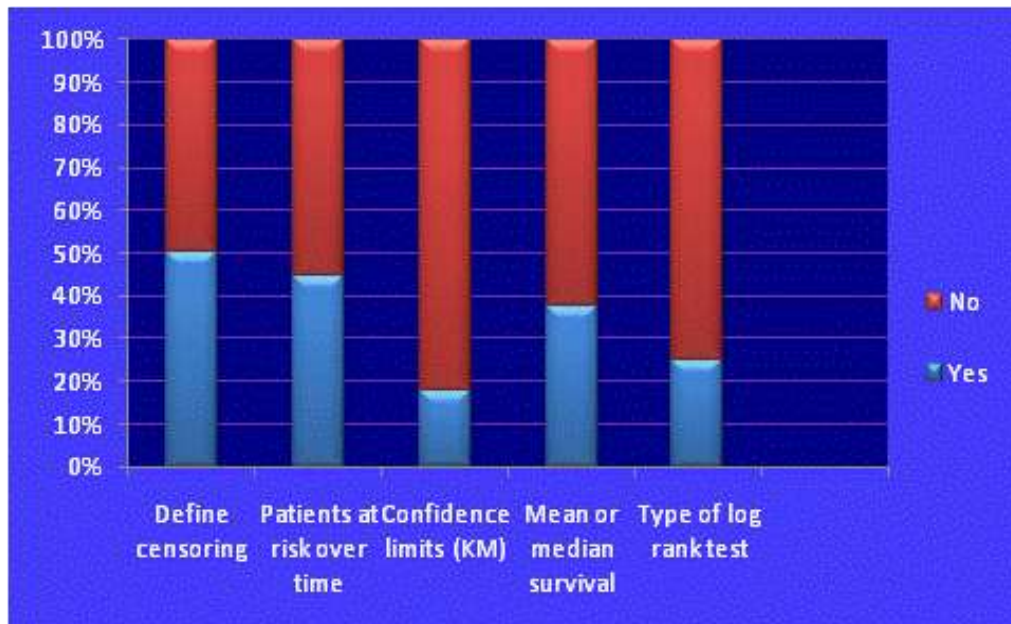


Figure (2): Level of detail in reporting survival statistic

A proportion of papers that a statistician was a co-author to the one without statistician, were compared on the quality of reporting and the quoting of confidence limits. The result shows that whether a statistician is a co-author on the paper does not make any significant difference to the quality of reporting, except in the quoting of confidence limits for survival analysis ($p=0.03$). All papers without a statistician as a co-author did not report these confidence limits.

Figure 3 and 4 shows the distribution of number of P-values. The number of P-values referring to a comparison of therapeutic outcome was counted and the inferred number of P-values, judged to have been calculated but not necessarily reported, was estimated. When there are a large number of statistical tests for difference in outcome, the effective significance level, α will be larger than the nominal 5% α .

Due to the multiple comparisons, there is a high chance of a false-positive result even if the null hypothesis is correct in reality. Very few papers, 11%, used a statistical correction for multiple comparisons.

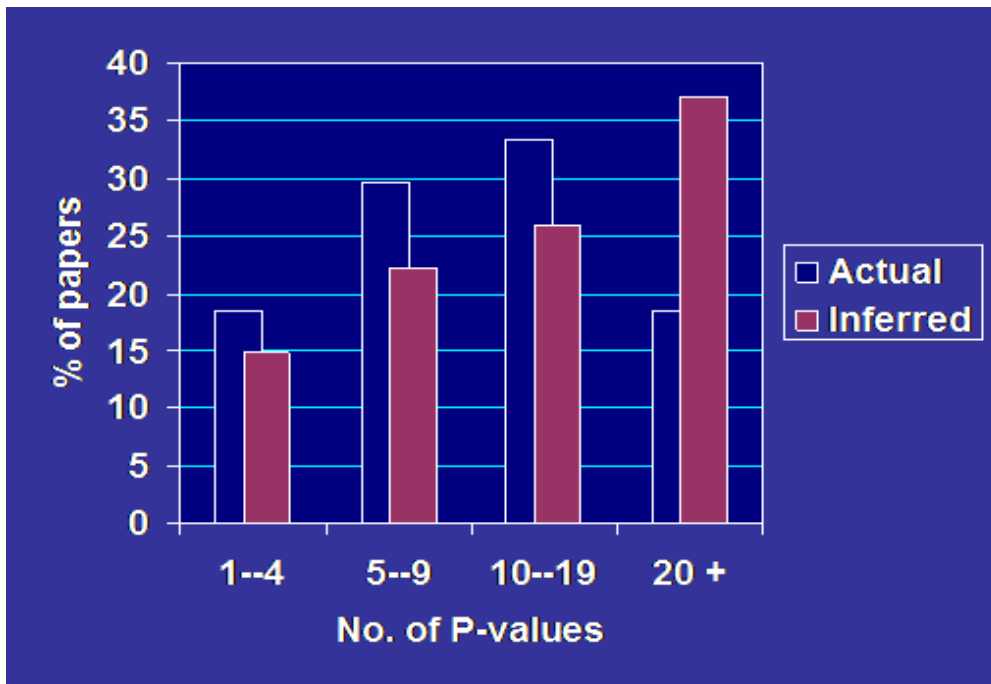


Figure (3): The distribution of number of P-values by % of papers

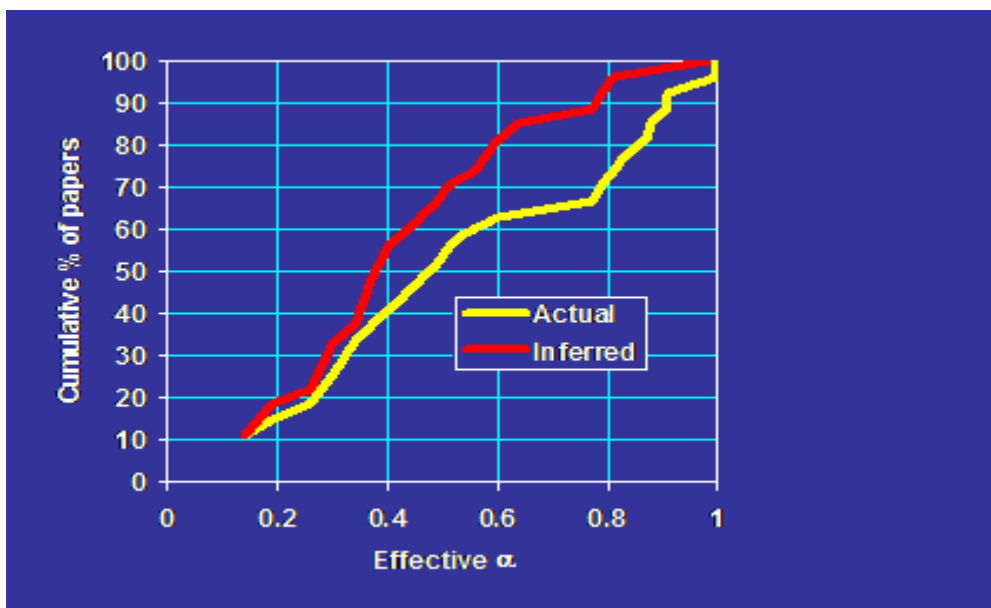


Figure (4): Cumulative (%) of papers by effective α for actual and inferred p-values

SUMMARY & COCLUSION

This paper reports on results obtained from 27 of the 66 papers selected for our systematic review of the quality of reports of randomised clinical trials in cancer and radiotherapy. Our conclusions are many papers are still not meeting basic CONSORT criteria. More than 80% of the studies did not have sufficient statistical power to resolve a 20% enhancement in effect with 90% probability. Basic statistical information is still under reported.

Most reports contain multiple p-values relating to outcome and this increases the risk of a false- positive finding.

A statistician as co-author does not make any significant difference to the quality of the reporting of most statistical issues.

Our overall conclusion is that despite CONSORT and the acceptance of these guidelines by many biomedical journals the quality of reporting of randomised clinical trials in radiotherapy and cancer still needs to be improved.

Reference

1. Gardner MJ, Machin D, Campbell MJ. The use of checklists in assessing the statistical content of medical studies *BMJ* 1986; 292: 810-2
2. JÜni p., Altman D. G. and Egger M. *Systematic Reviews in health care: Assessing the quality of controlled clinical trials*, *BMJ* 2001; 323: 42-46.
3. Pocock SJ, Hughes MD, Lee RJ. Statistical problems in reporting of clinical trials. *N Engl J Med* 1987; 317:426 -32.
4. Renni D. Reporting randomised controlled trials: an experiment and a call for responses from readers, *JAMA* 1995; 273: 1054 – 5. [Medline]