

Variables affecting evaluation and publication of oncology case reports: a systematic analysis

Antonio Florita¹, Elena Morittu¹, Carlotta Galeone², Antonette E. Leon³, Rossella Ballarini¹, Giulio Zuanetti⁴

¹Fondazione IRCCS Istituto Nazionale dei Tumori, Milan - Italy

²Department of Clinical Sciences and Community Health, University of Milan, Milan - Italy

³Regional Center for Biomarkers, Department of Clinical Pathology and Transfusional Medicine, Azienda ULSS 12 Veneziana, Regional Hospital, Venice - Italy

⁴Wichtig Publishing, Milan - Italy

Antonio Florita and Elena Morittu contributed equally to this work.

ABSTRACT

Background: Studies on factors affecting editorial decisions of scientific journals are scarce. In this study, we focused on case reports submitted to oncology journals and analyzed whether their nature or other relevant variables affected the chances of their acceptance.

Methods: We analyzed case reports submitted to 2 oncology journals: *Tumori Journal* and *The International Journal of Biological Markers*, and split them into 3 predefined groups: those (a) describing rare or unusual presentation of diseases, (b) describing the side effects of an intervention or (c) describing the success of a novel intervention. Publication status was retrospectively retrieved from the submission system, and acceptance rates were calculated taking into account other variables including geographic location of corresponding author.

Results: A total of 326 case reports were suitable for analysis. The acceptance rate was 35.4% for group (a), 27.9% for group (b), 19.6% for group (c) ($p = 0.01$). After correcting for other variables, the odds ratio (OR) of being accepted for group (c) was 0.58 (95% CI, 0.33-1.00) compared with the other groups combined. There was a highly significant difference of acceptance rates between manuscripts with authors coming from developed vs. developing countries that remained significant (OR = 5.94; 95% CI, 3.05-10.09) after correcting for multiple variables.

Conclusions: The nature of a case report in oncology may affect acceptance rate, with case reports describing successful approaches or side effects of treatment being accepted with a higher frequency than case reports describing a rare clinical or diagnostic scenario. Also, works coming from developed countries are accepted significantly more frequently than case reports coming from developing countries.

Keywords: Case reports, Oncology, Peer review, Publication bias

Introduction

Despite its ups and downs (1, 2), editorial evaluation and peer reviewing of manuscripts remains the backbone of scientific journals. Several studies over the past several

years have evaluated whether there is a bias in peer review based on the positive or negative outcome of randomized control trials (3), the behavior of US vs. non-US peer reviewers (4), the type of industry involvement (5) and others, but evidence remains relatively scarce when case reports are concerned.

Therefore, in this study we approached the issue from a different angle and focused our attention on case reports, which represent a relatively homogenous type of article, generally do not have industry support at variance with clinical trials and can be broadly categorized into different groups.

We tested the hypothesis that the country of affiliation of the corresponding authors and/or the nature of the case reports could per se influence the final outcome of the editorial decision (acceptance or rejection) of case reports.

Received: August 25, 2016

Accepted: October 3, 2016

Published online: November 8, 2016

Corresponding author:

Dr. Antonio Florita

Fondazione IRCCS Istituto Nazionale dei Tumori di Milano

Via Giacomo Venezian, 1

20133 Milan, Italy

antonio.florita@istitutotumori.mi.it



Methods

Study protocol

The full text of manuscripts labeled as “case reports,” received by the Editorial Offices of the *Tumori Journal* (TJ) and *The International Journal of Biological Markers* (IJBM) for which a decision had been made between January 1, 2015, and June 30, 2016, were selected for the study.

This interval was chosen as it represented a time when there were no changes in the Editorial Board of either journal and particularly in the editors of the sections of reference for the case reports submitted.

Countries of the corresponding author were collected, and cases were classified by at least 2 independent evaluators into 3 broad categories and a total of 9 subcategories, according to the following classification:

- 1a. Report of a rare disease;
- 1b. Report of a rare presentation of a disease or of an elusive diagnosis or of an unusual biomarker(s) phenotype/genotype;
- 2a. Report of successful diagnosis or successful predictive use of markers;
- 2b. Report of successful treatment (drug);
- 2c. Report of successful treatment (device, radiotherapy, other);
- 2d. Report of successful treatment (surgery);
- 3a. Report of a side effect of a treatment (drug);
- 3b. Report of a side effect of a treatment (device, radiotherapy, other);
- 3c. Report of a side effect of a treatment (surgery).

When the report was dealing with different scenarios (e.g., successful novel treatment of a relatively rare disease), the evaluators allocated the case to the prevalent category. In the few cases of discrepancy between the 2 evaluators regarding the classification, the case would be evaluated by a third evaluator.

Countries of corresponding authors were clustered into 2 predefined categories: Developed Countries (United States, Canada, Western European countries, Japan, Australia and New Zealand) and Developing Countries (Mexico and Latin America, Eastern European countries, other Asia Pacific countries), to evaluate whether the country of the corresponding author could influence the acceptance rate.

Data analysis

Categorical data were presented as numbers and percentages, and comparisons between groups were performed using contingency table analysis with the chi-square test. The odds ratios (ORs) of acceptance of case reports and the corresponding 95% confidence intervals (CIs) were derived using unconditional multiple logistic regression models. Multivariate models included terms for country (developing vs. developed), topic of case reports (rare diseases or elusive diagnoses vs. other topics) and calendar period (2015 vs. 2016).

All tests were 2-sided, and a *p* value of less than 0.05 was considered as statistically significant. Data analyses were

conducted using SAS version 9.2 (SAS Institute, Cary, NC, USA) statistical software.

Results

A total of 327 manuscript labeled as case reports were received by the Editorial Offices in the period taken into consideration. One was clearly mislabeled and sent back to authors for correction. Out of the remaining 326, a total of 83 (25.5%) were accepted for publication either in regular issues (6-50), or in a dedicated case reports supplement (51).

The acceptance rate was significantly different when the case reports were clustered by topic, with successful diagnosis or treatment case reports having an acceptance rate of 35/99 (35.4%) followed by report of an adverse event (12/43, 27.9%) and report of a rare disease (36/184, 19.6%). Acceptance rate declined throughout the study period, with acceptance of 65/224 (29%) during 2015 and 18/102 (17.6%) during the first 6 months of 2016 (*p* = 0.03).

When comparing developing and developed countries of affiliation of the corresponding authors, a significant difference was observed in acceptance rates: 66/162 (40.7%) vs. 17/164 (10.4%; *p* < 0.001).

Multivariate models including terms for country (developing vs. developed), topic of case reports (rare diseases vs. other topics) and calendar period (2015 vs. 2016) showed that the difference between developed and developing countries remained highly significant. The difference of topic remained of borderline significance with an adjusted OR of 0.58 (95% CI, 0.33-1.00), and the temporal trend was also significant (Tab. I).

Interestingly, although several manuscripts received by the Editorial Office had a title explicitly referring to a “literature review” as a complement to the description of the case report, a careful analysis of the full text indicated that a thorough review of the literature was indeed present in only a very few of those manuscripts (*n* = 3) thus preventing any meaningful analysis of its role in affecting acceptance of the manuscript.

Discussion

Editorial scrutiny and peer review of submitted manuscripts remains the main pillar of scientific literature. Despite the criticism inherent in the process itself (52), the development of alternative methods of evaluating the merits of scientific manuscripts, such as straight-away publication followed by post reviews and others, the vast majority of manuscripts ultimately published in the scientific literature, still go through the standard peer reviewing procedure, with an initial screening by the Editor in Chief (EIC) or the Associate Editors, and then review by experts in the field leading to the EIC’s final decision on the manuscript. Given the ubiquity of this process, it is surprising that data about what happens at peer review, and regarding which variables might affect acceptance or rejection of the manuscript are relatively scarce. Link (4) has evaluated whether US vs. non-US peer reviewers for JAMA would be more inclined to accept results obtained by US vs. non-US colleagues, thus focusing on the attitude of peer reviewers toward studies coming from the United

TABLE I - Association between selected factors and acceptance of case reports submitted to TJ and IJBM accepted between January 1, 2015, and June 30, 2016

	Crude OR (95% CI)	Adjusted OR (95% CI)*	Adjusted OR (95% CI)†
Country			
Developing	1 (Ref)	1 (Ref)	1 (Ref)
Developed	5.94 (3.29-10.75)	5.54 (3.05-10.09)	5.66 (3.10-10.31)
Topic			
Others	1 (Ref)	1 (Ref)	1 (Ref)
Rare diseases	0.49 (0.30-0.82)	0.59 (0.34-1.01)	0.58 (0.33-1.00)
Year			
2015	1 (Ref)	-	1 (Ref)
2016	0.52 (0.29-0.94)	-	0.50 (0.27-0.93)

CI = confidence interval; IJBM = *The International Journal of Biological Markers*; OR = odds ratio; TJ = *Tumori Journal*.

* Model adjusted for topic and country.

† Model adjusted for all variables reported in the table.

States. Link found that US reviewers showed a preference for US papers. Van Lent et al (3) evaluated whether the reporting of positive results might facilitate acceptance but did not show any significant difference in acceptance rates compared with manuscripts reporting negative results. In a more recent study, the same group (5) investigated whether industry sponsorship might affect acceptance and found that reviewers tended to identify fewer shortcomings in the design and statistical analysis of industry-related trials; however, the data showed that the research question and the methodological soundness were till the major drivers of acceptance.

In trying to quantify and model potential editorial bias, Wang et al (53) have proposed an agent-based model in which the process of peer review is guided mainly by the social interactions among authors, editors and reviewers, respectively. They applied the model to analyze a number of editorial behaviors such as decision strategy, number of reviewers and editorial bias in peer review and found that peer review outcomes were significantly sensitive to different editorial behaviors. While the simulation analysis was insightful, it is still unclear how this would apply to the day-to-day peer review process in any attempt to decrease bias (52).

In our study, we focused our analysis on the final outcome of the peer review process (rejection or acceptance), and we took into consideration the potential influence of 2 main variables: (a) the country of affiliation of the corresponding author and (b) the topic of the case reports. Because a progressive trend toward a lower acceptance rate was highlighted by comparing the acceptance rates of 2015 vs. those of the first 6 months of 2016, the analysis of the data gathered was corrected in a multivariate analysis to evaluate the time-independent influence of those variables on outcomes.

The results were particularly striking for the country of affiliation of the corresponding author, with case reports authored by researchers working in “developed” countries having at least a fivefold increase in acceptance rates compared with authors working in developing countries. This difference remained highly significant even adjusting for topic and time, as shown in Table I. It can be argued that

the highly significant difference in the acceptance rate was due to a different novelty, and in the quality of the description of the cases themselves, with the authors affiliated with institutions from developed countries perhaps describing more interesting or more thorough or better-written case reports, and that there was no bias toward where the work came from. But the finding remains that the authors affiliated with institutions coming from developed countries have a significantly higher chance of acceptance, and the data seem consistent with those reported by Link (4) where US peer reviewers tended to have a more positive approach toward US papers.

Perhaps more intriguing is the finding that the type of case report itself per se may independently influence the acceptance rate for the article. Indeed, in our study case reports describing a report of a rare disease, a report of a rare presentation of a disease or describing an elusive diagnosis or an unusual biomarker(s) phenotype/genotype had an overall much lower acceptance rate (19.6%) compared with either the description of a severe side effect of a treatment (i.e., a drug, a device, radiotherapy, surgery), or other (27.9%), and the report of successful diagnosis or successful predictive use of markers or of successful treatment (35.3%). This suggests that reviewers might be more prone to accept case reports where the diagnostic approach or medical or surgical intervention made a difference in the natural history of the disease. This observation needs confirmation in other case report series either in the same therapeutic areas or others.

Acknowledgment

We thank Elena Colombo for useful insights and comments on the manuscript.

Disclosures

Financial support: No grants or funding have been received for this study.

Conflict of interest: The authors declare they have no conflict of interest.



References

- Benos DJ, Bashari E, Chaves JM, et al. The ups and downs of peer review. *Adv Physiol Educ.* 2007;31(2):145-152.
- Jefferson T, Rudin M, Brodney Folse S, Davidoff F. Editorial peer review for improving the quality of reports of biomedical studies. *Cochrane Database Syst Rev.* 2007;(2):MR000016.
- van Lent M, Overbeke J, Out HJ. Role of editorial and peer review processes in publication bias: analysis of drug trials submitted to eight medical journals. *PLoS ONE.* 2014;9(8):e104846.
- Link AM. US and non-US submissions: an analysis of reviewer bias. *JAMA.* 1998;280(3):246-247.
- van Lent M, Int'Hout J, Out HJ. Peer review comments on drug trials submitted to medical journals differ depending on sponsorship, results and acceptance: a retrospective cohort study. *BMJ Open.* 2015;5(9):e007961.
- Bhagwandin SB, Salti GI. Hepatocellular carcinoma with peritoneal metastasis treated with cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy. *Tumori.* 2015;101(1):e1-e3.
- Franco P, Migliaccio F, Torielli P, et al. Bilateral breast radiation delivered with static angle tomotherapy (TomoDirect): clinical feasibility and dosimetric results of a single patient. *Tumori.* 2015;101(1):e4-e8.
- Lee A, Go SI, Lee WS, et al. Irinotecan and capecitabine combination chemotherapy in a patient with triple-negative breast cancer relapsed after adjuvant chemotherapy with anthracycline and taxane. *Tumori.* 2015;101(1):e9-e12.
- Priola AM, Priola SM. Thymoma of the left thymic lobe with a contralateral small pleural implant successfully detected with diffusion-weighted MRI. *Tumori.* 2015;101(1):e13-e17.
- Gurrieri L, Longhi A, Braghetta A. Lung cancer presenting as a metastasis to the tibial bones: a case report. *Tumori.* 2015;101(1):e18-e20.
- Matrone F, Sivoiella S, Bellavita R, Casciola L, Cristallini EG, Aristei C. Use of 18F-choline positron emission tomography/CT in high-risk prostate cancer: a case of solitary adrenal metastasis. *Tumori.* 2015;101(1):e21-e23.
- Biasco E, Antonuzzo A, Galli L, et al. Small-bowel neuroendocrine tumor and retroperitoneal fibrosis: efficacy of octreotide and tamoxifen. *Tumori.* 2015;101(1):e24-e28.
- Redondo A, Castelo B, Pinto A, Zamora P, Espinosa E. Prolonged response to aflibercept in ovarian cancer relapse: a case report. *Tumori.* 2015;101(1):e29-e31.
- Rafee S, Elamin YY, Joyce E, et al. Neoadjuvant crizotinib in advanced inflammatory myofibroblastic tumour with ALK gene rearrangement. *Tumori.* 2015;101(2):e35-e39.
- Cihan S, Atasoy A, Yildirim Y, Babacan NA, Kos TF. Hypersensitivity and tumor lysis syndrome associated with cetuximab treatment: should we be afraid? *Tumori.* 2015;101(2):e40-e45.
- Brandi G, De Lorenzo S, Di Girolamo S, Bellentani S, Saccoccio G, Biasco G. Fulminant hepatitis in a patient with hepatocellular carcinoma related to nonalcoholic steatohepatitis treated with sorafenib. *Tumori.* 2015;101(2):e46-e48.
- Chang H, Shih LY. Chronic lymphocytic leukemia-associated refractory immune thrombocytopenia successfully treated with eltrombopag. *Tumori.* 2015;101(2):e49-e50.
- Bordi P, Tiseo M, Buti S, Regolisti G, Arzidoni A. Efficacy and safety of long-term tolvaptan treatment in a patient with SCLC and SIADH. *Tumori.* 2015;101(2):e51-e53.
- Li M, Andrä C, Niyazi M, et al. Concomitant trimodality therapy of re-irradiation, chemotherapy and regional hyperthermia for a pretreated inoperable sarcoma recurrence. *Tumori.* 2015;101(2):e54-e56.
- Arcangeli S, Gambardella P, Agolli L, et al. Stereotactic body radiation therapy salvage reirradiation of radiorecurrent prostatic carcinoma relapsed in the prostatic bed. *Tumori.* 2015;101(2):e57-e59.
- Gambini D, Visintin R, Locatelli E, et al. Secondary breast angiosarcoma and paclitaxel-dependent prolonged disease control: report of two cases and review of the literature. *Tumori.* 2015;101(2):e60-e63.
- Vitale MG, Scagliarini S, Riccardi F, et al. Long progression-free survival with afatinib in a patient with EGFR-unknown lung adenocarcinoma after erlotinib failure: a case report. *Tumori.* 2015;101(2):e64-e66.
- Tatli AM, Besen AA, Kalender ME, et al. Association of vitiligo and response in patients with metastatic malignant melanoma on temozolomide. *Tumori.* 2015;101(2):e67-e69.
- Ginori A, Lo Bello G, Vassallo L, Tripodi SA. Amphicrine carcinoma of the ampullary region. *Tumori.* 2015;101(2):e70-e72.
- Bertocchi P, Meriggi F, Zambelli C, Zorzi F, Zaniboni A. Clear cell thymic carcinoma: a case report. *Tumori.* 2015;101(2):e73-e74.
- Giuliani J, Piacentini P, Bonetti A. Ampulla of Vater carcinoma in real-world clinical practice: a case series. *Tumori.* 2015;101(3):e75-e78.
- Messina C, Di Meglio A, Nuzzo PV, Boccardo F, Ricci F. Very late recurrence of renal cell carcinoma experiencing long-term response to sunitinib: a case report. *Tumori.* 2015;101(3):e79-e81.
- Bini R, Comelli S, Addeo A, et al. Inferior mesenteric artery chemoembolization and chemotherapy for advanced rectal cancer: report of a clinical case. *Tumori.* 2015;101(3):e82-e84.
- Shenoy S. PIK3CA mutations in small bowel adenocarcinoma. *Tumori.* 2015;101(3):e85-e87.
- Falcinelli L, Bellavita R, Rebonato A, et al. Bronchiolitis obliterans organizing pneumonia after radiation therapy for lung cancer: a case report. *Tumori.* 2015;101(3):e88-e91.
- Genestreti G, Di Battista M, Trisolini R, et al. A commentary on interstitial pneumonitis induced by docetaxel: clinical cases and systematic review of the literature. *Tumori.* 2015;101(3):e92-e95.
- Hwang KE, Jung JW, Oh SJ, et al. Transformation to small cell lung cancer as an acquired resistance mechanism in EGFR-mutant lung adenocarcinoma: a case report of complete response to etoposide and cisplatin. *Tumori.* 2015;101(3):e96-e98.
- Griguolo G, Mazzucchelli L, Cavalli F, Ceriani L, Zucca E, Stathis A. A case of Hodgkin lymphoma in a patient with a history of bone pain and an initial diagnosis of chronic osteomyelitis. *Tumori.* 2015;101(3):e99-e102.
- Petreni P, Mazzoni F, Meoni G, et al. Outcome of crizotinib treatment in a young woman with heavily pretreated ROS1-positive lung cancer. *Tumori.* 2015;101(3):e103-e106.
- Maniglio M, Capalbo E, Viganò S, Trecate G, Scaperrotta GP, Panizza P. Breast metastasis from cutaneous malignant melanoma mimicking a breast cancer. *Tumori.* 2015;101(3):e107-e109.
- Billè A, Girelli L, Colecchia M, Pastorino U. Single synchronous pulmonary metastasis from placental site trophoblastic tumor and teratoma. *Tumori.* 2015;101(3):e110-e111.
- Giuliani J, Martelli S, Remo A, Bonetti A. Primary TKI resistance in advanced non-small cell lung cancer with EGFR mutation: an open question. *Tumori.* 2015;101(4):e115-e117.
- Abbate MI, Cicchiello F, Canova S, et al. Isolated cardiac metastasis from squamous cell esophageal cancer. *Tumori.* 2015;101(4):e118-e121.
- Macerelli M, Mazzer M, Foltran L, Cardellino GG, Aprile G. Erlotinib-associated interstitial lung disease in advanced pancreatic carcinoma: a case report and literature review. *Tumori.* 2015;101(4):e122-e127.
- Di Girolamo M, Paris I, Carbonetti F, Onesti EC, Socciarelli F, Marchetti P. Widespread renal polycystosis induced by crizotinib. *Tumori.* 2015;101(4):e128-e131.
- Galetta D, Catino A, Misino A, et al. Bladder and gastric metastases from lung adenocarcinoma harboring codon 13 KRAS

- mutation: a case report with unusual clinical outcome. *Tumori*. 2015;101(5):e138-e140.
42. Schönknecht C, Hadjamu M, Oechsner M, Andratschke N, Duma MN. Long-term survival in metastasized leiomyosarcoma: a case report and review of the literature. *Tumori*. 2015; 101(5): e141-e144.
 43. Taberner Bonastre MT, Peralta Muñoz S, Boza FM, Gumà I, Padró J. Neutropenia secondary to exposure to levetiracetam. *Tumori*. 2015;101(5):e145-e146.
 44. Cetinkaya K, Benzer E, Dervisoglu H. Primary mucosal malignant melanoma of the cervix: case report and review of the literature. *Tumori*. 2015;101(5):e147-e150.
 45. Bellodi A, Rivoli G, Arboscello E, et al. Hepatosplenic T-cell lymphoma with aberrant expression of serum β -HCG: a case report. *Tumori*. 2015;101(6):e160-e162.
 46. Unal A, Yurtsever Kum N, Kum RO, et al. Giant cemento-ossifying fibroma of the maxilla. *Tumori*. 2015;101(6):e163-e166.
 47. Sponghini AP, Platini F, Rondonotti D, Soffietti R. Bevacizumab treatment for vestibular schwannoma in a patient with neurofibromatosis type 2: hearing improvement and tumor shrinkage. *Tumori*. 2015;101(6):e167-e170.
 48. Campos-Gomez S, Lara-Guerra H, Routbort MJ, Lu X, Simon GR. Lung adenocarcinoma with concurrent KRAS mutation and ALK rearrangement responding to crizotinib: case report. *Int J Biol Markers*. 2015;30(2):e254-e257.
 49. Trimboli P, Guidobaldi L, Locuratolo N, Piro FR, Giordano M, Giovanella L. Serum markers measured in FNA fluids of medullary thyroid carcinoma occurring as a cyst. *Int J Biol Markers*. 2016;31(2):e224-e227.
 50. Zampiga V, Danesi R, Tedaldi G, et al. Multiple primary tumors in a family with Li-Fraumeni syndrome with a TP53 germline mutation identified by next-generation sequencing. *Int J Biol Markers*. 2016 Aug 5:0. doi: 10.5301/jbm.5000227.
 51. Case Reports Supplement. *Tumori*. 2016;102(Suppl 2):S1-S140.
 52. Lee CJ, Sugimoto CR, Zhang G, Cronin B. Bias in peer review. *J Am Soc Inf Sci Technol*. 2013;64(1):2-17.
 53. Wang W, Kong X, Zhang J, Chen Z, Xia F, Wang X. Editorial behaviors in peer review. *Springerplus*. 2016;5(1):903.