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Abstract

Purpose: “Cure” is an important word in oncology but its use in the published literature has not been examined. I investigated all oncology articles using cure in the title field and published in 2012. The definition of cure was examined, specifically whether or not authors use the word to connote some surviving subset of patients who go on to experience outcomes similar to age-matched, normal controls—a definition favored by researchers and employed in survival function analyses. **Methods:** All articles published between January 1, 2012, and December 31, 2012, with the word cure in the title field were retrieved from Thompson Reuters’ Web of Science. After exclusions, articles were read in full to examine what definitions of cure was used. Additionally, for each situation (type of cancer, stage/grade) where the word cure was used, a literature search was performed to ascertain whether there existed documented cases of cure. **Results:** Twenty-nine oncology articles used the word cure in their title in 2012. Nearly half, 14 (48%) of 29, used the term in situations (cancer type, stage/grade) currently considered incurable. Approximately one-third (34.5%) of the articles used the word consistent with the definition that, after a set period of time, some surviving subset of patients experience survival similar to normal controls. **Conclusion:** There is heterogeneity in the use of the word cure in the literature.

Keywords

cure, oncology, language, cancer care, excellence

Introduction

In oncology, the word “cure” can be value laden, connoting different ideas to physicians and patients. A recent survey of practicing oncologists found that 80% of physicians are hesitant to use this term, and, if they do, a plurality (41%) would do so only 6 to 10 years after a cancer diagnosis.¹ Of the physicians, 20% state they would simply never use the word.¹ One prominent medical journalist considers the word cure to be among 7 taboo terms that should never be used in medical reporting, calling it “loaded and ill-defined.”² Others however find the term underused, noting that “using the word cured for cancer survivors may have positive outcomes.”¹

Although the word cure likely holds different meanings for different people, there have been several attempts to achieve consensus. In 2006, a group of pediatric cancer experts discussed the use of the word with respect to children’s cancers. The group felt that, while a canonical definition does not exist, for their purposes, children may be considered cured when “they have reached a time point at which the chance that they will die from their original disease is no greater than that of age peers in the general population of dying from any cause.”³

This definition of cure—that some fraction of patients eventually experience mortality comparable to age and sex-matched peers—was first articulated in 1963, regarding Hodgkin disease.⁴ Easson and Russell write “cure of a disease is taken to

connote that in time—probably a decade or two after treatment—there remains a group of disease free survivors whose annual death rate from all causes is similar to that of a normal population group of the same sex and age distribution.”⁴ Lambert et al⁵ codified this concept into a statistical model, which now serves as the basis of cure (or survival) function analysis.

To investigate whether or not the word cure is used as defined by Easson and Russell in the oncologic literature or what alternative meanings are favored, I set out to assemble a collection of representative cancer articles published in 2012 that use cure in the title.

Methods

Using *Thompson Reuters Web of Science*, I searched for all articles containing the word cure in the title and published between January 1, 2012, and December 31, 2012. I restricted my search to articles under the category “oncology.” Among document

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types “articles,” “editorial material,” “reviews,” and “letters” were included while “news items” and “meeting abstracts” were excluded. Meeting abstracts were excluded as the full posters and/or presentations were often unavailable, and news items were excluded as medical writers (and not academic oncologists) often author these pieces.

All articles meeting these criteria (41) were downloaded and read. Articles not in English (3), pertaining to animal studies (1), not related to cancer (5) or those using cure only as an abbreviation, part of hyphenated term, or as the title of an event (3) were excluded.

The remaining articles (29) were read in full. Data were extracted regarding the title of the article, the tumor type and stage and/or grade being discussed, and whether or not the word cure appeared solely in the title or in the text as well. Articles were then scored based upon prespecified criteria of whether or not the authors use the word cure as defined by Easton and Russell. If not, did authors provide an alternative definition of cure. If an alternative definition is offered, these sentences were extracted in full. Finally, for the specific cancer and stage/grade, a Medline search was performed to determine whether or not there were documented cases of cure.

Results

Twenty-nine articles that were published in the oncology literature in 2012 used the word cure in their title. Of these 29 articles, the word cure appeared nowhere in the body of the text of 2 (6.9%) articles. Of these 2 articles, in 1 case, the word cure was used in the title of an incurable malignancy and in the other case, the article did not focus on a single cancer but cancer vaccines in general.

In 10 (34.5%) of 29 articles, the word cure was used consistent with the definition advocated by Easton and Russell, specifically, that after a certain period of time, some surviving fraction of patients survive at rates comparable to that of the general population. For 15 (52%) of 29 articles, the specific cancer type and/or stage/grade discussed have had documented cases of cure but in 14 (48%) of 29 cases the word cure was used in the absence of any cases of cure. The results of all 29 articles are summarized in Table 1.

Two articles use cure in reference to chronic myeloid leukemia, 1 referring to a “functional” cure, where indefinite tyrosine kinase inhibitor use prevents disease progression,¹⁰ and the other referring to “therapy discontinuation without molecular response.”⁹ Four articles were paired in a single theme issue of the journal *Breast Cancer* and discussed the possibility for a cure in metastatic breast cancer.¹⁷⁻²⁰

Several articles use the word cure in the context of cure function analyses which proves mathematically that some surviving subset experiences mortality comparable to matched normal controls.^{25,29} A single article used the term to describe the outcome of 1 patient who used sorafenib in the neoadjuvant setting to allow an initially unresectable hepatocellular carcinoma to become resectable, thus serving as a bridge to transplant.³³ However, the length of follow-up for this patient posttransplant was not provided.³³

Discussion

Although the word cure carries important implications and meaning for cancer physicians and patients with cancer, there have been few empirical investigations regarding its use. From this review of the 2012 literature, 2 concerns emerged. The first was the use of cure in situations (cancer type, stage/grade) currently considered incurable. This was found in nearly half (14 of 29; 48%) of all oncology articles published in 2012 that used the word cure in the title. The second was the lack of rigor in defining cure. Only one-third (10 of 29; 34.5%) of the articles used the word consistent with a rigorous definition, specifically—after a set period of time—some surviving subset of patients experience survival similar to normal controls.

At times, the word cure is used to describe an incurable malignancy and does not appear in the text or is used only in a vague manner. In these cases, one may argue that the word is used in a “sensational fashion,” intended to draw attention to the article and not necessarily reflective of the realities of that cancer. However, such conclusions are a matter of judgment and taste. Additionally, the use of language such as cure often arises from a legitimate tension between wanting to inspire a research field, while avoiding sensationalistic claims.

There are several advantages to a clear and rigorous definition of cure. First, it eliminates ambiguity among physicians. Although there are methodology nuances to survival function analyses, the definition of Easton and Russell is generally clear and unambiguous. Second, a rigorous definition may better accord with our shared belief about what a cure really is—the idea that at some point after treatment, one’s life is no different than someone who had not experienced that disease.

There are several limits to the current investigation. First, although the articles selected were based on a systematic sample, they all originate from a single year. Since the use of language changes over time, the advantage of this strategy is that these articles capture the current use of the word. The disadvantage is that this study cannot inform us about historical patterns of use or trends in the literature. Additionally, this investigation required making decisions regarding classification which are inherently subjective. Thus, others may feel differently about some studies. However, whether or not authors use cure as defined by Easton and Russell is a relatively objective standard while the classification of alternate definitions may be less so. For this reason, the latter was reproduced verbatim (Table 1).

This is the first investigation to investigate the use of the word cure in the oncology literature. Prior attempts at understanding how oncologists use this term have focused on surveys of practicing physicians¹ which may not capture how the term is being used in among scholarly work. Neither methodology is inherently superior and both provide valuable information regarding the use of important language among physicians. Thus, the present investigation complements and expands prior work in this field.

In summary, I found that nearly half of articles used the word cure to describe a situation, which is presently incurable and that only a third of articles used the word cure to connote a return to

Table 1. Characteristics of 29 Articles Appearing in 2012 Which Use the Word “Cure” in the Title.

Reference	Title	Definition of cure			Is cure possible?	Comment
		Cancer type and/or stage	Easson and Russell	Other		
Kelsey et al ⁶	Combined-modality therapy for early-stage Hodgkin lymphoma: maintaining high cure rates while minimizing risks	Hodgkin lymphoma	Yes		Yes	
Shack et al ⁷	Cure by age and stage at diagnosis for patients with colorectal cancer in North West England, 1997-2004: a population-based study.	Colorectal cancer	Yes		Yes	
Liesveld ⁸	Management of AML: who do we really cure?	Acute myeloid leukemia		“Not had recurrence of disease for 3 years”	Yes	Definition used may be fair for patients not requiring stem cell transplant; not so for transplant patients—long-term survival is ~30% less than controls
Breccia et al ⁹	Can we safely discontinue imatinib? Searching for new endpoints in CML: a standardized definition of “cure”	Chronic myeloid leukemia (CML)		“Therapy discontinuation without molecular relapse”	No	
Cortes et al ¹⁰	Current issues in chronic myeloid leukemia: monitoring, resistance, and functional cure	CML		“Continued imatinib or second-generation TKI therapy that prevents progression to AP disease and the emergence of resistance may be thought of as an “operational” or a “functional” cure	No	The authors call this a “functional” cure
Kodeda et al ¹¹	Genomic CGH-assessed structural DNA alterations in rectal carcinoma as related to local recurrence following primary operation for cure	Rectal cancer	Yes		Yes	
Jansen et al ¹²	A new era for children with diffuse intrinsic pontine glioma: hope for cure?	Intrinsic pontine glioma		Not provided	No	The word cure is not found in the article
Frampton et al ¹³	Cancer vaccines: is prevention better than cure?	Cancer vaccines		Not provided		The word cure is not found in the article
Awada et al ¹⁴	New therapies in HER2-positive breast cancer: a major step towards a cure of the disease?	HER2+ breast cancer	Yes		Yes	
Othus et al ¹⁵	Cure models as a useful statistical tool for analyzing survival	Multiple myeloma		Not provided	No	

(continued)

Table 1. (continued)

Reference	Title	Definition of cure			Is cure possible?	Comment
		Cancer type and/or stage	Easson and Russell	Other		
Meyer ¹⁶	Playing bad cards properly: challenges to improving cure rates in rhabdomyosarcoma	Rhabdomyosarcoma	Yes		Yes	
Kobayashi ¹⁷	From improved survival to potential cure in patients with metastatic breast cancer	Metastatic breast cancer		Not provided	No	These studies are all from a single issue of the journal <i>Breast Cancer</i>
Cheng ¹⁸	Improvement of survival and prospect of cure in patients with metastatic breast cancer	Metastatic breast cancer		Not provided	No	
Ohno ¹⁹	Can patients with metastatic breast cancer be cured after introduction of newer and more effective agents?	Metastatic breast cancer		Not provided	No	
Kobayashi et al ²⁰	Possible clinical cure of metastatic breast cancer: lessons from our 30-year experience with patients having oligometastatic breast cancer and literature review.	Metastatic breast cancer		Not provided	No	
Garraway ²¹	Will identification of a prostate cancer stem cell lead to its cure?	Metastatic prostate cancer		Not provided	No	
Dawood et al ²²	Brain metastasis in breast cancer: last barrier to the cure?	Metastatic breast cancer		Not provided	No	
Rea et al ²³	Curing chronic myeloid leukemia	CML		Not provided	No	
Fossa et al ²⁴	Two escalated followed by 6 standard BEACOPP in advanced-stage high-risk classical Hodgkin lymphoma: high cure rates but increased risk of aseptic osteonecrosis.	Hodgkin lymphoma	Yes		Yes	
Moulliet et al ²⁵	Pathologic complete response to preoperative chemotherapy predicts cure in early-stage nonsmall-cell lung cancer combined analysis of 2 IFCT-randomized trials	Early stage lung cancer	Yes		Yes	
Ito et al ²⁶	Role of age and tumor stage in the temporal pattern of cure from stomach cancer: a population-based study in Osaka, Japan	Gastric cancer	Yes		Yes	Uses the word cure exceptionally precisely
Bartlett et al ²⁷	Can metastatic colorectal cancer be cured?	Metastatic colorectal cancer		Not provided	Yes	

(continued)

Table 1. (continued)

Reference	Title	Definition of cure			Is cure possible?	Comment
		Cancer type and/or stage	Easson and Russell	Other		
Maithel ²⁸	Metastatic colorectal cancer: potential for cure?	Metastatic colorectal cancer	Yes		Yes	
Dubecz et al ²⁹	Temporal trends in long-term survival and cure rates in esophageal cancer a SEER database analysis	Esophageal cancer	Yes		Yes	Cure is clearly defined
Bajpai ³⁰	Locally advanced breast cancer: prevention is better than cure!	Locally advanced breast cancer		Not provided	Yes	Uses the word cure only tangentially
Li et al ³¹	Diagnosis and cure experience of hepatolithiasis-associated intrahepatic cholangiocarcinoma in 66 patients	Intrahepatic cholangiocarcinoma		Not provided	No	
Kunkler ³²	What price cure?	All tumor types		Not provided	Yes	Cure is vague
Di Benedetto ³³	Is advanced hepatocellular carcinoma amenable of cure by liver transplantation with sorafenib as a neoadjuvant approach plus m-TOR inhibitors monotherapy?	Advanced hepatocellular carcinoma + sorafenib to bridge to transplantation		Not provided	No	Single case report, length of follow-up posttransplant not given
Israels ³⁴	Wilms tumor in Africa: challenges to cure	Wilms tumor		Not provided	Yes	

Abbreviations: AP, accelerated phase; AML, acute myeloid leukemia; BEACOPP, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisolone; CML, chronic myeloid leukemia; CGH, comparative genomic hybridization; IFCT, French Intergroup of thoracic Oncology; HER2, human epidermal growth factor receptor 2; m-TOR, mammalian target of rapamycin; SEER, Surveillance, Epidemiology, and End Results; TKL, tyrosine kinase inhibitor.

survival similar to normal controls. One can argue that there should be consistency in the use of the term cure. Much like the World Health Organization criteria and then *Response Evaluation Criteria In Solid Tumors* (RECIST) were developed to provide investigators a common metric, so too should we have such a metric for cure, a case where a “complete response” is very durable. And one could also argue that in this respect, the definition of Easton and Russell is generally clear and unambiguous and should be adopted. Where for some reason an investigator disagrees, at a minimum, a clear understanding of how the term is being used should be provided to make sense of research claims.

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