Should We Reestablish the Lung Cancer Study Group?

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The hallmark of the Lung Cancer Study Group (LCSG) was its multidisciplinary approach to cancer management, based on close collaboration among thoracic surgeons, medical oncologists, radiation oncologists, pathologists, biostatisticians, and data managers. Discontinuation of funding for the group dispersed a critical mass of thoracic oncologists and had serious adverse effects on clinical trials in early-stage thoracic malignancies, on translational research, and on oncologic education. The use of an intergroup mechanism for clinical trials has been partially successful in continuing the work started by the LCSG, but a sustained effort will be necessary to recreate the framework for clinical investigation provided by the group.

The question “should we reestablish the Lung Cancer Study Group?” indirectly asks whether the Lung Cancer Study Group (LCSG) could accomplish something that other cooperative groups cannot. To answer this question, it is necessary to examine the way the LCSG functioned, and to understand some of the problems that are unique to performing clinical trials in early-stage thoracic malignancies.

The hallmark of the LCSG was its multidisciplinary approach to cancer management, based on close collaboration among thoracic surgeons, medical oncologists, radiation oncologists, pathologists, biostatisticians, and data managers. With respect to administrative and scientific leadership, there was an equal partnership among all specialties. In essence, the group was composed of individuals who perceived themselves and each other primarily as thoracic oncologists, not as surgeons or medical oncologists or radiation oncologists. To achieve this equal partnership, each specialty had to develop a broader knowledge of oncology than is traditionally taught in most residency programs. Surgeons had to understand how specific chemotherapeutic agents or radiation treatments might affect an operation. Medical and radiation oncologists had to understand the nuances of staging and how to integrate surgical resections with other treatment modalities. All of the pathologists had specific expertise in thoracic malignancy and had a close working relationship with the thoracic surgeons. Accurate staging and pathology quality control were considered vital, and not merely a footnote to the activities of the group. Biostatisticians and data managers were considered active participants in the planning and execution of clinical trials, and not merely faceless individuals who rendered a service.

This organization, which ignored the traditional separation of specialties in favor of a collaborative multidisciplinary approach, emulated from the way in which the LCSG was established. The LCSG was founded as a multidisciplinary group to perform adjuvant postoperative clinical trials in early-stage lung cancer. Other, larger cooperative groups such as the Cancer and Leukemia Group B (CALGB), the Eastern Cooperative Oncology Group (ECOG), and the Southwest Oncology Group (SWOG) were founded to study new chemotherapeutic agents in hematologic malignancies. Subsequently, they expanded their efforts into the treatment of solid tumors but continued to focus on the management of advanced cancers. For historical reasons, these groups have been dominated by hematologists and medical oncologists. Inclusion of radiation oncologists and of surgeons has been a relatively recent event, and none of the groups has successfully integrated all of the oncologic specialties to the extent that was achieved in the LCSG.

In addition to ignoring the importance of this multidisciplinary approach, the decision to discontinue funding for the LCSG disregarded several problems that are unique to clinical trials in thoracic malignancies. Surgical residency programs often provide relatively little training in oncology, and virtually never include training in biostatistics or clinical trials methodology. The 1994 directory of the Society of Surgical Oncology lists only 1,300 physicians who have met the criteria for membership because of additional specific training in some area of surgical oncology. The General Thoracic Surgical Club, composed of Canadian and American surgeons who are board certified in cardiothoracic surgery and who devote at least 50% of their practice to general thoracic surgery, includes just over 200 members. Not all of these individuals have specific interest or training in thoracic oncology. None of the accredited cardiothoracic surgical residency programs currently include specific training in biostatistics or clinical trials methodology. Moreover, until recently, no cardiothoracic residency program provided more than 6 months of training in general thoracic surgery. Most of the 2-year residency focused on cardiac surgery. In contrast, there are thousands of board-certified medical oncologists, all of whom have been exposed to clinical trials methodology as an integral part of their fellowship training. The lack of properly trained surgical oncologists makes it difficult to perform well-designed clinical trials in early-stage cancers because surgeons are the gatekeepers to patient accrual in these trials and are responsible for performing the careful operative staging that leads to accurate patient eligibility. This lack of adequately trained surgical oncologists is particularly acute in thoracic surgery.

The LCSG was criticized for taking 5 to 7 years to complete some of its phase 3 randomized trials, and it was assumed that the larger cooperative groups would be able to complete such trials more quickly because of access to a larger pool of patients. It was also assumed that those groups would automatically have in place knowledgeable and enthusiastic thoracic surgical oncologists, and that the close collaboration among oncologic specialties present in the LCSG would quickly be duplicated. However, many of the medical and radiation oncologists had no experience working with each other or with surgical oncologists in this manner. The mutual fund of knowledge and the interchange necessary for successful multidisciplinary trials...
were absent. Since the dissolution of the LCSG in 1989, none of the other cooperative groups has individually been able to complete a phase 3 randomized trial because they simply did not have in place the proper framework to do so. Adequate accrual to such trials is only beginning to occur through the intergroup mechanism that has brought back together some of the critical mass of thoracic oncologists dispersed by dissolution of the LCSG.1,2

The discontinuation of funding for the LCSG had serious ramifications in two other areas. Because the group was small, had a flexible administrative structure, and free interchange among specialties, it allowed young thoracic oncologists to learn about clinical trials, to present new scientific ideas, and to participate in the group. This was particularly important for thoracic surgeons who are often intimidated into not participating in other groups because of their personal inexperience in clinical trials methodology, the dearth of surgical leadership, and the cumbersome administrative structure in the larger cooperative groups. Rather than fostering surgical participation by a larger number of thoracic surgeons, the dissolution of the LCSG has made it harder to organize and encourage such participation. Indeed, virtually all thoracic surgeons actively participating in cooperative group trials today were either participants in the LCSG or were trained by members of the LCSG.3,4

The final consequence of the dissolution of the LCSG was the interruption of a burgeoning effort in translational research. The LCSG recognized that combining standard treatment modalities in adjuvant or neoadjuvant trials led to only modest changes in clinical outcome, and that significant improvements in therapy would depend on understanding the fundamental biology of cancer. The group also understood that it was uniquely positioned to perform translational research because of its ability to correlate pathologic and molecular biologic alterations with the stage and clinical course of disease. In the latter half of its existence, the LCSG made a conscious decision to pursue collaborative research efforts with several basic scientists. As illustrated by the reports provided in this supplement, these collaborative efforts were remarkably successful in a very short period of time. Unfortunately, this was an idea slightly ahead of its time. The importance of translational research by cooperative groups was not generally recognized, and the LCSG was severely criticized at its site visits for pursuing “nontherapeutic ancillary trials.” Now, each of the larger cooperative groups is struggling unsuccessfully to recreate the scientific efforts established by the LCSG. Straightforward correlations of molecular biologic abnormalities with clinical findings that were planned by the LCSG and that could have been accomplished easily within another 2 to 3 years were never done because of discontinued funding. At best, it will be years before other cooperative groups can ask and answer similar questions. Important information about the biology of cancer that could have contributed to the design of clinical trials today is not available because of the single short-sighted decision not to continue funding for the LCSG.

In light of all this, it is impossible for members of the LCSG not to be embittered by the decision to discontinue funding for the group. However, as much as possible, it is important to think passionately about what we can learn from the LCSG and how we can redevelop an effective framework for clinical trials in early-stage thoracic malignancies. There are perhaps six areas on which we need to focus our efforts: (1) the support of committed surgeons; (2) the education and participation of surgeons not currently participating in cooperative group trials; (3) the education of nonsurgical oncologists inexperienced in clinical trials in early-stage cancers; (4) the education of data managers; (5) the support of the intergroup effort; and (6) ensuring adequate peer review.

Support of committed surgeons requires that they have support from well-educated data managers at a level equal to that currently available to medical and radiation oncologists. Busy clinicians, no matter what their specialty, do not have time to ensure that every test or data form required by a protocol is properly completed. It has been assumed that surgeons do not require data management support and that data managers do not have to understand or help enforce the meticulous staging necessary for clinical trials in early-stage cancers. In fact, proper surgical and pathologic staging, and the proper submission of surgical data forms is pivotal in such trials and is relatively labor-intensive. Funding for this portion of clinical trials must be allocated either through separate grant mechanisms for surgeons, through capitation funding for patient accrual, or through inclusion of surgeons and their data managers on the institutional grants submitted at each cooperative group site visit. Surgeons also need funding to travel to cooperative group meetings so that they can participate in scientific and administrative activities on a par with medical and radiation oncologists.

Nonparticipating surgeons will participate in clinical trials only if they have the knowledge, the incentive, and the ability to do so. Many lack knowledge about clinical trials methodology, about the cooperative groups, and how they function. It is incumbent upon surgeons experienced in these areas to share that knowledge through postgraduate courses at thoracic surgical meetings, through publications, including summaries of active cooperative group trials4 and surgical handbooks that codify guidelines for staging and resection in clinical trials.5 Most importantly, residents and fellows must be educated, or future generations of surgeons will also fail to contribute to clinical trials. Specific didactic courses in biostatistics and clinical trials methodology should be a required part of thoracic surgical training. Residents and fellows should be taken to cooperative group meetings by mentors in their training program so they can learn how the groups function and how oncologists from various specialties interact. Individuals planning to focus on general thoracic surgery must be taught that participation in clinical trials is an important and integral part of their practice just as it is for the vast majority of medical and radiation oncologists.

The education of oncologists unused to performing clinical trials in early-stage cancers will be difficult. It will require patience, persistence, and leadership by oncologists more experienced in this area. Many oncologists consider accurate staging superfluous, and view surgeons as individuals of limited education and intelligence whose function it is to perform an undefined type of resection and
to deliver appropriate amounts of tissue on request. The
lack of oncologic expertise in the surgical community at
large contributes to this impression, and the few well-
trained surgical oncologists are left struggling constantly
to dispel it. Only a sustained effort by oncologists, both sur-
gical and nonsurgical, who understand the importance of
a close collaborative and collegial effort in clinical trials
will ultimately eliminate this very real problem.

The education of data managers is more straightforward
but will also require a sustained effort. Data managers
come to their jobs from a variety of backgrounds and do
not necessarily continue in that capacity for long periods
of time. The corporate memory about clinical trials
methodology is short, and for this reason, the cooperative
groups provide educational sessions for data managers at
each of their semiannual meetings. It is vital that seminars
on staging and on clinical trials in early cancers be included
in those educational sessions. The principles of data
management for such trials are similar across all malignancies.
Therefore, not every session need address thoracic malign-
nancy, but repetition of the principles on a regular basis is
critical.

The failure of any of the individual cooperative groups
to complete a phase 3 trial during the past 5 years
emphasizes the importance of an intergroup effort to draw
on the critical mass of thoracic oncologists. The National
Cancer Institute has recognized this need and has strongly
supported the intergroup effort in the last couple of years.
Very brief intergroup meetings twice a year cannot
substitute for the constant dialogue that occurred within
the LCSG, but they at least provide a forum in which to
set scientific priorities. The success of this intergroup effort
depends on the enthusiastic participation of all thoracic
oncologists. Without it, no phase 3 trials in early-stage
thoracic cancers will be completed because of the large
numbers of patients required for such trials.

The paucity of well-trained thoracic oncologists, par-
ticularly surgical oncologists, has made it difficult to find
individuals who can provide qualified peer review at co-
operative group site visits. Qualified peer review and
thoughtful but firm critique will lead the cooperative
groups to understand the importance of surgical quality
control, of strong surgical participation, and of multidis-
ciplinary collaboration in their clinical trials. Finding
qualified surgical oncologists for review of the cooperative
groups remains a problem, but the importance of this is at
least somewhat better recognized by the National Cancer
Institute than it was several years ago.

There is no current mechanism or forum that can really
replace the LCSG. The discontinuation of funding for the
group had serious adverse consequences for clinical trials,
translational research, and oncologic education. In fact, the
LCSG does need to be reestablished, but it is unlikely that
funding for such a group will ever be made available again.
Hopefully, it will be possible to redevelop an effective
framework for clinical trials in early-stage thoracic cancers
and to expand this framework to a larger number of aca-
demic and community institutions, but a sustained effort
at several levels will be required to achieve this.

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