Lung cancer is the leading cause of cancer-related mortality in the world. The advent of population-based screening programs is expected to result in a greater proportion of patients being diagnosed with stage I non–small-cell lung cancer (NSCLC). The optimal management hinges on multidisciplinary collaboration, with treatment options ranging from surgery (i.e., lobar or sublobar resection) to radiotherapy (i.e., stereotactic body radiotherapy [SBRT] or stereotactic ablative radiotherapy) and best supportive care. Our current understanding of the comparative effectiveness of these modalities is based primarily on several nonrandomized studies of varying quality. Although overall survival is thought to favor surgery over SBRT, lung cancer–specific survival has been shown to be similar across modalities (1). Given seemingly similar oncologic outcomes, patient–centered outcomes and health-related quality of life (HRQOL) considerations are of paramount importance to facilitate treatment decision-making in this patient population.

In this issue of *AnnalsATS*, Nugent and colleagues (pp. 988–997) provide important longitudinal data on self-reported quality of life (QOL) among patients treated with surgery or SBRT for stage I NSCLC (2). This is a prospective, multicenter, observational cohort study of 127 patients, evaluating changes in HRQOL before, during, and after (4–6 wk, 6 mo, and 12 mo) treatment. The authors use several validated measures (i.e., European Organization for Research and Treatment of Cancer [EORTC] QLQ-C30/QLQ-LC13, Functional Assessment of Cancer Therapy–Lung [FACT-L], and St. George’s Respiratory Questionnaire) for a comprehensive evaluation of patient-centered outcomes, including global QOL, physical wellbeing, and emotional wellbeing, as well as the severity and impact of lung cancer–specific symptoms (e.g., dyspnea, chest tightness).

Their findings indicate that approximately 30% of patients with stage I NSCLC may have a clinically significant decrease in global QOL one year after SBRT or surgical resection. Pain and dyspnea were among the most common side effects of treatment, with nearly 40% of all patients experiencing a clinical deterioration in fatigue at 12 months, which is similar to prior reports of symptom trajectory in the year following diagnosis of early-stage lung cancer (3). Surgical resection was associated with a steeper decline, particularly in global and physical QOL, during and four to six weeks after treatment compared with SBRT. This decline, however, was not permanent and recovered within a year for most patients. The authors appropriately used mixed effects modeling to study changes in QOL, allowing them to better account for more than one source of random variability in the data, including uneven time point spacing, as well as inherent differences among patients and instruments. The authors also completed an exhaustive number of sensitivity analyses, all yielding consistent and credible results. This confirms that their results are robust to alternative comparison groups (e.g., patients found to not have stage I disease or those not undergoing treatment) and enhances the generalizability of their findings (4).

This article is an important addition to the current body of literature, which consists of low-quality institutional data with small sample sizes and limited generalizability (5–9). In a systematic review of nine prospective studies, there were few clinically significant changes noted in HRQOL scores after SBRT (4). The included studies, however, had variable survey response rates (59–95% within 1 yr of treatment), with relatively short follow-up periods (three studies had a maximum follow-up of <1 yr). This time interval, however, may be sufficient to examine the trajectory of symptoms after SBRT versus surgery, in which the decrease in HRQOL has been reported to manifest within six months of surgery and may persist for up to two years (8). There still remains a paucity of high-quality direct comparisons of surgery and SBRT with respect to QOL. In an exploratory analysis of 22 patients in the ROSEL trial, global HRQOL was significantly more favorable with SBRT than surgery (9). This trial, however, was terminated early due to poor patient accrual.

There a few limitations that require discussion because they impact the extent to which the reader can trust the conclusions that spring forth from this study. To their credit, authors have explicitly identified these limitations. One issue that is germane to one of the central conclusions of this article is the impact of surgical modality on patient-reported outcomes. The authors were unable to adjust for invasiveness of surgery, in part due to sample size limitations. Video-assisted thoracic surgery (VATS) is thought to be associated with reduced pain, and better physical and emotional HRQOL, as well as quicker recovery of symptoms after surgery compared with thoracotomy (10, 11). The
study results suggest that surgery comes at the cost of reduced HRQOL during and immediately after the acute treatment period. Minimally invasive surgery and the use of enhanced recovery after surgery are thought to confer a protective effect against this reduction in HRQOL (10, 12). If the early reductions in HRQOL are driven even partially by perioperative pain, then it is entirely plausible that VATS and robotic surgery advancements are likely to abrogate those deficits. Furthermore, there is a new wave of advancements in minimally invasive surgery that have the potential to reduce the early issues associated with surgery. These include uniporal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14). The inclusion of uniportal VATS, and subxiphoid and tubeless thoracic surgery (13, 14). The addition of surgical modality as a covariate and tubeless thoracic surgery (13, 14).

The article by Nugent and colleagues sheds valuable light on the longitudinal impact of surgery and SBRT on HRQOL in patients receiving curative-intent treatment for stage I NSCLC. An important finding in this study is that there is a significantly worse decline in HRQOL during active treatment with surgery compared with SBRT but that the slope of decline did not appear to be different after the acute treatment period. Thus, this finding in HRQOL mirrors a similar phenomenon described in perioperative clinical outcomes: that of the early dip in survival curves that then stabilizes over time. Only time, and the pursuit of randomized trials, will answer the question whether the upfront morbidity costs with surgery allow patients to reap the benefits of increased long-term survival. There are certainly believers on either side of that debate, each armed with their own fusillade of imperfect data.

Until such a time when randomized trials fully clarify the tradeoffs of surgery versus SBRT in the treatment of stage I lung cancer, studies like this can help to inform the conversation regarding the optimal therapeutic choice in this population and, more importantly, can be used to facilitate shared decision-making with patients. Studies such as this should also serve as a call to action to continue to improve our interventions and identify ways to minimize the deleterious impact on the QOL of our patients. ■

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