Metastasectomy on the Rise Across Several Cancer Types

An article about a recent study reported that over the past decade, metastasectomy has been increasingly performed and done more safely, even in patients with a higher number of comorbidities (Cancer. [published online ahead of print November 6, 2014]. doi: 10.1002/cncr.29134).

Researchers investigated national trends in surgery for isolated metastases in 4 common cancer types and set out to determine whether better and more readily available systemic therapies, and/or varying tumor responsiveness to systemic therapies, influenced these trends.

The authors used the National Inpatient Sample database to identify patients admitted to the hospital who underwent a metastasectomy for colorectal cancer, breast cancer, lung cancer, or melanoma from 2000 through 2011. The National Inpatient Sample includes a sample of approximately 20% of nationwide hospital admissions. Along with reporting data on cancer type and surgical procedure, other variables included inpatient mortality, number of comorbidities, and hospital volume. Hospital volume was calculated for each tumor separately, and a high-volume center was defined as one within the top 10% with regard to the number of metastasectomy procedures performed; all others were deemed low-volume centers.

Colorectal cancer was the most frequent reason for metastasectomy followed by lung cancer, breast cancer, and melanoma. Liver resection was most common in patients with colorectal cancer and brain surgery was most common in patients with lung cancer, breast cancer, and melanoma. Patients with lung cancer had the highest comorbidity scores and the highest inpatient mortality rate at 3.2%.

Metastasectomy for colorectal cancer increased from 6046 procedures in the year 2000 to 11,587 in 2011, for an annual average percent change (AAPC) of 6.8%. Liver and lung resections were the main types of surgery. Metastasectomy for lung cancer also increased in the study period, with an AAPC of 5.8% reported between 2000 and 2012. In 2006, the trend became more pronounced with an annual percent change of 3.3% before 2006 and 8.7% thereafter. Brain resections were the main surgical procedures driving this increase. Metastasectomies for breast cancer increased from 1680 procedures in the year 2000 to 2991 in 2011, yielding an AAPC of 5.5%. Metastasectomies for melanoma were less common than the other tumors studied and had the slowest rate of increase, with an AAPC of 4.0%.

Inpatient mortality was very uncommon across all tumor types, ranging from 1.6% (melanoma) to 3.2% (lung cancer). Inpatient mortality rates fell for all tumor types, but were significant only for patients with colorectal and lung cancer. Metastasectomies for lung cancer had the highest initial rate of mortality and had the biggest decrease in mortality rate over the study period, with an AAPC of −6.2%. The type of metastasectomy performed affected patient outcomes. Small bowel resection was associated with the highest mortality rate at 6%, followed by brain (2.2%), adrenal (1.8%), liver (1.4%), and lung (0.92%) metastasectomies.

Over the study period, the mean number of comorbidities increased significantly across all tumor types. The majority of metastasectomies were performed at high-volume centers and ranged from 60% to 70% of procedures across all 4 tumor types. The increasing trends for the performance of metastasectomy were almost completely driven by increases at high-volume centers, and the mortality rates at high-volume centers were significantly lower compared with low-volume institutions.

Further Research Needed
“The main point of the paper is that we are doing more metastasectomies for various cancers more safely, probably secondary to a variety of reasons including: one, as systemic therapies improve, many patients with stable oligometastatic disease will come to be considered for surgery; and two, as surgical techniques improve and mortality rates improve, patients who...
historically would otherwise be considered too high risk for surgery, [such as] older more medically frail patients, may now be offered surgery,” says corresponding author Giorgos Karakousis, MD, assistant professor of surgery at the Abramson Cancer Center of the University of Pennsylvania in Philadelphia.

Researchers point out that the highest increases in metastasectomies were observed for colorectal cancer, for which there was the most efficacious systemic treatments during the study period. Melanoma had the lowest rates, corresponding with a lack of effective systemic treatments available during the study period. The authors speculate that melanoma metastasectomy may increase now, as more efficacious systemic therapies have become available over the past several years.

“Another contributor may be the widespread availability of better imaging such as low-dose high-resolution CT [computed tomography] scan which can potentially identify more patients with metastatic disease,” says Mark Ferguson, MD, professor of surgery and head of thoracic surgery at the University of Chicago Medical Center.

Dr. Ferguson also points out that physician-patient psychological factors can drive increases in surgical rates, even in the absence of strong data showing a benefit, because it is more appealing for everyone to have an active treatment and talk about a cure.

“With this surgical trend, we as clinicians need to investigate more critically and learn the influence of surgery in this setting on the natural history of these diseases,” says Dr. Karakousis. “Phase 3 trials may not necessarily be feasible, but collecting longitudinal long-term data on clinical outcomes at the institutional levels and national database levels can, and should, be done,” says Dr. Karakousis.

There is in fact one phase 3 ongoing trial examining resection of pulmonary metastasis in patients with colorectal cancer that is mentioned in the current article. “The study is seeking to analyze surgical benefit by removing the inherent selection bias present in nonrandomized studies. Patients eligible for surgery are likely to be the ones who are in better shape and more likely to have better outcomes anyway,” says Dr. Ferguson. Although he is not sure how the accrual is progressing, he points out that the same study group has conducted a challenging trial in the past involving surgery versus no surgery in the upfront management of patients with mesothelioma, so it is likely feasible.

**Study Limitations**

Limitations of the current study include that the study database provided information regarding inpatient admissions only, potentially affecting mortality rates, because deaths occurring during follow-up were not available. Inherent to these types of databases are limits to administrative/coding accuracy. Furthermore, indications for metastasectomy could not be ascertained, and therefore it is unknown whether the procedure was palliative or for curative intent.

Therefore, the conclusions of the study are that the rates of metastasectomy procedures are increasing across several tumor types, these procedures are being performed in patients with higher numbers of comorbidities but with lower mortality than in the past, and that these trends are being driven mainly by high-volume centers.

In addition, the availability of more effective systemic therapies does not decrease rates of performance of metastasectomy. The study authors believe that these findings justify further study of long-term outcomes. Although being able to perform the procedures more safely can increase the number of eligible patients, it does not determine the impact on survival. Determining which patients will achieve real clinical benefits from surgical resection of metastatic disease is crucial.

“As systemic therapies continue to evolve in parallel with advances in surgical techniques and perioperative care, these data need to be continuously reevaluated to better inform appropriate indications for these procedures,” concludes Dr. Karakousis.

“Patient selection is critical and there likely is a small subset that will derive real clinical benefit from metastasectomy,” says Dr. Ferguson. “If biological factors can be found that correlate with benefit from surgery, we could be entering an era of personalized medicine for metastatic as well as primary disease.”

doi: 10.3322/caac.21269