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Esophageal Carcinoma Metastatic to the Brain: Clinical Value and Cost-effectiveness of Routine Enhanced Head CT before Esophagectomy

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PURPOSE: To assess the value of screening enhanced head CT before esophagectomy for carcinoma, identify increased risk factor(s) for brain metastases, and determine metastasis incidence. **METHODS:** Thoracic surgery files of patients undergoing esophagectomies for squamous carcinomas, adenocarcinomas, and undifferentiated carcinomas between January 1984 and March 1993 were reviewed regarding sex, size (length) of neoplasm, and brain metastases. Surgical pathology and tumor registry files also were reviewed. Records of patients with brain metastases were reviewed in detail. **RESULTS:** Three hundred thirty-four esophagectomies were performed for 230 adenocarcinomas (202 male, 28 female) and 104 squamous carcinomas (61 male, 43 female). In 9 males and 1 female with adenocarcinomas and 1 male and 1 female with squamous carcinomas, brain metastases developed. Surgical pathology files identified 293 additional esophageal carcinomas, including 2 males with adenocarcinomas metastatic to brain. Tumor registry files identified 1 additional male with brain metastasis from an undifferentiated esophageal neoplasm. No statistically significant preoperative characteristic of esophageal carcinomas with proneness to brain metastases was found, except large size of primary neoplasm. Preoperative screening head CT done on approximately 240 patients who underwent esophagectomies showed no metastases. **CONCLUSIONS:** Brain metastases from carcinomas of the esophagus are relatively uncommon (3.6% in the esophagectomy cohort). They tend to occur in patients with large primary neoplasm, probably especially adenocarcinomas involving the esophagogastric junction, and with findings of local invasion and lymph node metastases by CT and/or microscopically. It may be reasonable to obtain head CT as a last preoperative staging procedure in such patients. Routine preoperative head CT for staging is not cost effective.

Index terms: Brain neoplasms, metastatic; Carcinoma; Computed tomography, in treatment planning; Economics

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Carcinoma of the esophagus has been considered a very uncommon source of metastatic neoplasm to the brain. Nevertheless, we have encountered several such cases in our routine clinical work during the last several years. Undoubtedly in part because one of us (M.B.O.) has had a special interest in carcinomas of the esophagus and has popularized the technique of transhiatal esophagectomy without thoracotomy (1, 2), many patients with esophageal carcinomas have been evaluated in our hospital during the last decade. Using this clinical material, the present study has the following three main goals: (*a*) assess the medical value and cost effectiveness of obtaining contrast-enhanced head computed tomography (CT) as part of the routine preoperative staging evaluation before esophagectomy; (*b*) attempt to establish an updated incidence of brain metastases from carcinomas of the esophagus; and (*c*) attempt to identify any characteristic(s) of esophageal carcinomas associated with proneness to metastasize to the brain,

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possibly also suggesting indication(s) for head CT scanning.

Material and Methods

Because preliminary inspection of patient data files showed relatively few patients with carcinomas of the esophagus encountered in our hospital each year before 1984, but with a striking increase thereafter, the period from January 1, 1984, to March 31, 1993, was selected for retrospective review of certain features of squamous (epidermoid) carcinomas, adenocarcinomas (including mucinous adenocarcinomas), and undifferentiated (or anaplastic) carcinomas of the esophagus, including a few adenocarcinomas with origins at the esophagogastric junction. This cut-off date permitted at least 18 months of follow-up after the initial histologic diagnosis was made. Detailed files, including follow-up, of patients who had esophagectomies for carcinomas of the esophagus during this period have been maintained in the Section of Thoracic Surgery. This group of patients was the basic cohort in the present study. Separate computerized searches for such carcinomas of the esophagus also were made in the data banks maintained in surgical pathology and the tumor registry in our institution. In addition, these computerized data banks were searched for cases of carcinomas of the esophagus with metastases to the brain.

Data on these patient groups were first entered on floppy disks and subsequently transferred to separate data files for reference and cross reference (matching). Information on the patients included name, hospital registration number, sex, and type of carcinoma.

The clinical records, including the available imaging studies, on those patients identified as having developed metastases to the brain from carcinomas of the esophagus were reviewed in detail for any possible special predisposing characteristic(s) associated with such spread.

The two-tailed Fisher's Exact Test and *t* test were used for the statistical analysis.

Results

The findings obtained from the thoracic surgery, surgical pathology, and tumor registry files first were analyzed separately and then correlated.

In the thoracic surgery files of patients having undergone esophagectomies for carcinomas of the esophagus in our institution during the stated period, a total of 334 patients had available documentation of the specified histologic diagnoses. Two hundred thirty (68.9%) had adenocarcinomas (202 male, 28 female), 104 (31.1%) had squamous carcinomas (61 male, 43 female), and none had undifferentiated carcinomas. In the entire cohort of 334 patients, 12 (3.6%) were found to have brain metastases after undergoing esophagectomies. Of these, 9 male and 1 female subject with adenocarcinomas and 1 male and 1 female subject with squamous carcinomas had brain metastases. Of the 202 male subjects with adenocarcinomas, 9 (4.5%) developed brain metastases.

By cross matching the patient lists from thoracic surgery and surgical pathology, the surgical pathology search identified 293 additional patients not included on the thoracic surgery list. Of these, 178 (60.8%) had adenocarcinomas (157 male, 21 female), 115 (39.2%) had squamous carcinomas (89 male, 26 female), and none had undifferentiated carcinomas. These 293 cases represented two categories. The first, larger group consisted of patients with biopsy-proved carcinomas of the esophagus on the basis of biopsies done in our institution, but who were not deemed to be suitable candidates for esophagectomies. The criteria for resectability have been published elsewhere (2). The second, smaller group represented patients who had biopsies and/or esophagectomies elsewhere, but with review of the tissue(s) by surgical pathology in our hospital. Among these additional surgical pathology cases, 2 male subjects with adenocarcinomas had known brain metastases.

A central tumor registry of patients with malignant neoplasms has been maintained in our institution for many years. By cross matching the lists obtained from thoracic surgery and surgical pathology against the patient list from the tumor registry, 95 additional patients with carcinomas of the esophagus not appearing on the first two lists were identified. Of these, 78 (82.1%) had adenocarcinomas (32 male, 46 female), 15 (15.8%) had squamous carcinomas (7 male, 8 female), and 2 (2.1%) had undifferentiated carcinomas (1 male, 1 female). Of these additional patients found in the tumor registry, only the single male subject with undifferentiated neoplasm had a known brain metastasis. This tumor registry group consisted mostly of patients with carcinomas of the esophagus proved by biopsies and/or esophagectomies done elsewhere, but with evaluation and often also subsequent treatment other than esophagectomy in our institution.

The Table is a summary of data on the 15 patients with known brain metastases, including sex, age at histologic diagnosis of esophageal carcinoma, type and length of carcinoma, duration between esophagectomy and time of dis-

Summary of findings in 15 patients with brain metastases from esophageal carcinomas

Case	Sex/Age, y*	Histology/Length	Year of Diagnosis	Reason for Head CT or MR	Time from Esophagectomy to Diagnosis of Brain Metastasis	CT and/or MR Findings	Treatment of Brain Metastasis and Follow-up
1	M/62	Adenocarcinoma/ 7 cm	1984	Headaches and leg numbness	4 mo	CT done elsewhere—L cerebellar mass	Supportive care; died 2 wk after diagnosis of brain metastasis made
2	M/59	Squamous/6 cm	1985	Developed dysarthria and obtundation 2 d after esophagectomy	3 d	CT—enhancing L frontoparietal and R temporal masses	Radiation therapy to brain; died 6 wk after esophagectomy
3	M/64	Adenocarcinoma (Original diagnosis: undifferentiated carcinoma)/10 cm	1986	Recent onset of L arm numbness and weakness	12 mo	CT—R parietal lobe 2- to 3-cm enhancing mass	Metastasis resected—adenocarcinoma; radiation therapy; recurrence resected; another adenocarcinoma metastasis in R caudate nucleus later; died 15 months after diagnosis of 1st metastasis
4	M/72	Undifferentiated/ 11 cm	1986	R-sided numbness and difficulty finding words for 3 wk	Diagnosis of brain mass made 2 wk before esophageal carcinoma found; no esophagectomy	CT—L parietal lobe mass	Radiation therapy to brain; died about 7 wk after brain mass found
5	M/63	Adenocarcinoma/ 6 cm	1986	Dizziness	31 mo	Diagnosis of brain metastasis made elsewhere; details unknown	Radiation therapy and chemotherapy; suicide 14 months after diagnosis of brain metastasis
6	M/43	Adenocarcinoma/ 11 cm	1986	Headaches for 2–3 wk	6½ mo	CT and MR—frontal, parietal, and cerebellar metastases; obstructive hydrocephalus	Radiation therapy; died 11 months after esophagectomy
7	M/61	Adenocarcinoma/ 5 cm	1988	Unknown	39 mo	Diagnosis made elsewhere; details unknown	Unknown
8	F/48	Adenocarcinoma/ 10 cm	1990	Unknown	6½ mo	Diagnosis made elsewhere; details unknown	Treatment unknown; died 7 months after esophagectomy
9	M/55	Adenocarcinoma/ 13 cm	1991	Seizures with face twisting, last 4 wk	5 mo	CT—L parietal lobe enhancing 1.5-cm mass	Metastasis resected; radiation therapy; second unresectable R cerebral hemisphere metastasis seen on CT 4 wk before death, 12 months after brain metastasis surgery
10	M/45	Adenocarcinoma/ 10 cm	1991	R-sided headache for 3 mo	Brain metastasis diagnosis made 3 days before esophageal carcinoma found; no esophagectomy	CT—2-cm enhancing mass in R temporal lobe	Chemotherapy and radiation therapy; alive with several symptoms at last follow-up 5 months after brain surgery
11	M/64	Adenocarcinoma/ 8.5 cm	1991	Headaches, nausea, vomiting, and stumbling for 5 wk	6 wk	CT and MR—3.5-cm L cerebellar enhancing mass and 1-cm R frontal lobe enhancing mass	Chemotherapy and radiation therapy; also had liver and adrenal metastases; died 5 months after esophagectomy

Table continues

TABLE: Continued

Case	Sex/Age, y*	Histology/Length	Year of Diagnosis	Reason for Head CT or MR	Time from Esophagectomy to Diagnosis of Brain Metastasis	CT and/or MR Findings	Treatment of Brain Metastasis and Follow-up
12	M/62	Adenocarcinoma/ 12 cm	1991	L-sided weakness for 8 d	Brain metastasis diagnosis made 2 wk before esophageal carcinoma found; no esophagectomy	MR—1.5-cm enhancing R frontoparietal mass	Metastasis resected; last follow-up 7 months later; alive; pain from L hip metastasis
13	F/69	Squamous/9 cm	1992	Progressive L arm weakness for 3 wk	7 wk	CT—2.5 to 3-cm R parietal lobe enhancing mass	Metastasis removed; died next day with 3rd degree heart block
14	M/77	Adenocarcinoma/ 8 cm	1992	Difficulty walking for 1 mo	3 mo	CT—4 × 4 × 3-cm R cerebellar enhancing mass	Metastasis resected; radiation therapy; in bad condition, at home, at last follow-up 5 months later
15	M/65	Adenocarcinoma/ 3 cm	1992	Weakness in L hand for 2 wk and seizure	7½ mo	MR—R frontal lobe 2-cm enhancing mass near motor strip	Metastasis resected; radiation therapy; lung metastasis resected 6 mo after brain metastasis surgery; 2 × 2.4 × 3-cm R cerebellar metastasis resected 12 mo after first craniotomy; died 5 mo later

* Age at time of histologic diagnosis of esophageal carcinoma

covery of cerebral metastasis, the reason for performing head CT, and a brief description of the CT findings as well as resultant treatment and outcome.

Of the entire group of 15 patients with brain metastases, there were 12 (80%) adenocarcinomas (11 male, 1 female), 2 (13%) squamous carcinomas (1 male, 1 female), and 1 man with undifferentiated carcinoma. Thirteen (87%) patients were men. All available CT and magnetic resonance findings (MR) of the documented brain metastases showed a characteristic, although not pathognomonic, appearance of metastatic neoplasm to the brain.

The surgical pathology files obviously contained only histologically proved brain metastases of esophageal carcinoma, so that some patients on the surgical pathology list of esophageal carcinomas may have been diagnosed only clinically, even in other institutions, as having brain metastases (although not recorded in the surgical pathology files). Therefore, no reliable true total incidence of brain metastases from esophageal carcinoma could be obtained from surgical pathology.

The tumor registry patients were coded for stage of neoplasm at initial entry, including a subheading for central nervous system metastasis. However, reliable follow-up data regarding brain metastases were not available from this source, especially beyond 4 months after primary entry date.

A statistically highly significant finding was the tendency of male subjects to have adenocarcinomas of the esophagus compared with female subjects having squamous carcinomas of the esophagus ($P < .001$). The preponderance of male subjects with brain metastases from adenocarcinomas reflects this phenomenon. Using the initial data, no statistically significant characteristic or predictive feature correlating esophageal neoplasm with propensity for brain metastases was found. However, as a trend, adenocarcinomas were more prone than squamous carcinomas to metastasize to the brain ($P = .16$).

Review of the cases with brain metastases showed that the primary neoplasms tended to be large (Table). The esophageal neoplasms were especially large (10, 11, and 12 cm long) in the three patients diagnosed as having brain metastases before their primary neoplasms were found.

We proceeded to explore further a possible statistically significant correlation between sizes of esophageal neoplasms and brain metastases. Using computerized data, the lengths of the esophageal neoplasms in a large group of patients (N = 496, including those patients referred to in "Material and Methods") having undergone transhiatal esophagectomies for cancer, and without known brain metastases, were compared with the lengths of the esophageal neoplasms of the 15 patients listed in the Table. The mean length of the esophageal cancers without brain metastases was 5.12 cm (SD, 2.56 cm), and the mean length in patients with brain metastases was 8.63 cm (SD, 2.79 cm). There was a statistically highly significant correlation between large size of primary neoplasm and risk of brain metastasis ($P < .001$). Even if the 3 patients with brain metastases as their initial clinical presentations were excluded, the size correlation still was statistically highly significant ($P = .004$).

Review of the pathologic reports on the esophagectomy specimens from the 12 patients listed in the Table revealed ominous prognostic features in 8 patients, who all had extension of neoplasm through the muscularis propria into the adventitia, with neoplasm involving the margin of surgical resection in 2 of these cases. Six of these 8 patients also had regional (mediastinal and/or perigastric) lymph node metastases, 2 of whom additionally had distant lymph node metastases (1 celiac, 1 scalene). One of the 8 patients with adventitial invasion and regional metastases had extensive angiolymphatic permeation. The 8 patients with ominous prognostic features included the 2 patients who were found to have brain metastases 6 and 7 weeks after esophagectomy, both having invasion of adventitia and positive regional nodes. One of these also had distant (celiac) lymph node metastases, and the other one had neoplasm in the surgical margin of resection.

Of the eight patients with ominous microscopic features, preoperative CT correctly predicted adventitial invasion in one case and lymph node metastases in that same case as well as in three other cases. Preoperative CT reported lymphadenopathy (enlarged nodes) in three additional patients who did not have subsequent pathologic confirmation of lymph node metastases. However, in one of these cases, the operative note stated that gross neoplasm was left behind on pericardial and periaortic fascial planes, although the pathology report failed to mention presence of neoplasm at the surgical margin.

Of the eight patients with ominous microscopic features, the esophageal neoplasm extended to involve the esophagogastric junction in four cases, and in a fifth case the neoplasm arose at the esophagogastric junction. In a ninth patient who developed a brain metastasis from a small primary neoplasm without ominous prognostic microscopic features of the types mentioned, the primary neoplasm also arose at the esophagogastric junction (case 15).

In early December 1985, a head CT done on a patient 3 days after undergoing esophagectomy for squamous carcinoma showed a brain metastasis (case 2 in the Table). Thereafter, routine preoperative head CT was instituted on all esophagectomy candidates, and this policy was continued until the end of April 1991. About 240 patients underwent esophagectomies for cancer during that period. All these head CTs were negative for brain metastases. Six of these patients (cases 3 and 5 through 9, in the Table) subsequently were discovered to have brain metastases (5, 6½, 6½, 12, 31, and 39 months after surgery).

Discussion

Well-known textbooks published about 30 years ago state that the great majority of primary esophageal carcinomas are epidermoid carcinomas, often poorly differentiated, and that adenocarcinomas almost always occur in the terminal portion of the esophagus, often representing secondary spread from gastric carcinomas (3, 4). Such incidences are in sharp contrast to the much higher incidence of apparent primary adenocarcinomas of the esophagus in the present clinical material, as also reported previously (5). There can be little doubt that the high incidence of primary adenocarcinomas of the esophagus is associated with reflux esophagitis and development of Barrett mucosa with its malignant predisposition.

All of the esophagectomy cases on the thoracic surgery list also were found in the surgical pathology files. The fact that many additional patients were found in the surgical pathology files is partly attributable to review of tissues obtained in other institutions, but mostly a reflection of ineligibility for esophagectomy after initial staging of esophageal carcinoma in our hospital. Some patients had medical contraindications to esophagectomy, but most of these patients were deemed inoperable because of distant metastases that precluded potential surgical cure. As compared with squamous carcinomas, an even higher percentage of adenocarcinomas already had unresectable metastatic spread at the time of initial diagnosis.

Not unexpectedly, the patients who developed brain metastases had primary neoplasms that tended to be large, had locally invasive tendencies, and usually had lymph node metastases microscopically. Some of these ominous features were diagnosed correctly by preoperative CT. In the present material, neoplastic involvement of the esophagogastric junction and even extension of an apparent primary esophageal neoplasm into the gastric cardia was not rare. Such involvement, a poor prognostic sign in our experience, was present in 6 of the 12 esophagectomy patients with brain metastases.

We did not review the preoperative CT or surgical pathology reports of all esophagectomy patients, specifically regarding location of neoplasm, invasive characteristics, and metastatic spread. Nevertheless, we believe that the stated ominous findings in those patients with brain metastases are prognostically significant, though of unknown magnitude.

It is noteworthy that about 240 patients undergoing esophagectomies for cancer during the December 1986 through April 1991 period underwent head CT as a routine, preoperative screening procedure, and that no brain metastasis was discovered by such CT. Those patients not deemed eligible for esophagectomies were excluded on other grounds. Thus, head CT done on these patients had no value in determining eligibility for esophagectomy. All patients who had esophagectomies for esophageal carcinomas and who subsequently were shown to have metastases to the brain underwent head CT because of symptoms consistent with, or suspicious for, metastatic spread to the brain.

Before routine preoperative head CT was instituted, 2 patients were found to have brain metastases 3 days and 4 months after esophagectomy. Of the approximately 240 patients undergoing esophagectomy during the period of routine preoperative head CT, 6 later were found to have brain metastases. Even the 3 with the shortest duration between esophagectomy and diagnosis of brain metastases (5, 6½, and 6½ months) had normal preoperative head CT. After routine preoperative head CT was stopped, brain metastases were diagnosed in 4 patients (6 weeks, 7 weeks, 3 months, and 7½ months) after the esophagectomies (see the Table). It is unlikely that the 2-cm-diameter frontal lobe metastasis discovered 7½ months after esophagectomy (case 15 in the Table) could have been detected by preoperative head CT, because the 2 × 2.4 × 3-cm-diameter cerebellar metastasis diagnosed 12 months after esophagectomy was not apparent on the CT done 4½ months earlier (7½ months after esophagectomy).

One may speculate that only 3 (0.9%) of 334 patients may have had brain metastases diagnosable by CT when evaluated as esophagectomy candidates. Because they had no clinical evidence of brain metastases before esophagectomy, their identification would have required routine preoperative screening head CT (or MR), arguably on all 334 patients in the esophagectomy cohort, at an estimated approximate cost of $200 400 (based on $600 per contrast-enhanced CT). If esophagectomies could have been avoided in 3 patients, the associated estimated approximate savings would have been $75 000 ($25 000 × 3). Purely from a financial aspect, using these cost estimates, there would have been $125 400 ($200 400 − $75 000) savings by not performing screening head CT as a last step of the routine preesophagectomy evaluation on these 334 patients. If head CT had been obtained earlier in the preoperative evaluations (including patients subsequently shown by other imaging for staging to have intrathoracic and/or intraabdominal metastases), many more patients would have had head CT, and far greater costs would have ensued.

If it is assumed that the 2 patients who were found to have brain metastases 3 and 4 months after esophagectomy (cases 14 and 1, respectively, in the Table) also could have been diagnosed by preoperative CT, 5 (1.5%) of the 334 patients in the esophagectomy cohort would have been considered ineligible for esophagectomy. The revised savings by not performing routine preoperative head CT then would have been $75 400 ($200 400 − $25 000 × 5).

Accurate analysis of professional and hospital costs and charges is a very complex matter. The analysis shown above is a very simple, even simplistic, approach, which admittedly is vulnerable to legitimate criticism in several ways.

The present study assumed a fee-for-service model of billed charges, which no longer is the most prevalent system. Billed CT and esophagectomy charges might more realistically be viewed as potential cost savings. Additional complicating factors are significantly lower collected than billed charges, both for CT and esophagectomies, and frequent reimbursement differences between outpatient and inpatient services. We did not try to tabulate CT done on an outpatient versus inpatient basis. Lower reimbursed than billed charges for both CT and esophagectomies would tend to offset each other, but still probably would result in somewhat lower estimated cost savings because routine preoperative head CT would not be performed. Furthermore, many institutions charge less than $600 per contrast-enhanced head CT, although the prevailing local charges are even higher.

We believe that the detailed cost analysis with extensive discussion, which would be required for great accuracy, is beyond the scope of this report. We are confident that the imaging/medical findings are reliable, and we also believe that even this simplified cost analysis shows such a strong trend that we are justified in our conclusion that routine enhanced preesophagectomy head CT is not cost-effective.

It is difficult to compare the relatively small risk and discomfort associated with contrast-enhanced CT, multiplied many times, with the much greater risk, morbidity, and discomfort of esophagectomy, multiplied only a few times. It also is difficult to assess the possible palliative benefits of improved swallowing and nutrition after esophagectomy if survival time is short because of brain metastases. Furthermore, excision of a brain metastasis may offer worthwhile palliation.

Unfortunately, a reliable true total incidence of brain metastases from esophageal carcinomas in this material cannot be determined. We believe that the 3.6% incidence in the esophagectomy cohort, presenting initially without clinical or imaging evidence of metastatic spread, is very accurate for purposes of clinical management in this select group of patients. A significant percentage of the patients undergoing esophagectomies had no evidence of persistent or recurrent neoplasm at 2 years (and even 4 years) after esophagectomy. The incidence of brain metastases for all cases of esophageal carcinomas undoubtedly is significantly higher. One also would expect to find an even higher frequency of brain metastases in an autopsy series.

The incidence of radiologically detectable brain metastases from esophageal carcinomas in our institution appears to be so low that we do not now consider it either cost effective or medically indicated to obtain screening head CT as a routine part of the evaluation for esophagectomy candidacy or for staging of esophageal carcinoma in general. In patients with esophageal carcinomas, regardless of treatment status or candidacy, we now perform head CT and/or MR only for the presence of neurologic symptoms and/or signs consistent with (but not necessarily attributable to) metastatic neoplasm. As is well known, enhanced head MR is more sensitive than CT in detecting small brain metastases and could be expected to increase the preesophagectomy incidence of detecting brain metastases, but this small increase in yield also would result in significantly higher imaging costs. It may be reasonable to obtain contrast head CT as a last imaging evaluation in only those patients with very large esophageal neoplasms and/or CT evidence of local invasion or metastatic spread, perhaps especially if treated with preesophagectomy chemotherapy and radiation therapy, with the attendant delay of the esophagectomy.

References

1. Orringer MB, Sloan H. Esophagectomy without thoracotomy. *J Thorac Cardiovasc Surg* 1978;76:643–654
2. Orringer MB. Transhiatal esophagectomy without thoracotomy for carcinoma of the thoracic esophagus. *Ann Surg* 1984;200:282–288
3. Ackerman LV, Butcher HR Jr. *Surgical Pathology*. 3rd ed. St Louis: CV Mosby Co; 1964:370–374
4. Ackerman LV, del Regato JA. *Cancer*. 3rd ed. St Louis: CV Mosby Co; 1962:557–561
5. Orringer MB, Marshall B, Stirling MC. Transhiatal esophagectomy for benign and malignant disease. *J Thorac Cardiovasc Surg* 1993;105:265–276