Interactive CardioVascular and Thoracic Surgery 17 (2013) 720–724
doi:10.1093/icvts/ivt300 Advance Access publication 6 July 2013

Is a thoracotomy rather than thoracoscopic resection associated with improved survival after pulmonary metastasectomy?

Amy Greenwood and Douglas West*

Department of Thoracic Surgery, Bristol Royal Infirmary, Bristol, UK

* Corresponding author. Department of Thoracic Surgery, Bristol Royal Infirmary, Upper Maudlin Street, Bristol BS2 8HW, UK. Tel/fax: +44-117-3423132; e-mail: douglas.west@uhbristol.nhs.uk; dgwest@rcsed.ac.uk (D. West).

Received 25 March 2013; received in revised form 28 May 2013; accepted 13 June 2013

Abstract

A best evidence topic in thoracic surgery was written according to a structured protocol. The question addressed was 'in patients undergoing pulmonary metastasectomy, does a thoracotomy (rather than a thoracoscopic approach) affect survival?' Altogether >153 papers were found using the reported search, of which seven represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated. No papers were greater than level-three evidence. Length of stay and length of chest drainage were found to be significantly shorter in the minimally invasive groups in one study, although this result is undermined by significant differences between the two cohorts. One paper demonstrated that, although there was a significantly closer resection margin in thoracoscopic resections, this had no effect on survival or recurrence rates. A prognostic analysis found no correlation between surgical approach and survival across a number of primary pathologies. However, by analysing the results by primary pathology, the sample groups were small. Despite no difference being found in outcome, more complications were seen with open resections in one study, and although there was a trend towards improved disease survival following resection of single resections by video-assisted thoracoscopic surgery (VATS), this did not reach significance. We conclude that there have been few high-quality studies to date, and further studies would be beneficial. From the published data, VATS metastasectomy has been associated with shorter hospital stays, chest drainage times and perioperative complications. We did not find evidence for a survival difference with either approach, and the lack of high-quality data makes it impossible to recommend any particular surgical approach in terms of long-term survival.

Keywords: Review • Video-assisted thoracoscopic surgery • Thoracotomy • Survival • Pulmonary metastasis

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This is fully described in the *ICVTS* [1].

THREE-PART QUESTION

In [patients undergoing pulmonary metastasectomy] does [a thoracotomy rather than a thoracoscopic approach] affect [survival]?

CLINICAL SCENARIO

A sixty-nine-year old gentleman is referred with a suspected single pulmonary metastasis following treatment for colorectal cancer 22 months ago. On computed tomography (CT) scan, the nodule is resectable. On discussion with the patient, he expresses concern about undergoing a thoracoscopic resection, having searched the internet and found an article suggesting that nodules are missed during thoracoscopy. You resolve to review the literature.

SEARCH STRATEGY

We searched the Medline database from 1946 to November 2012 and Embase 1974 to November 2012, using OVID interface. The search strategy is detailed below.

[[[Pulmonarymetastasis.mp OR lung secondary.mp OR pulmonary secondary] AND surgery.mp] OR lung metastasis/su] AND [thoracotomy.mp OR thoracoscopic.mp OR VATS.mp OR video assisted thoracoscopic surgery.mp OR minimally invasive surgery.mp OR lung metastasectomy.mp] AND [overall survival.mp OR surgical mortality.mp OR long term survival.mp OR survival rate.mp OR mortality.mp].

Limit search to adults, humans.

The reference lists of the selected papers were also searched for relevant articles.

SEARCH OUTCOME

One hundred and fifty-three papers were found using the reported search. From these, six papers were identified that provided the best evidence to answer the question. A further relevant

Table 1: Best evidence papers

Author, date journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Gossot *et al.* (2009), Ann Thorac Surg, France [2] Single centre non-randomized control study (level 3)	60 patients undergoing excision of sarcoma metastases between 2000 and 2007. Inclusion criteria: up to two nodules per lung field; max nodule diameter <30 mm; feasible wedge resection; no mediastinal or chest wall involvement Thoracotomy group (TT), 29 patients underwent 60 resections by thoracotomy only Thoracoscopic group (TS), 31 patients undergoing surgery involving at least 1 by thoracoscopy (63 operations; 42 (66.7%) thoracoscopic, 21 (33.3%) thoracotomy) Staged bilateral procedures in 11 patients; 7 thoracoscopic on 1 side, thoracotomy on the other, 4 bilateral VATS Mean follow-up 34 months	Mean nodule diameter (mm) Repeat resections Complications Overall 5-year survival Disease-free survival at 3 years Local recurrence Length of chest drainage postoperatively Length of stay	Group TS 13 Group TT 17 $P < 0.05$ Group TS 36% Group TT 41% No P-value given One haemopneumothorax in group TS Group TS 52.5% (25.6–79.1) Group TT 34% (15.3–52.7) $P = 0.20$ Group TS 26.4% (9.4–43.4) Group TT 24.8% (12.7–36.9) $P = 0.74$ One patient in each group Group TS 1.5 days (1.2–1.8) Group TT 3 days (2.5–3.5) $P < 0.0001$ Group TS 3.7 days (3.1–4.7) Group TT 6.2 days (5.5–6.8) $P < 0.0001$	This retrospective study showed no survival difference between a thoracotomy only and a mixed thoracotomy/ thoracoscopy group. Length of stay and length of chest drainage significantly lower in group TS Choice of approach was dependant upon nodule location (deep or subpleural) and surgeon preference, leading to a risk of bias. No adjustment for confounding in the analysis
Chao *et al.* (2011), Thorac Cardiovasc Surg, Taiwan [3] Single centre, case-matched study (level 3)	Patients undergoing first-time resection of colorectal metastasis 1997–2008 Excluded: previous pulmonary metastastectomy, incomplete resection, biopsy procedures 35 matched pairs chosen from 143 patients. Case matched 1:1 thoracoscopy/thoracotomy by resection type and by preoperative CT findings (size, laterality and number of lesions). Following matching, 35 pairs included in study Surgical procedure performed: Thoracotomy group, 6 lobectomy; 29 wedge resection VATS group, 4 lobectomy; 31 wedge resection Mean follow-up 50 months	Overall 5-year survival Tumour recurrence at 50 months mean follow-up Resection margin	Mean 5-year survival: Thoracoscopy 42% Thoracotomy 58% $P = 0.22$ Overall: Thoracoscopy 40% Thoracotomy 54% $P = 0.23$ Pulmonary recurrence: Thoracoscopy 22.9% Thoracotomy 25.7% $P = 0.78$ Ipsilateral pulmonary recurrence: Thoracoscopy 20% Thoracotomy 14.3% $P = 0.75$ Nearest staple margin (cm): VATS 0.44 ± 0.28 Thoracotomy 0.89 ± 0.54 $P = 0.01$	This case-matched study showed no difference in 5-year survival or recurrence between thoracoscopy and thoracotomy. Staple margins were closer in VATS procedures, but there was no obvious clinical consequence of this

Continued

Table 1: (*Continued*)

Author, date journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Hornbeck *et al.* (2011), J Thorac Oncol, Denmark [4], Single centre follow-up study (level 3)	Patients undergoing pulmonary metastastectomy with curative intent from 2002 to 2006 256 resections, 60 thoracoscopic (23%), 53 initiated as VATS but converted to thoracotomy (21%), 143 thoracotomy (56%) Minimum follow-up 36 months. Survival status obtained from National Danish Registry. Prognostic factors analysed, including surgical approach Results presented by primary pathology	Thirty-day mortality Unadjusted association between surgical approach and 5-year survival. Significance calculated by primary tumour type	1.9% (5/256) Not reported by surgical approach, only overall Colorectal cancer $P = 0.54$ Sarcoma $P = 0.82$ Melanoma $P = 0.92$ Renal cell carcinoma $P = 0.66$ Miscellaneous cancers $P = 0.46$ Measures of effect not reported, only *P*-values	This study of prognostic factors affecting survival following pulmonary metastastectomy demonstrated no significant effect of surgical approach. Statistical analysis did not adjust for confounders, and no multivariable model was reported. Statistical power reduced due to analysis by tumour type, which reduced numbers
Nakajima *et al.* (2008), Interact CardioVasc Thorac Surg, Japan [5] Non-randomized retrospective comparison study (level 3)	143 patients who underwent 199 metastastasectomy procedures (112 thoracoscopic and 87 thoracotomy) between 1987 and 2005. Thoracoscopy was introduced in 1996 Only macroscopically complete resections included Follow-up by CT and Carcinoembryonic antigen titre	Patients in the thoracotomy group had more (3.4 vs 1.6 $P = 0.0007$) and larger (27.4 vs 15.0 mm, $P = 0.015$) metastases, and were more likely to have an anatomical resection (45 vs 8%, $P < 0.0001$) than the thoracoscopy group Unadjusted overall 5-year survival Unadjusted recurrence-free 5-year survival Multivariate analysis of prognostic factors	Open group 39.5% Thoracoscopy group 49.3% $P = 0.047$ Open group 21.1% Thoracoscopy group 34.4% $P = 0.064$ Surgical approach was not associated with overall or event-free survival. However, wedge resection, which most thoracoscopy patients underwent, was associated with poorer overall survival (odds ratio 4.24, $P = 0.026$)	A non-randomized comparison study. Thoracoscopy was associated with improved overall and event-free survival in unadjusted analyses, but significant confounding makes this difficult to interpret. When adjusted in a multivariable model, surgical approach was not prognostic
Mutsaerts *et al.* (2002), Eur J Surg Oncol, Netherlands [6] Non-randomized, retrospective comparison study with historical control (level 4)	35 patients with a peripheral solitary pulmonary nodule up to 3 cm diameter following treatment of primary malignancy between 1992 and 1998 Group 1: 19 patients 1992–1996 underwent thoracoscopic resection followed by confirmatory thoracotomy Group 2: 16 patients 1993–1998 underwent thoracoscopic resection only 7 patients (20%) technically impossible to perform procedure thoracoscopically included in the thoracotomy group (1)	Two-year overall survival Two-year disease-free survival Pulmonary recurrence during the follow-up Perioperative complications	Group 1: 70% Group 2: 67% $P = 0.85$ Group 1: 42% Group 2: 50% *P*-value not stated Group 1: 42% Group 2: 38% *P*-value not stated Group 1: 14% Group 2: 0% $P = 0.049$	Small retrospective study, with relatively short follow-up More complications were seen in the thoracotomy group. Although two additional lesions were identified during thoracotomy in Group 1, pulmonary recurrence rates were not different between the groups. Confirmatory thoracotomy after thoracoscopy did not improve survival. Conclusions limited by study design, size and limited follow-up

Continued

Table 1: (*Continued*)

Author, date journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
	Only 20 patients with histologically confirmed metastases included in survival analysis			
Nakajima *et al.* (2001), Surg Endosc, Japan [7] Non-randomized control trial (level 3)	Retrospective review of patients undergoing initial resection of metastases between 1994 and 1999 100 patients grouped into open resections (n = 55) and thoracoscopic resections (n = 45) 47 solitary nodule resections performed (13 open, 34 thoracoscopic) 15 patients excluded (9 had too many foci of pulmonary metastases, 5 had primary lung cancer or intrapulmonary lymph nodes, and 1 patient who died 2 days postoperatively from pulmonary embolism)	Actuarial 3-year survival Percentage free from pulmonary recurrence at 3 years (actuarial) Actuarial 3-year survival rate in solitary metastasis resection Actuarial 3-year rate of freedom from tumour recurrence in solitary metastasis resection	Thoracoscopy group 62.3% Open group 52.7% P = 0.819 Thoracoscopy group 43.1% Open group 19% P = 0.126 Thoracoscopy group 58.1% Open group 46.3% P = 0.84 Thoracoscopy group 50.0% Open group 12.6% P = 0.059	Thoracoscopic resection of pulmonary metastases showed equivalent survival compared with open resection. There was a trend towards improved disease-free survival of single lesions by thoracoscopy rather than thoracotomy, which did not reach significance
Watanabe *et al.* (1998), J Laparoendosc Adv Surg Tech, Japan [8] Historically controlled study (level 4)	27 patients undergoing thoracoscopic resection of 1–2 peripheral metastases measuring <3 cm diameter on CT, from 1992 to 1998 Of thoracoscopic patients, 23 (85%) underwent wedge resection, and 4 (15%) lobectomy. Five (18%) were converted to minithoracotomy 15 of these, patients had metastatic colorectal cancer, and were compared with 16 historical thoracotomy controls Follow-up 1–60 months	Median survival of all patients undergoing thoracoscopic resection Median survival of patients with colorectal cancer metastasis (n = 15) undergoing thoracoscopic resection Three-year survival rate following pulmonary metastastectomy for colorectal cancer	22 months No figures provided for open resection cohort 23 months No figures provided for open resection cohort Thoracoscopic resection 56.4% Historic thoracotomy control 48.6% No significant difference but no P-value provided	This historically controlled study demonstrated no difference in 3-year survival between thoracoscopic and open resection of colorectal metastases 3 (11%) thoracoscopy patients were reoperated for recurrence. Two were at port sites, and another recurrence in the lung. Figures for open surgery are not given Patients with three or more lesions were excluded, so results are not generaliszable to this population

paper referenced was also included, bringing the total to seven. These are presented in Table 1.

RESULTS

Gossot *et al.* [2], in 2009, performed a retrospective review of 60 patients who underwent resection of pulmonary sarcoma metastases. They found no difference in 5-year survival (52.5% thoracoscopy vs 34% thoracotomy, P = 0.20) or disease-free survival at 3 years (26.4% thoracoscopy vs 24.8% thoracotomy P = 0.74). Those undergoing thoracoscopic surgery had shorter lengths of stay (3.7 vs 6.2 days P < 0.0001) and shorter chest drainage times (1.5 vs 3 days P < 0.0001). The authors acknowledge selection bias within the study, as patients were selected for a thoracoscopic approach according to surgeon preference, and location of the nodules. There is some contamination bias, as the thoracoscopic group underwent a mixture of thoracoscopic and thoracotomy approaches. Confounding factors were not adjusted for in the analysis.

In 2012, Chao *et al.* [3] compared long-term outcomes following resection of pulmonary metastases from colorectal cancer by thoracoscopy or thoracotomy. This case-matched study demonstrated no difference in 5-year survival (58% thoracotomy vs 42% thoracoscopy, $P = 0.22$), or tumour recurrence (54 vs 40%, $P = 0.23$), between the two approaches, despite significantly smaller resection margins in the thoracoscopy group (0.89 vs 0.44 cm, $P = 0.01$). The study was limited by the exclusion of incomplete resections.

An analysis of prognostic factors in pulmonary metastasectomy performed in 2011 by Hornbeck *et al.* [4] also found no effect of surgical approach on outcome for any of the primary cancers analysed. Patients were analysed in small groups by primary pathology, limiting statistical power.

Nakajima *et al.* [5] found a better unadjusted disease-free survival at 5 years (34.4 vs 21.1%, $P = 0.047$) in patients undergoing thoracoscopic metastasectomy compared with thoracotomy. However, there were significant confounding differences between the two cohorts, with patients in the thoracotomy group having a larger mean tumour diameter (27.4 vs 15.0 mm, $P = 0.015$), and undergoing a lobectomy or segmentectomy more frequently (45 vs 8%, $P < 0.0001$). When these were adjusted for in a multivariable model, surgical approach did not predict survival.

Mutsaerts *et al.* [6] performed a small non-randomized retrospective study of 35 patients in 2002. This demonstrated a greater rate of complications in patients undergoing video-assisted thoracoscopic surgery (VATS) followed by confirmatory thoracotomy ($P = 0.049$), but no difference in 2-year survival ($P = 0.85$) or disease-free survival compared with VATS alone. Only 20 patients were available for survival analysis, limiting the strength of the conclusions drawn.

An earlier retrospective study by Nakajima *et al.* [7] compared patients undergoing pulmonary metastastasectomy via a thoracoscopic approach with those via a thoracotomy. The demographics of these two groups were again significantly different, with more bilateral procedures (51 vs 4% $P < 0.0001$) and multiple nodules (74 vs 24% $P < 0.0001$) in the thoracotomy group, and with more wedge resections (93 vs 69% $P = 0.0026$) in the thoracoscopic group. The study also excluded a postoperative mortality secondary to pulmonary embolism. It showed no difference in unadjusted survival over 3 years between the two groups ($P = 0.819$).

Finally, Watanabe *et al.* [8] performed a retrospective, historically controlled study, comparing patients undergoing thoracoscopic resection of colorectal metastases with a historical cohort of patients undergoing open resections. No difference was found in 3-year survival rates between the two groups. Unfortunately, no comparison was made between the demographics of the two cohorts, and outcomes for the historical group were not fully reported. Port site recurrences were seen in 2 patients after thoracoscopic resection.

CLINICAL BOTTOM LINE

The current data are limited to non-randomized retrospective studies. Most of these did not fully adjust for confounding variables in their analysis.

Thoracoscopic resection was associated with improved short-term outcomes; shorter hospital stays, chest drainage duration and fewer perioperative complications in two studies. No survival benefit has been shown with either approach. The lack of high-quality data makes it impossible to recommend any particular surgical approach in terms of long-term survival.

Conflict of interest: none declared.

REFERENCES

[1] Dunning J, Prendergast B, Mackway-Jones K. Towards evidence-based medicine in cardiothoracic surgery: best BETS. Interact CardioVasc Thorac Surg 2003;2:405–9.
[2] Gossot D, Radu C, Girard P, Le Cesne A, Bonvalot S, Boudaya MS *et al*. Resection of pulmonary metastases from sarcoma: can some patients benefit from a less invasive approach? Ann Thorac Surg 2009;87:238–43.
[3] Chao YK, Chang HC, Wu YC, Liu YH, Hsieh MJ, Chiang JM *et al*. Management of lung metastases from colorectal cancer: video-assisted thoracoscopic surgery versus thoracotomy—a case-matched study. Thorac Cardiovasc Surg 2012;60:398–404.
[4] Hornbeck K, Ravn J, Steinbrüchel DA. Outcome after pulmonary metastasectomy: analysis of 5 years consecutive surgical resections 2002–2006. J Thorac Oncol 2011;6:1733–40.
[5] Nakajima J, Murakawa T, Fukami T, Takamoto S. Is thoracoscopic surgery justified to treat pulmonary metastasis from colorectal cancer?. Interact CardioVasc Thorac Surg 2008;7:212–7.
[6] Mutsaerts EL, Zoetmulder FA, Meijer S, Baas P, Hart AA, Rutgers EJ. Long term survival of thoracoscopic metastasectomy vs metastasectomy by thoracotomy in patients with a solitary pulmonary lesion. Eur J Surg Oncol 2002;28:864–8.
[7] Nakajima J, Takamoto S, Tankaka M, Takuci E, Murakawa T, Fukami T. Thoracoscopic surgery and conventional open thoracotomy in metastatic lung cancer: a comparative clinic analysis of surgical outcomes. Surg Endosc 2001;15:849–53.
[8] Watanabe M, Deguchi H, Sato M, Ozeki Y, Tanaka S, Izumi Y *et al*. Midterm results of thoracoscopic surgery for pulmonary metastases especially colorectal cancers. J Laparoendosc Adv Surg Tech 1998;8:195–200.