Long term survival with thoracoscopic versus open lobectomy: propensity matched comparative analysis using SEER-Medicare database

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STUDY QUESTION

What are the differences in short term and long term outcomes after thoracoscopic (minimally invasive) and open thoracotomy lobectomies?

SUMMARY ANSWER

In a propensity matched analysis, patients undergoing thoracoscopic lobectomy had similar overall, cancer specific, and disease-free survival compared with those undergoing open thoracotomy lobectomy.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Thoracoscopic lobectomy is associated with fewer postoperative complications than thoracotomy lobectomy, but whether the long term outcomes are compromised is unclear. Minimally invasive techniques do not seem to compromise the long term outcomes after lobectomy in this largest study to date representing modern practice in the United States.

Participants and setting

Between 2007 and 2009, we identified 6008 patients with lung cancer undergoing lobectomies (n=1293 (22%) thoracoscopic). The median age of the entire cohort was 74 (interquartile range 70-78) years. The matched analysis included 1195 patients in each group. We matched on the basis of patients' age, sex, and race; tumor stage, site, histology, and size; diagnosis of diabetes, hypertension, congestive heart failure, coronary artery disease, peripheral vascular disease, or hypertension; and hospital volume and metropolitan location.

Design, size, and duration

This was an observational, longitudinal cohort study using the Surveillance, Epidemiology and End Results (SEER) linked to Medicare database. We did a propensity matched comparative analysis of thoracoscopic versus open thoracotomy lobectomies. The median follow-up was 40 months.

Main results and the role of chance

In matched analysis, we found no statistical difference in three year overall, disease-free (treated recurrence), and cancer specific survival between the groups undergoing thoracoscopic versus open thoracotomy lobectomies (overall survival: 68.1% *v* 70.6%, P=0.5543; disease-free survival: 85.4% *v* 86.2%, P=0.46597; cancer specific survival: 89.5% *v* 92%, P=0.0509). Cox proportional hazards models accounting for clustering supported these results; only the difference in cancer specific survival was statistically significant favoring thoracoscopy (hazard ratio for overall survival 0.9, 95% confidence interval 0.78 to 1.04; disease-free survival 0.86, 0.69 to 1.07; cancer specific survival 0.74, 0.56 to 0.97).

Bias, confounding, and other reasons for caution

The study is based on analysis of data from a large longitudinal registry; inherent selection biases exist, which can be adjusted for but never completely eliminated. We attempted to account for known confounders in our propensity matching. However, we could not account for differences between the two groups that are not known, such as the experience of surgeons and institutions. VIOLET (video assisted thoracoscopic lobectomy versus conventional open lobectomy for lung cancer), a multicenter randomized controlled trial, may be able to answer some key questions related to the extent of the bias and confounding, along with its primary objective of comparing functional outcomes after thoracoscopic and open lobectomies

Generalizability to other populations

The study included a nationally representative cohort of Medicare patients over 65 years of age with lung cancer who underwent a lobectomy in the time period 2007-09. The results might not be generalizible to younger patients who are a minority of patients undergoing surgery for lung cancer in the United States and western Europe.

Study funding/potential competing interests

AS received funding from the US Food and Drug Administration for establishing the MDEpiNet Science and Infrastructure Centre at Weill Cornell Medical College.

Lung cancer surgery outcomes after thoracoscopic versus open thoracotomy lobectomies in propensity matched cohort

	Events (%)			
	Thoracoscopy	Thoracotomy	Hazard ratio (95% CI)	Hazard ratio (95% CI)
Propensity matched cohort				
Overall survival	339 (28.3)	371 (31.1)		0.90 (0.78 to 1.04)
Cancer specific survival	90 (7.5)	120 (10.0)		0.74 (0.56 to 0.97)
Disease-free survival	149 (12.5)	171 (14.3)		0.86 (0.69 to 1.07)

Impact of sending email reminders of the legal requirement for posting results on ClinicalTrials.gov: cohort embedded pragmatic randomized controlled trial

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- Research: Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis (*BMJ* 2012;344:d7292)
- Research: Compliance with mandatory reporting of clinical trial results on ClinicalTrials.gov: cross sectional study (*BMJ* 2012;344:d7373)
- Research news: Half of drug trials with results on ClinicalTrials.gov are not published in journals (*BMJ* 2013;347:f7219)

STUDY QUESTION

Do email reminders to responsible parties of trials not complying with the Food and Drug Administration Amendments Act section 801 (FDAAA 801) to post results, increase the rate of posting on ClinicalTrials.gov?

SUMMARY ANSWER

Email reminders to responsible parties of trials not complying with the FDAAA 801 regulation improved the posting of results on ClinicalTrials.gov at six months but not at three months.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Despite a policy added to the FDA Amendments Act on 27 September 2007 for the posting of basic results to registries, and despite potential penalties for not complying with the regulation, the proportion of posted results remains low.
Our study showed that sending email reminders, in a simple and automatic way, might be an additional efficient tool for increasing compliance.

Design

We derived a cohort of all phase IV trials registered on ClinicalTrials.gov and under the FDAAA 801 regulation but not complying with the regulation. A sample of half of these trials was randomly selected (by a computer generated randomization list) to receive the intervention. The other half received no intervention. The intervention consisted of personalized emails, sent at baseline then at day 7 and at two and five months, to non-compliant responsible parties of trials, reminding them of the legal requirement and potential penalties of non-compliance with the regulation. Emails were sent from one of us (PR) and constructed like surveys, asking for reasons for not complying.

Outcomes

The primary outcome was the proportion of basic results posted on ClinicalTrials.gov three months after the first email reminder. The secondary outcome was the proportion at six months. Two assessors blinded to the intervention group collected the posting date.

Main results

Among the 379 trials included in the cohort, 190 were randomized to receive the intervention. The rate of posting of results did not significantly differ between trials with and without the intervention at three months (36/190 (19%) and 24/189 (13%), respectively, relative risk 1.5, 95% confidence interval 0.9 to 2.4, P=0.096) but did at six months (46/190 (24%) *v* 27/189 (14%), 1.7, 1.1 to 2.6, P=0.014).

Results of sensitivity analysis

A sensitivity analysis excluding 48 (13%) wrongly included trials (that is, trials for which results had been posted on ClinicalTrials.gov before randomization but did not appear as posted because of the posting process) showed a significant increase in posting rate at both three and six months.

Main limitations of study

Because we aimed for the trial to be simple and pragmatic, data were extracted after being automatically downloaded from ClinicalTrials.gov. Trials not meeting the inclusion criteria (for example, trials incorrectly registered by responsible parties) might have been wrongly included. In contrast, the number of trials not complying was probably larger than the number included because we restricted the cohort to studies registered as phase IV trials so as to use stringent criteria ensuring that they indeed were under the FDAAA 801 regulation; closed trials that did not appear as closed because their status was not updated were not included and for 14% of trials, the intervention was not received (email returned with an error message). Finally, emails were sent from one of us: direct reminders by health authorities may have had greater impact.

Study funding/potential competing interests

This study received no funding. We have no competing interests.

Proportion of trials with results posted on ClinicalTrials.gov at three and six months. Values are numbers (percentages) unless stated otherwise

Analysis	Intervention	Control	Risk difference (95% CI)*	Relative risk (95% CI)	P value
Primary analysis:	n=190	n=189			
3 months	36 (19)	24 (13)	6.2 (−1.1 to 13.6)	1.5 (0.9 to 2.4)	0.096
6 months	46 (24)	27 (14)	9.9 (2.1 to 17.8)	1.7 (1.1 to 2.6)	0.014
Sensitivity analysis†:	n=164	n=167			
3 months	10 (6)	2 (1)	4.9 (0.9 to 8.9)	5.1 (1.1 to 22.9)	0.02
6 months	20 (12)	5 (3)	9.2 (3.6 to 14.8)	4.1 (1.6 to 10.6)	0.001

Three month assessment corresponds to posting results on 1 December 2012.
Six month assessment corresponds to posting results on 1 March 2013.
*Asymptotic 95% confidence interval.
†Excluding 48 trials not meeting inclusion criteria because "results first received date" were before randomization.

Variation in patients' perceptions of elective percutaneous coronary intervention in stable coronary artery disease: cross sectional study

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STUDY QUESTION

What are patients' perceptions of the urgency and benefits of an elective percutaneous coronary intervention in stable coronary artery disease and do they vary across sites?

SUMMARY ANSWER

Patients have a poor understanding of the benefits of elective percutaneous coronary intervention. Although no sites had a high proportion of patients accurately understanding the benefits, there was significant variability in patients' perceptions across sites and the way in which the informed consent process was conducted at each institution.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Prior single center studies have suggested that patients overestimate the benefits of an elective percutaneous coronary intervention in the management of stable coronary artery disease. No study has examined if patients' perceptions of percutaneous coronary intervention in stable coronary artery disease vary by site.

Participants and setting

1004 patients with stable coronary artery disease undergoing elective percutaneous coronary intervention across 10 US academic and community hospitals between 2009 and 2011.

Design

Cross sectional study.

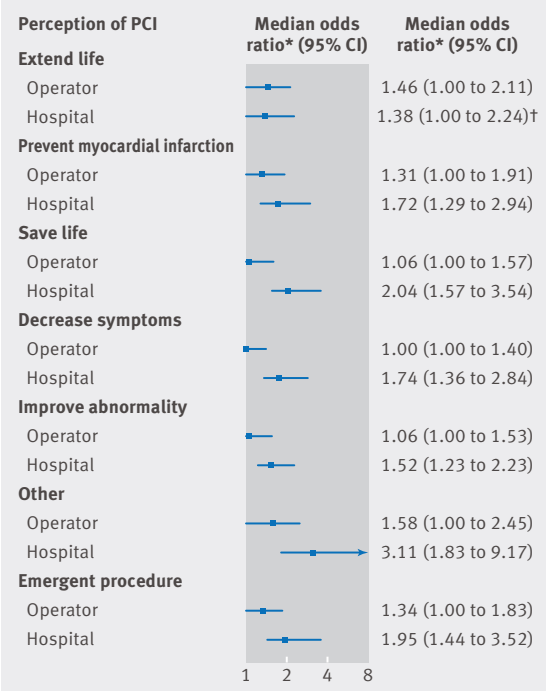
Primary outcome

Patients' perceptions of the urgency and benefits of elective percutaneous coronary intervention, assessed by a standardized interview. Median odds ratios were calculated using multilevel hierarchical logistic regression models, adjusted for patient and operator characteristics, to examine variation in patients' understanding across centers and operators.

Main results and the role of chance

991 patients (98.7%) participated in the interview. Twenty per cent (site range 4-38%) of patients classified their procedure as "emergent," despite all procedures being elective. The most commonly reported benefits from percutaneous coronary intervention were to extend life (90%, n=892; site range 80-97%) and to prevent future heart attacks (88%, n=872; 79-97%), followed by to save life (69%, n=684; 31-85%). Although nearly two thirds (site range 52-87%) of patients did report that percutaneous coronary intervention was done for improvement of symptoms, only 1.0% (n=9) identified this as the only benefit from treatment.

Median odds ratios (95% confidence intervals) of patients' perceptions of the urgency and benefits of elective percutaneous coronary intervention (PCI) by hospitals and operators within a hospital



*Adjusted for patient and operator (interventional cardiologist) characteristics
†Confidence interval comes close to 1.00 but does not include it, P≤0.05

The median odds ratios showed significant variation in patients' perceptions of percutaneous coronary intervention across sites (range 1.4-3.1) but not across operators within a site.

Bias, confounding, and other reasons for caution

Limitations of our study include that we did not directly observe the informed consent process, we did not assess physicians' perceptions of the benefits of percutaneous coronary intervention in patients with stable coronary artery disease, and we were unable to account for unmeasured confounding.

Generalisability to other populations

We achieved a high response rate among a contemporary cohort of patients with stable coronary artery disease undergoing an elective percutaneous coronary intervention across 10 US sites.

Study funding/potential competing interests

The study was supported by an American Heart Association Outcomes Research Center grant (0875149N) and the National Heart Lung and Blood Institute (R01-HL096624). The funding agencies had no role in data collection, analysis, interpretation, or the decision to submit the results.

Antibiotic treatment failure in four common infections in UK primary care 1991-2012: longitudinal analysis

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STUDY QUESTION

Has failure of antibiotic treatment for four common infection groups in primary care in the United Kingdom changed over the 22 years to 2012?

SUMMARY ANSWER

Overall rates of treatment failure increased by more than 10% from 1991 to 2012, with most of the increase occurring in more recent years.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Antibiotic prescribing in primary care is associated, at a country level, with hospital based antibiotic resistance, but the frequency and pattern of failure of antibiotic treatment in primary care are unknown. Our study suggests that treatment failure rates in UK primary care increased by 12% from 1991 to 2012, with the greatest increase being from 2000 and in lower respiratory tract infections.

Participants and setting

We used routine anonymised primary care data from the UK Clinical Practice Research Datalink (CPRD).

Design, size, and duration

We carried out a longitudinal analysis of treatment failure rates in first line antibiotic monotherapies for upper and lower respiratory tract infections, skin and soft tissue infections, and acute otitis media started anytime in 1991-2012.

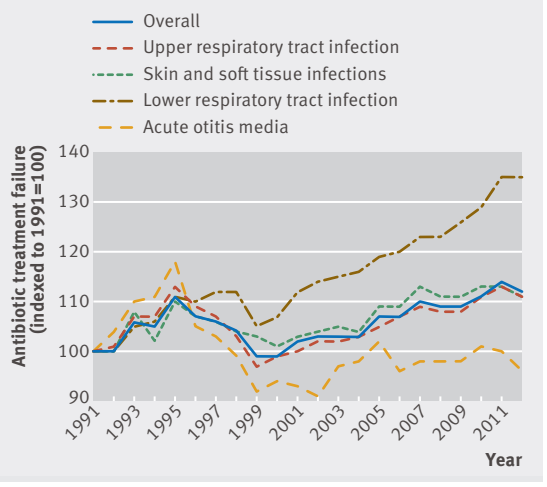
Primary outcome

Rates of failure of antibiotic treatment identified by standardised criteria, adjusted for age, sex, infection diagnosis, and antibiotic and indexed to 1991.

Main results and the role of chance

We identified 10 967 607 first line antibiotic monotherapies in 3 809 587 patients: 4 236 574 (38.6%) for upper respiratory tract infections; 3 148 947 (28.7%) for lower respiratory tract infections; 2 568 230 (23.4%) for skin and soft tissue infections; and 1 013 856 (9.2%) for acute otitis media. In 1991, overall, 13.9% of antibiotic treatments failed; 12.0% of treatments failed for upper respiratory infections, 16.9% for lower respiratory infections, 12.8% for skin and soft tissue infections, and 13.9% for acute otitis media. By 2012, the overall failure rate was 15.4%, representing an adjusted increase of 12% compared with 1991. The highest increase was seen in lower respiratory tract infections, where the adjusted failure rate was 35% higher in 2012 than in 1991. For upper respiratory tract and skin and soft tissue infections, adjusted failure rates were 11% higher in 2012 than in 1991; for acute otitis media, the adjusted failure rate was 4% lower. In the most commonly prescribed antibiotics (amoxicillin, phenoxymethylpenicillin, and flucloxacillin) failure rates remained below 20%, and rates were largely stable in those recommended for first line treatment, such as the broad spectrum penicillins and the macrolides. There were, however, some notable increases in failure rates for antibiotics that are not usually recommended as first line treatments for the conditions under study—for example, trimethoprim in the treatment of upper respiratory tract infections and ciprofloxacin and cefalexin in the treatment of lower respiratory tract infections.

Failure rates for antibiotic treatment indexed to 1991



Bias, confounding, and other reasons for caution

Unnecessary or inappropriate prescribing for viral or self limiting infections within primary care might have attenuated the rates of antibiotic treatment failure observed here. We did not investigate treatment dose because precise dose instructions are not always recorded in CPRD, but a preliminary exploration suggested that antibiotic doses might have increased over time.

Generalisability to other populations

Data in CPRD are broadly representative of the UK as a whole. The generalisability of our results to primary care in other countries is unknown.

Study funding/potential competing interests

The study was funded by Abbott Healthcare Products. Co-authors from the funding body helped to design the study and suggested editorial changes. Full details of authors' links with the funders and other agencies are on thebmj.com.