

Extended resection of non-small cell lung cancer invading the left atrium, is it worth the risk?

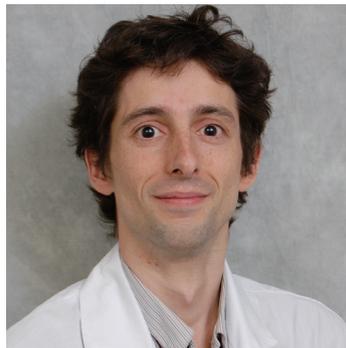
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Author's introduction: Geraud Galvaing is currently assistant professor in thoracic surgery in Jean Perrin comprehensive cancer center in Clermont-Ferrand, France. His main areas of interest involve thoracic oncology, minimally invasive thoracic surgery, thoracic trauma and invasive respiratory support. His current research implies thoracic rehabilitation and muscle physiology. He is also involved in teaching gross anatomy in Clermont-Ferrand Medical School. He attends to the French Thoracic and Cardio-Vascular Society.



Geraud Galvaing

Abstract: Only few reports of surgical approach to T4 lung carcinoma invading the heart have been reported in the medical literature. It is also controversial if such cancer should be treated by surgery. The aim of this review is to assess the current risk/benefit ratio of the surgical management of non-small cell lung cancer (NSCLC) invading the left atrium, especially in the light of a multidisciplinary approach. We also expose our surgical experience and the procedure we have developed in order to increase our rate of complete resection as this criterion appears to be mandatory as well as patients' nodal status in order to increase life expectancy.

Keywords: Left atrium; T4; extended resection

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Introduction

Surgical resection remains a critical component of multidisciplinary therapy for locally advanced non-small cell lung cancer (NSCLC), thus, extended resection may improve survival of selected patients. Left-atrial resection is infrequently performed and surgical techniques are rarely reported; moreover, oncological results and survival rates remain uncertain. Currently, 5-year survival rate is about 24% in stage IIIA and 9% in stage IIIB (T4N2M0) disease (1). However, with modern advances in imaging, surgical techniques and perioperative care, highly selected patients may benefit from multimodal therapy.

Surgical procedure

With the advent of cardiopulmonary bypass (CPB) in the late 1950s, thoracic surgeons realized the potential for extracorporeal circulation to facilitate resection of pulmonary malignancies invading the heart or great vessels. Bailey and colleagues (2) were the first to report an extended left pneumonectomy invading the left atrium performed under CPB. Two patients had been operated on: the first one died in the early postoperative course from coagulopathy, whereas, the 2nd patient survived 14 months before succumbing to metastatic disease.

The use of CPB in cancer surgery has been debated for many years: it has been thought to increase the risk of disseminated metastasis or the likelihood of recurrence. Only recently, Muralidaran and colleagues (3) demonstrated that planned CPB usage does not decrease patients' life expectancies. It's the surgeon's duty to estimate how much of the left atrium has to be removed to ensure en bloc R0 resection. Based on preoperative CT-scan and cardiac MRI, the thoracic surgeon must evaluate if a patch graft will be necessary in order to maintain a functional left atrium, if so, CPB is mandatory. Experimental studies on dogs (4) showed that up to a third of the left atrium could be resected without hemodynamic disturbance. However, to our knowledge, no study in humans has provided precise information on this limit.

We know that right-sided tumors can invade the left

atrium faster than left-sided tumors, as pulmonary veins are shorter. This unfavorable anatomical condition is counterbalanced by good exposure of the right aspect of the left atrium, the ending of the right pulmonary veins, and the junction of the two atria. Moreover, this junction is superficially marked by the interatrial groove, and can be dissected to increase the length of the atrial cuff.

In our institution, we have developed a surgical procedure based on the dissection of the interatrial septum (IAS) in order to increase surgical margins without the need of CPB in case of right-sided pulmonary resection extended to the left atrium. Our surgical and oncological results have been published recently (5).

Surgical technique

Under general anesthesia and selective bronchial intubation, a muscle-sparing lateral thoracotomy or a postero-lateral thoracotomy is performed. Resectability is ensured prior any further step. The dissection begins in the sulcus, just behind the connection to the superior vena cava with the right atrium, and is continued caudally where the sulcus is hardly noticeable. The atrial roof attaching the superior and anterior aspects of both atria is composed of interatrial muscles fibers. This musculature leads to the posterior aspect of the aortic root and increases the length of dissection in the upper part of the interatrial groove by two-fold (facing the upper pulmonary vein). The limits of depth of the dissection are represented by the limbus of the fossa ovalis and by the Koch triangle at the lower extremity. In addition, the resectable left atrial cuff can be a mean distance of 40 mm at the level of the upper pulmonary vein after sectioning the interatrial muscle (*Figure 1*).

We propose 3 levels of left-atrial resection (5) in order to precise the operative technique used. The IAS can be dissected down to the ascending aorta root. The extra-length of left-atrial cuff permits a complete resection. The left atrial surgical margin can be analyzed by frozen section: in cases of microscopically invaded section, the interatrial groove can be dissected a step forward to achieve a complete resection with no need for CPB.

Discussion

Lung cancers invading the heart are only a small subset of T4 tumors. Acquiring sufficient randomized data in order to provide evidence-based medicine will likely never be possible. Therefore, we must analyze reported experiences to make clinical decisions.

We should first define what is considered to be an invasion of the left atrium: we believe the cornerstone of the definition is the presence of cancer cells within cardiac muscle fibers on the pathologic specimen; it means that intrapericardial section of the pulmonary veins should not be classified as extended resection to the left atrium (involving a down-staging from T4 to T3 tumors). This precise point is almost never assessed in the surgical literature.

The impact of neoadjuvant therapy is still debated (6-8) especially in the subset of cT4N2 disease. We believe the aim of induction chemotherapy or chemoradiotherapy is to downstage locally advance NSCLC by reducing tumor size and lymph node involvement, as well as potentially

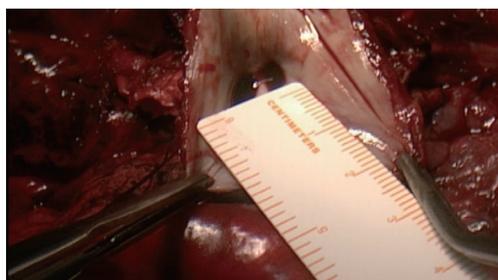


Figure 1 Operative view of the atrial cuff after a complete dissection of the interatrial septum. Distance show from the ostium of the right superior pulmonary vein to the surgical margin.

eradicating micrometastatic disease. To date, very little data are available and no recommendation can be made. Most of the reported studies involving NSCLC invading the left atrium did not assess this issue.

Here are summarized the main results of reported retrospective studies involving pulmonary resection extended to the left atrium (*Table 1*).

Unanimously, good survival rates were obtained by resection of T4 tumors in cases of N0 or N1 nodal status and if complete surgical resection is achieved. The influence of the N status on survival is well recognized (15). Fukuse and colleagues (9) reported a median survival time of 29 months in patients T4N0 NSCLC and 9 months in T4N2 NSCLC. It emphasizes the need for accurate mediastinal staging to exclude patients with occult N2 disease who would have only few benefits from aggressive surgical therapy.

It is also clear that operative morbidity and mortality of extended resection have improved over time, yet the risks are still high. Such procedures should only be suitable for highly selected patients: i.e., those with a minor medical history, and who have good physical health and nutritional status.

We achieved a 5-year survival rate of 43.7%. This result is higher than that reported in the literature, which ranges from 0-36%. This difference may be due to several factors including the rate of complete R0 resection ranging from 35-100%.

A large majority (all postoperative survivors but one) of patients (68.4%) underwent complete neoadjuvant therapy, and 84.2% also underwent complete adjuvant therapy including at least 50 grays of radiation therapy and chemotherapy.

Table 1 The main results of reported retrospective studies involving pulmonary resection extended to the left atrium

Authors	n	Neoadj (%)	PN0 (%)	PN1 (%)	PN2-3 (%)	R0 (%)	R+ (%)	Mortality (%)	Morbidity (%)	5-year SR (%)
Fukuse (9)	42	14	14	6	22	35	65	2.4	NR	17 (3-year SR)
Ratto (10)	19	15	15	26	57	58	42	0	36	14
Bobbio (11)	23	17	56	22	17	83	17	9	22	10
Spaggiari (12)	15	60	13	33	53	100	0	0	16.5	39 (3-year SR)
Wu (13)	46	NR	30.5	47.8	21.7	NR	NR	0	52.1	22
Wang (14)	25	NR	20	48	32	92	8	NR	NR	36
Galvaing (5)	19	68.5	5.2	57.9	36.9	89.4	10.6	52.6	10.5	43.7

Neoadj, neoadjuvant therapy; NR, non-reported; SR, survival rate.

Although pathologic N2 status is considered a predictor for a poor prognosis (16), in our study, pN2 status did not appear to be a pejorative risk factor, probably because of the smaller number of patients. Persistent N2 after induction therapy probably don't benefit from surgery, confirming the need for accurate restaging. Mediastinoscopy and/or EUS-EBUS-TBNA should be of systematic use to evaluate this therapeutic response.

We reported (5) an overall postoperative morbidity rate of 52.6% (n=10). The postoperative mortality rate was 10.5% (n=2) and the 90-day mortality rate was 15.7% (n=3). The 5-year survival rate was 43.7%, and the median survival time was 28.9 months. The recurrence rate was 21.0%. Three patients (15.7%) were alive for >6 years post-surgery and were considered cured.

Conclusions

Extended lung surgery with partial resection of the left atrium is a feasible procedure with acceptable morbidity and mortality rates. In highly selected patients, who eventually underwent neoadjuvant treatment, it enabled complete resection of the disease. Current data suggest that resection should be considered in such advanced tumors in relation to multidisciplinary care. Probably, experienced, high volume centers are best suitable to offer such therapeutic options. This resulted in improved long-term survival, which should be the surgeon's goal.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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