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ORIGINAL ARTICLE

呼吸困難で発症した中枢気道の腫瘍性病変に対する二期的手術
—硬性気管支鏡下 core out の有用性—

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Usefulness of Emergency Coring Out of Airway Neoplastic Tumors Obstructing the Central Airway with a Rigid Bronchoscope Prior to Radical Surgery

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ABSTRACT —— ***Objective.*** We retrospectively analyzed the results of emergency coring out with a rigid bronchoscope for symptomatic malignant or benign tumors obstructing the central airway prior to radical resection. ***Patients and Methods.*** We performed rigid bronchoscopic interventions on 103 patients with symptomatic central airway obstructions from January 2007 to December 2010. Among these, we enrolled 6 patients (5 men; 1 woman; median age, 63 years) who underwent emergency coring out with a rigid bronchoscope of tumors on the day of referral to our institution prior, to radical resection. The primary site of the tumor was the trachea in 4 patients and the left main bronchus in 2. ***Results.*** All 6 patients recovered from dyspnea immediately, and none suffered postoperative complications. We histopathologically confirmed that the obstructions comprised adenoid cystic carcinoma (n = 5) and neurofibroma (n = 1). The second radical procedure was a left sleeve pneumonectomy and tracheal resections in 1 and 3 patients, respectively. The remaining 2 elderly patients declined radical surgery. ***Conclusion.*** Emergency coring out with a rigid bronchoscope for malignant or benign neoplastic obstructions of the central airway appears to be a safe initial treatment prior to a radical procedure.

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KEY WORDS —— Rigid bronchoscope, Endotracheal tumor, Airway stenosis

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要旨 —— **目的.** 呼吸困難で発症した中枢気道の腫瘍性病変に対して，二期的手術を企図し緊急硬性気管支鏡（RBS）下 core out を施行した症例を検討した．**対象.** 2007年1月から2010年12月までに気道狭窄に対してRBS下に治療が施行されたのは103例で，二期的手術を企図しRBS下 core out を施行した6例を対象とした．男女比は5：1，年齢中央値63歳．腫瘍の原発部位は気管4例，左主気管支2例．**結果.** 当院初回受診当日に全症例で緊急RBS下に腫瘍を core out した．呼吸困難は全例で改善．術後合併症を認めなかった．切除した病理組織学的検索では腺様嚢胞癌5例，神経線維腫1例であった．二期的根治手術は4例に施行し，気管環状切除再建術3例，左 sleeve pneumonectomy 1例であった．2例は高齢を理由に手術を拒否された．**結語.** 中枢気道の腫瘍性病変に対する緊急RBS下 core out は安全で，二期的根治手術を安全に行う上で有用であった．

索引用語 —— 硬性気管支鏡，気管内腫瘍，気道狭窄

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はじめに

気管支内視鏡下治療の進歩に伴い，中枢気道に発生した腫瘍性病変に対する気道狭窄解除の有用性が報告されており，quality of life の向上に寄与している.[1-4] その多くは姑息的治療となることが多いが，気道狭窄解除により全身状態を改善させ，根治術が施行可能となる症例も報告されている.[5]

今回我々は呼吸困難で発症した中枢気道病変に対して二期的根治術を企図した硬性気管支鏡（rigid bronchoscope：RBS）下に腫瘍の core out を施行した症例を後ろ向きに検討した.

対象と方法

2007年1月より2010年12月までの4年間で，当センターにおいて気道狭窄に対して RBS 下に治療が施行されたのは103例であった．RBS による腫瘍の core out を施行したのは36例（35%）であり，中でも二期的根治手術を企図して RBS 下 core out を施行した6例（5.8%）を対象とした．腫瘍の core out を先行させ二期的根治術を企図した根拠は，①腫瘍が endoluminal type であり気道内に限局した病変であること，②縦隔リンパ節転移陰性例であることであった．加えて，腫瘍により末梢気道に炎症を来しており一期的根治術が困難と考えられた症例（1例），組織学的確定診断が得られていない症例（5例）も，二期的手術を選択した理由であった.[5,6] また小細胞癌例は対象から除外した.

各症例の背景因子を Table 1 に示す．男女比は5：1，年齢中央値63歳（範囲：33～76歳），全例呼吸困難を主訴として前医を受診し治療目的に当院に紹介され緊急入院となった．腫瘍の原発部位は気管4例，左主気管支2例であり RBS 前に確定診断が得られていたのは1例のみであった．左主気管支発生の1例では，左肺下葉の閉塞性肺炎を認めており前医での抗生物質投与では改善が得られていなかった.

麻酔の導入は，純酸素吸入下に1% プロポフォール注射薬（丸石製薬（株），大阪）を用いて行い，塩酸レミフェンタニル（アルチバ®，ヤンセンファーマ（株），東京）を併用した．ラリンゲルマスクもしくは気管内チューブを

Table 1. Patient Characteristics

No. of patients	6
Gender (M/F)	5/1
Age, median (range)	63 y (33-76 y)
Primary site of tumors	
Trachea	4
Left main bronchus	2

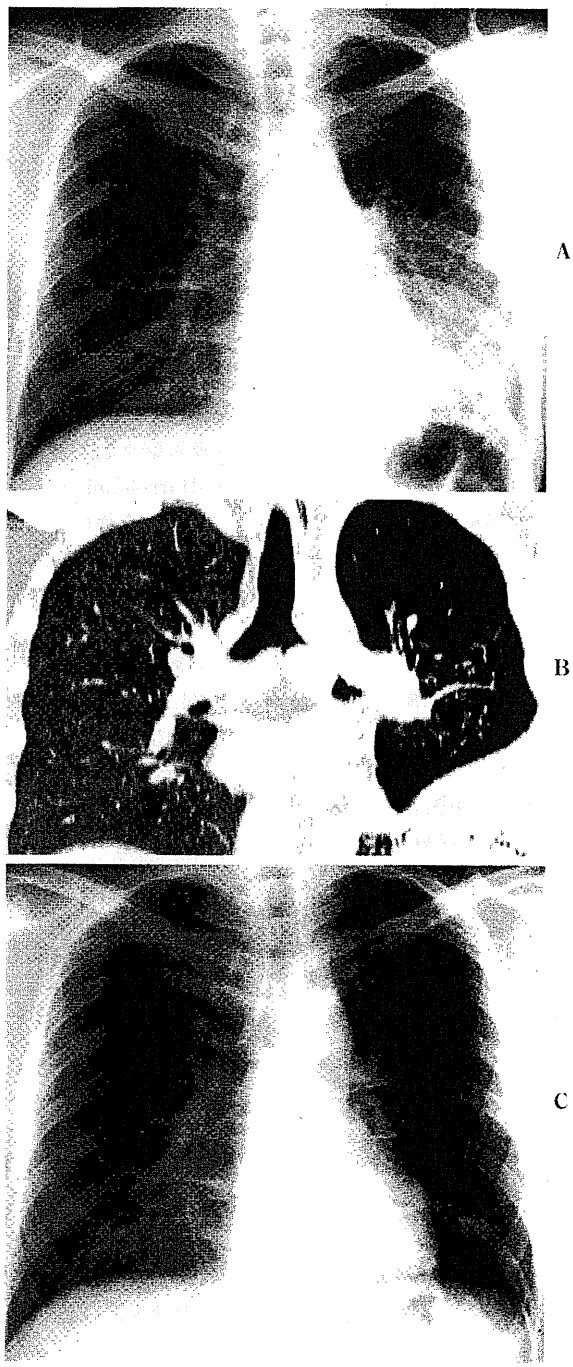

Figure 1. Preoperative chest radiography shows atelectasis and inflammatory change in the left lung and an elevated left-side diaphragm (**A**). A preoperative computed tomography scan (sagittal view) reveals an endoluminal tumor in the left main bronchus (**B**). Postoperative chest radiography demonstrates improvement of the atelectasis and inflammatory changes (**C**).

Table 2. Rigid Bronchoscopic Interventions

Age	Gender	Primary site	Histology	Waiting time for radical operation (days)	Radical operation procedure
33	M	LMB	ACC	25	Lt-PN
53	M	Trachea	ACC	53	TR
76	M	Trachea	ACC	42	TR
74	M	LMB	ACC		
73	F	Trachea	Neurofibroma		
39	M	Trachea	ACC	31	TR

LMB, left main bronchus; ACC, adenoid cystic carcinoma; Lt-PN, left pneumonectomy; TR, tracheal resection.

挿入し用手的に換気を維持した後，RBSを挿入した．RBS挿入後SpO_2をモニターしながら吸入酸素濃度は可能な限り低く抑えた．[7] RBSはDumon-Harrell universal bronchoscope（EFER, La Ciotat, France）を使用し，5 mmの直視鏡を挿入し内腔を観察した．腫瘍がendoluminal typeであり，末梢気道の開存が得られていることを確認した後，臭化ロクロニウム（エスラックス®，MSD（株），東京）を投与し，RBS外筒による腫瘍のcore outを施行した．[7,8] 止血はRBS外筒の圧迫止血と高周波電気メスによる焼灼止血，そしてボスミン加生理食塩水の散布を併用した．腫瘍片の除去および末梢気道へのたれ込みを十分に吸引した後手術を終了した．手術操作中の換気の維持は麻酔科医師により用手的に行った．[4,8]

結　果

当院初回受診当日に全例全身麻酔下にRBS下core outを施行した．平均手術時間は37.5分（範囲：18～63分）で全例合併症なく経過した．全例において呼吸状態は速やかに改善し，閉塞性肺炎を来していた1例では肺炎像も治癒した（Figure 1A, 1B, 1C）．病理組織学的検索では，腺様嚢胞癌5例，神経線維腫1例であった．高齢のため追加治療を拒否された2例を除いて二期的根治手術を施行した．RBS施行から二期的根治手術までの待機期間は中央値36.5日（範囲：25～53日）であり，二期的根治術の術式は気管環状切除3例，左sleeve pneumonectomy 1例であった（Table 2）．二期的根治手術の術後死亡および合併症の発生は認めなかった．気管環状切除を施行した2例で切除断端陽性となり，術後放射線療法（70 Gy）を追加照射した．二期的根治術後の平均追跡期間は29±14.5ヶ月（中央値34ヶ月）であり，全例再発および転移を認めていない．

考　察

悪性腫瘍による中枢気道狭窄は，病勢の進行により急性呼吸不全を来し致死的になることがあり，[9] このような症例に対するステント留置など気管支内視鏡下治療の有用性が報告されている．[8,10] 気道閉塞症例の中でも気道内に進展するendoluminal typeの狭窄に対しては速やかに腫瘍のdebulkingを図ることが重要である．[1,3] 本邦では，RBS下処置に対する準備の煩雑さ，全身麻酔が必要であること，人手も要すること，手技に対する不慣れがあることからRBSを施行しない施設も多い．[11] そのため軟性気管支内視鏡を用いたレーザー照射，冷凍凝固，高周波メスによるスネア切除などが報告されている．[10,12,13] しかしながら呼吸不全に陥った状態での軟性気管支内視鏡での処置は安全が担保できないことが多い．[4,8,12] このような症例では腫瘍のdebulkingを行うだけでは呼吸状態の改善を図ることは困難であり，末梢側への血液のたれ込みや粉砕された腫瘍片の吸引および末梢側の気道内分泌物の吸引が必要となる．[5,12] RBS下での気管内処置は全身麻酔下に気道確保しながら施行でき，処置孔も大きく複数の鉗子も挿入可能であるため安全かつ迅速に施行可能である．[1,5,8,10,14]

我々は2007年1月より2010年12月までの4年間に103例に対してRBS下での気道狭窄解除を施行しているが，core outを施行した36例（35%）の中で17例にステント留置を追加した．これらの症例では，endoluminal typeの狭窄にextraluminal typeの狭窄を伴っており，腫瘍のdebulkingのみでは気道の拡張が得られない症例であった．[6,10,12] 今回検討した6例はendoluminal typeの狭窄を来した限局性病変であり，core outのみで気道の拡張が得られ，core out後は残存する狭窄病変を認めなかったためステント留置は不要であった．[6,14] また腫瘍が広基性に進展する場合はcore outのみでは気道の拡張が得られることは困難であるが，高周波電気メスによる焼灼を行った後にcore outを行うことで気道の拡張が得られた．二期的根治手術を企図した6例を除く30例のcore out後の治療は，化学療法17例，化学放射線療法6例，放射線療法3例であり，高齢もしくは全身状態不良のためbest supportive careのみの症例は4例であった．core out前に化学放射線療法が施行されていたのは4例で，遠隔転移を有していたのは7例であった．

腫瘍が大きく，狭窄部位が長ければレーザー照射，冷凍凝固，高周波メスによるスネア切除などのみでは腫瘍のdebulkingを図ることは難しく，狭窄の解除は不完全になることが多い.[14,15] RBS外筒を回転させながら腫瘍の除去を行うcore outは，短時間で腫瘍を除去することができ，RBS以外に特別な機器を必要としない．RBS下core outによる合併症としては，歯牙口唇の損傷，気道損傷，出血があげられる.[10,12] 気道損傷を回避するために，我々は末梢側の確認の際にはX線透視下にFogarty 7 Frバルーンカテーテル（エドワーズライフサイエンス（株），東京）もしくは硬性気管支鏡用鉗子を腫瘍の末梢側に進めてガイドとし，進行方向を十分に確認しながら外筒を進めている.[4,8] また咳嗽反射が強い症例では，超短時用型の筋弛緩剤臭化ロクロニウム（エスラックス®）を併用し気道損傷を避けるようにしている.[1,4,8,12] 出血に対してはRBS外筒による圧迫止血が有効であり，必要により高周波電気メスによる焼灼やボスミン加生理食塩水の散布を併用している．しかしながらこれらの合併症は操作技術に習熟すれば稀であり，[5,8] RBS下core outは安全かつ迅速に施行可能であった.

我々はこの4年間に施行したRBS下治療症例において，経皮的心肺補助装置などの補助循環を使用しなかった．高度気道狭窄例，換気障害を来すことが予想される症例では経皮的心肺補助装置下でのステント留置が報告されている.[16] 我々は，換気不良となればRBSを一旦中断し気管内挿管を施行して換気を十分行うことで対処が可能であり，またhigh frequency jet ventilationの併用などにより補助循環の使用は避けることができると考えている.[8,17] 補助循環使用による易出血性，perfusion injuryの可能性もあるため通常補助循環を使用せずにRBSを施行している.[8,15] しかしながら下部気管と気管分岐部にまたがる病変の場合は，末梢側へのたれ込みを吸引することが困難となることも考えられ，補助循環の使用を念頭におく必要があるかもしれない.

今回core out前に確定診断が得られていたのは6例中1例のみであったが，core outにより生検も安全に施行でき，治療方針の決定が可能となった．またcore outにより呼吸状態を改善させるとともに，閉塞性肺炎を起こしていた症例でも末梢側気道の清浄化も得られ，全身状態の安定を図ることができ根治術を待機的に施行することが可能となった．呼吸困難を呈したendoluminal typeの狭窄では，RBS下core outはまず考慮すべき選択肢であると考えられた.[1,5]

結　語

中枢気道の腫瘍性病変に対して緊急RBS下core outを安全に施行し得た．術前に末梢側気道の清浄化も得られるとともに，全身状態も改善し二期的根治手術は待機手術が可能であった.

本論文内容に関連する著者の利益相反：なし

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症　例

左 B^{1+2} 分岐異常領域に発生した肺癌の1切除例

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中嶋　　隆，多田　弘人

要　　旨

症例は62歳女性．右乳癌術前精査中に胸部CTにて左 S^{1+2} に28×26 mm大の腫瘤陰影を認めた．気管支鏡検査を施行したところ左 B^{1+2} と考えられる気管支が左主気管支より直接分岐する分岐異常を認め，同気管支より生検を施行し腺癌と診断した．左原発性肺癌（cT1bN0M0）と診断し左上葉切除，リンパ節郭清を施行した．術中，肺動脈の背側を左上葉に進入する索状物を認めた．上下葉間は不全分葉で上区とS6間を形成する際に前述の索状物を肺組織とともに自動縫合器にて切離したところ，索状物が左 B^{1+2} であったことが判明した．左 B^{1+2} が左主気管支から直接分岐し肺動脈の背側を走行する解剖学的特徴が認められた．気管支分岐異常の頻度は0.4～0.6%であり，左 B^{1+2} 分岐異常の発生頻度は全気管支分岐異常の0.02～0.2%と稀である．左 B^{1+2} 分岐異常では気管支が肺動脈の背側を走行する場合があることを念頭に置く必要がある．

索引用語：気管支分岐異常，肺癌
B^{1+2}，anomalous bronchi, lung cancer

はじめに

左 B^{1+2} 分岐異常は稀な分岐異常である．左 B^{1+2} 分岐異常領域に発生した肺癌に対し左上葉切除を施行した．分岐異常気管支と肺動脈の解剖学的特徴を中心に文献的考察を加えて報告する．

症　　例

症　例：62歳，女性．

主　訴：胸部異常陰影．

既往歴・家族歴：特記事項なし．

喫煙歴：なし．

現病歴：右乳癌に対する術前精査で施行された胸部CTにて左肺異常陰影を指摘され，経気管支的組織診にて腺癌と診断された．乳癌は非浸潤性であったため，原発性肺癌 cT1bN0M0，stage 1A と診断し肺切除を先行する方針となった．

入院時現症：身長149 cm，体重37 kg（体重減少なし）．身体所見に異常は認めなかった．

入院時検査所見：腫瘍マーカーを含めた血液検査，呼吸機能検査，血液ガス分析において異常所見は認めなかった．

胸部レントゲン：左上肺野に25 mm大の腫瘤陰影を認めた（Fig. 1a）．

胸部CT：左 S^{1+2} に胸膜陥入像を伴う辺縁不整な28×26 mm大の腫瘤陰影を認めた（Fig. 1b）

気管支鏡検査：左 B^{1+2} が左主気管支から直接分岐する気管支分岐異常を認め（Fig. 2a），$B^{1+2}a$ から経気管支生検を施行し腺癌と診断した（Fig. 2b）．

手術所見：左第4肋間前側方開胸，胸腔鏡補助下に手術を施行した．左 S^{1+2} は過分葉を呈し同部位に胸膜陥入を伴う25 mm大の腫瘍を認めた．胸膜面への腫瘍の露出を認めず，胸水貯留，播種，肺内転移も認めなかった（P0，E0，D0，PM0）．左上葉切除術を施行することにした．肺門部背側の縦隔胸膜を切開し肺動

大阪市立総合医療センター　呼吸器外科
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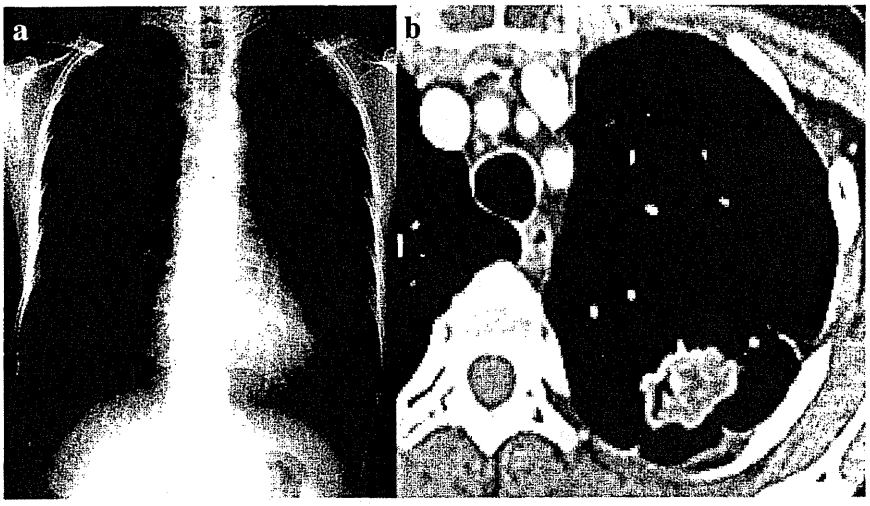

Fig. 1 **a**: A chest radiograph showed a tumor shadow in the left upper lung field. **b**: Chest CT showed a tumor shadow with pleural indentation in the left S^{1+2}.

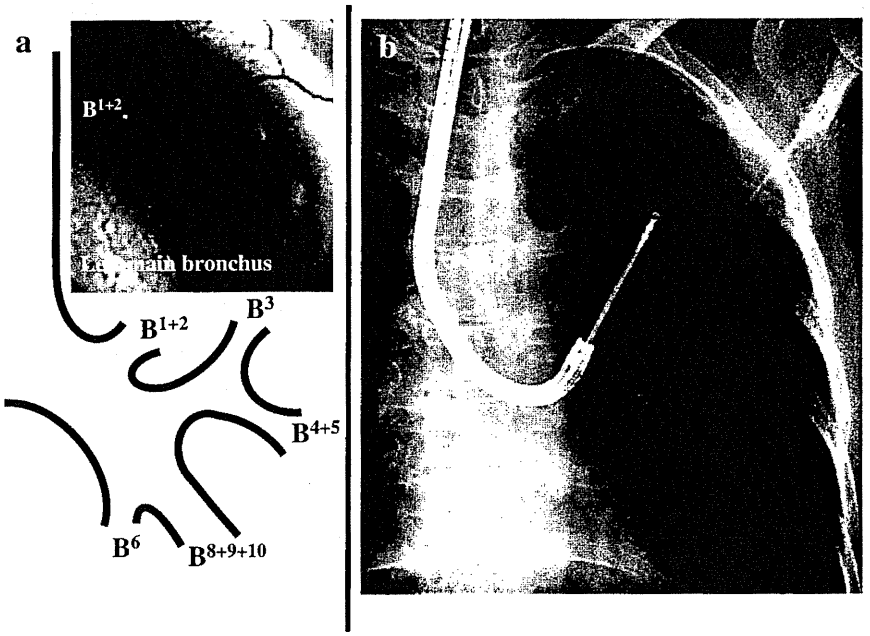

Fig. 2 **a**: A bronchoscopic examination showed that the left B^{1+2} diverged from the left main bronchus. **b**: A trans-bronchial biopsy was performed through the left B^{1+2}a, and lung adenocarcinoma was diagnosed.

脈を露出すると，肺動脈の背側を左上葉に進入する索状物を認めた（Fig. 3a）．上下葉間は不全分葉であった．上区と S6 間を形成する際に前述の索状物を肺組織とともに自動縫合器にて切離したところ，索状物が左主気管支から直接分岐する左 B^{1+2}であったことが判明した(Fig. 3b)．B^{1+2}気管支断端は 5－0 PDS にて追加縫合処置を施行した．肺動脈の走行異常は認めず，肺動脈を A^{4+5}，A^{1+2}c，A^{1+2}b，A^{1+2}a の順に切離し上肺静脈を切離したのちに A^3を切離し，最後に左上葉気管支（B^{3+4+5}）を切断した．肺門リンパ節（No10）および縦隔リンパ節（No4，5，6）を郭清した．

病理組織所見：左 S^{1+2}は過分葉を呈し，同部位に25

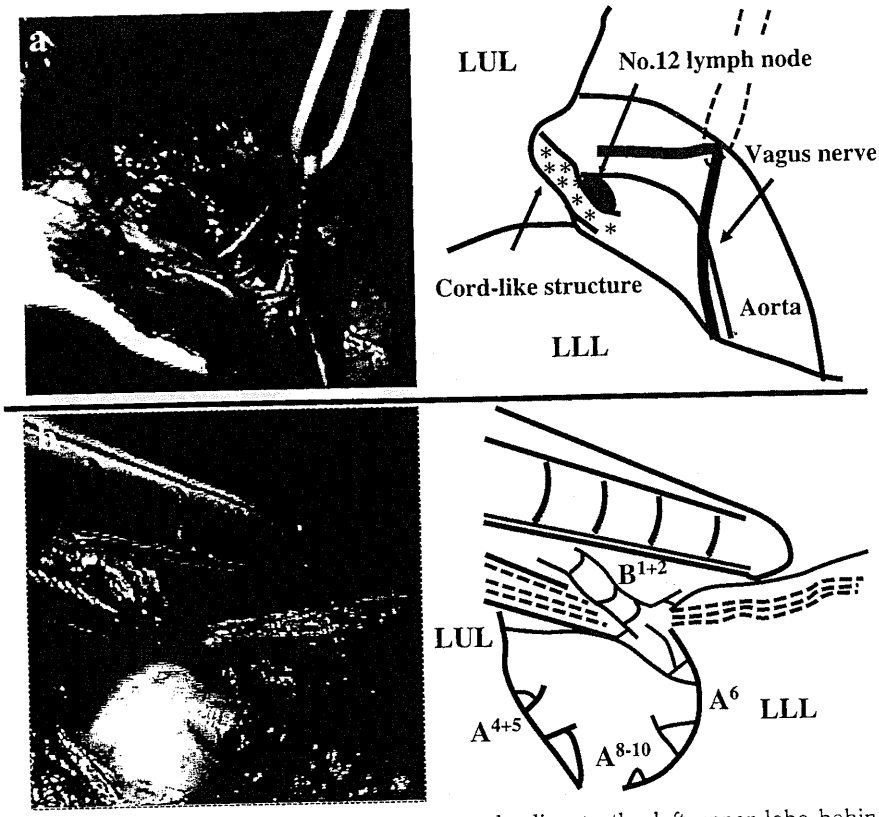

Fig. 3　**a**: There was a cord-like structure leading to the left upper lobe behind the left pulmonary artery. **b**: B^{1+2} was cut while separating the left upper lobe from the lower lobe using a stapling device. LUL, left upper lobe; LLL, left lower lobe.

mm大の腫瘍を認めた．組織学的には腫瘍細胞の乳頭状増殖と辺縁部では肺胞壁を置換するような増殖部位も認められ，胸膜浸潤およびリンパ節転移は認められなかった．以上より肺腺癌（papillary and bronchiolo-alveolar subtypes），pT1bN0M0と診断された．

術後経過：術後3日目に胸腔ドレーンを抜去し，術後8日目に退院となった．

考　　察

転位気管支と過剰気管支を含めた気管支分岐異常の発生頻度は0.4～0.6%と報告されている[1,2]．右側発生が気管支分岐異常の80～90%を占め，特に上葉気管支に関係する場合が全気管支分岐異常の67～80%を占める[3]．左B^{1+2}分岐異常の発生頻度は全気管支分岐異常の0.02～0.2%と極めて稀である[2,4]．気管支は胎生5から6週目に発生する．気管支分岐異常症例には同時期の発生異常である心房中隔の形成不全などを合併することがあり，気管支分岐異常には胎生5から6週目にかけての子宮内環境が影響していると考えられる[2]．

左肺の場合，肺門部背側の縦隔胸膜を切開すると肺動脈と分岐するA^{1+2}の亜区域枝やA^6が確認でき，葉間形成の際に指標となる．自験例ではB^{1+2}が左主気管支から直接分岐し，B^{1+2}とB^{3+4+5}の間を肺動脈が走行していた（Fig. 4a）．B^{1+2}が肺動脈の背側に位置するため，肺門部の背側でA^{1+2}の亜区域枝を確認することが出来なかった．上下葉間は不全分葉で葉間形成を施行する際に葉間肺動脈を露出し，血管鞘にそって背側にトンネリングしテーピングした．この時点で不全分葉の肺組織とともにB^{1+2}がテーピングされることになった．自動縫合器はB^{1+2}の頭側に挿入され（Fig. 4a:→），葉間を形成した際に切離面に気管支が含まれていることからB^{1+2}を切離したことが判明した．術前の気管支鏡検査でB^{1+2}分岐異常を認識していたが

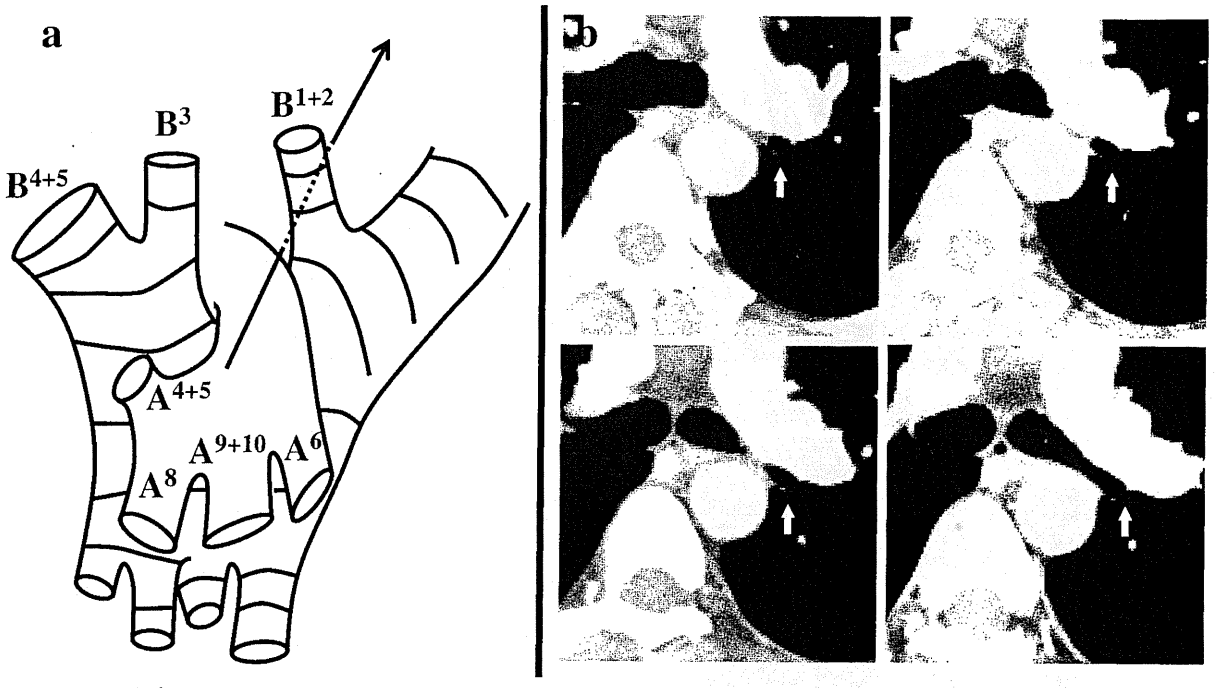

Fig. 4 **a**: B^{1+2} diverged from the left main bronchus directly. The left pulmonary artery was located between B^{1+2} and the left upper bronchus (B^{3+4+5}). A stapling device was inserted on the cranial side of B^{1+2} (→). **b**: Preoperative chest CT showed an anomalous bronchus that diverged from the left main bronchus and arose cranially behind the left pulmonary artery.

肺動脈の背側を B^{1+2} が走行することを念頭に置いていなかったため，葉間形成の際に B^{1+2} を切離してしまった．自験例は上葉切除を目的としていたため B^{1+2} を葉間形成の際に切離しても支障はなかったが，下葉切除を目的としていた場合などでは気管支再建，または S^{1+2} の追加切除が必要になっていたと考えられる．

左上葉に関連する分岐異常領域に発生した肺癌症例についての報告は public medline と医学中央雑誌にて検索した限り，本邦からの2例のみであった．本橋らは左肺全摘後に $B^{1+2}a$ が左主気管支から独立分岐し，その分岐異常領域に腫瘍が発生していた症例を報告している[5]．島本らは左 B^{1+2} が左主気管支から直接分岐する分岐異常領域に発生した肺癌症例に対し，左 S^{1+2} 区域切除を施行している[6]．島本らの報告例においても B^{1+2} は肺動脈の背側を走行していた．自験例と同様に葉間形成の際に B^{1+2} を切離し切離面に気管支が含まれていることから，B^{1+2} と肺動脈の位置関係が判明している．島本らは術前に肺動脈の3D構築と virtual bronchoscopy を作成し分岐異常を認識していたが，分岐異常気管支と肺動脈との位置関係は認識していなかったと報告している．左 B^{1+2} の分岐異常は稀な分岐異常であり肺動脈との位置関係を検討した報告は認められない．自験例では術前気管支分岐異常についての情報は，気管支鏡検査以外には胸部CT水平断のみであった．術前の胸部CTを再検討すると，B^{1+2} と考えられる気管支が左主気管支から分岐し肺動脈の背側を肺尖方向に向かっていることが確認できる（Fig. 4b）．気管支レベルでの分岐異常であれば胸部CTの水平断のみで確認出来ると考えられるが，解剖学的位置関係を念頭に置かなければ自験例のように術前に認識できない可能性がある．また，胸部CTで発見される小型肺癌症例では術前に気管支鏡検査を施行しない症例も多い．術前に気管支鏡検査を施行しなかった症例には気管支の3D構築を作成するか，麻酔導入後に気管支鏡検査を施行するなどの手段で気管支分岐異常の有無を確認するべきである．気管支分岐異常の存在が確認できれば肺動脈との解剖学的位置関係に留意して術前画像検査を見直し，術中は気管支や肺動脈周囲の剥離を慎重に施行する必要がある．

左 B^{1+2}が左主気管支から独立分岐する分岐異常領域に発生した肺癌症例を経験した．左 B^{1+2}分岐異常症例では B^{1+2}が肺動脈の背側を走行する場合があることを念頭に置く必要がある．

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A case of lung cancer arising from abnormal bronchi

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A 62-year-old woman was referred to our hospital due to an abnormal shadow in left S^{1+2} on chest CT, which was performed for the preoperative examination of right breast cancer. Bronchoscopic examination showed that the left B^{1+2} diverted from the left main bronchus. A trans-bronchial biopsy was performed through the left B^{1+2}a, and primary lung adenocarcinoma was diagnosed. Left upper lobectomy was performed. The left B^{1+2} was cut while separating the left upper lobe from the lower lobe using a stapling device. The left B^{1+2} diverged from the left main bronchus directly and rose to S^{1+2} behind the left pulmonary artery. Such anomalous divergence of the left B^{1+2} is rare. It is important to recognize that B^{1+2} might arise behind the left pulmonary artery when it diverges from the left main bronchus directly.

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Long-term results of surgical resection for pulmonary metastasis from renal cell carcinoma: a 25-year single-institution experience

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Abstract

Objective: Despite the report of new treatment options, surgery remains the best treatment for pulmonary metastases from renal cell carcinoma (RCC). Repeat resection is also an effective means for recurrent pulmonary metastases. The aim of the present study was to define the prognostic factors for survival after pulmonary metastasectomy from RCC based on a 25-year single-centre experience. **Methods:** Between 1973 and 2008, 59 thoracotomies on 48 patients (38 men, 10 women) were performed in our hospital. Repeat resections were performed in eight patients. The clinicopathological and surgical data of these patients obtained from the medical records were analysed. The time interval between lung resection and death, or latest follow-up, ranged from 3 to 177 months (median 39 months). Survival analysis was conducted by the Kaplan–Meier method and log-rank test. Multivariate analysis was performed using the Cox multivariate proportional hazard model. **Results:** The cumulative 3-, 5- and 10-year survival rates were 60%, 47% and 18%, respectively. Multivariate analysis identified disease-free interval (DFI) (≥2 years) and complete resection as significant prognostic factors for survival. Among eight patients, who underwent repeat resection, two remain alive with no evidence of disease. These two patients had long DFI and long DFI-2 (time from first pulmonary metastasectomy to diagnosis of recurrent pulmonary metastasis). **Conclusions:** The results showed that (1) surgical resection of pulmonary metastasis from RCC has a favourable outcome in selected patients, (2) DFI and completeness of resection are prognostic markers for survival after pulmonary metastasectomy and (3) repeat lung resection for metastatic RCC is a safe procedure that provides satisfactory patient outcomes.

Keywords: Renal cell carcinoma; Lung; Metastasectomy

1. Introduction

Renal cell carcinoma (RCC) accounts for about 2% of all cancers [1] and 25–30% of patients with an RCC have a metastasis at the time of diagnosis. The most common site of the initial recurrence in patients, who have undergone radical nephrectomy for RCC, is the lung; 30–50% of patients with RCC subsequently have pulmonary metastases [2]. The effect of conventional chemotherapy or radiotherapy in RCC is poor. Immunotherapy, such as the administration of recombinant human interleukin-2 or interferon-alpha, has limited overall response rate ranging from 15% to 20% [3]. The treatment of RCC with tyrosine kinase inhibitors (TKIs), such as sorafenib and sunitinib, has been reported recently to prolong the time to progression compared with interferon therapy [4,5]. However, few patients achieve complete remission by TKIs, and hence, most patients treated with TKIs experience disease progression. Therefore, surgery remains the best treatment for pulmonary metastases from RCC if potentially curative resection is expected. In 1939, Barney and Churchill [6] were the first to describe pulmonary metastasectomy from RCC. Surgical resection of pulmonary metastases is an established treatment modality in patients with metastatic disease. The reported 5-year survival rate after pulmonary metastasectomy is 21–60%, which is higher than the 3–11% reported for non-operated patients [7].

Repeat resection is also effective for recurrent pulmonary metastasis [8]. Several studies have examined the prognostic factors for repeat pulmonary metastasectomy for various types of tumours other than RCC, such as osteosarcoma [9], soft-tissue sarcoma [10] and colorectal cancer [11]. To the best of our knowledge, however, there are no reports on repeat pulmonary metastasectomy for RCC or on the prognostic factors after repeat resection.

The aim of the present study was to determine the prognostic factors for pulmonary metastasectomy from RCC based on a 25-year single-centre experience. Specifically, the study focussed on details of treatment and outcome of

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patients with recurrent lung metastases after first lung resection and the significance of repeat resection.

2. Patients and methods

The present study is a retrospective analysis of consecutive patients who underwent pulmonary metastasectomy from RCC with curative intent between 1973 and 2008 in our hospital. A total of 59 thoracotomies on 48 patients (38 men, 10 women) were evaluated. In all patients, the primary tumour was treated by radical nephrectomy. Patients underwent resection of pulmonary metastases after meeting the following criteria: (1) pulmonary metastases were deemed completely resectable by preoperative radiological examinations; (2) absence of apparent mediastinal lymph node metastases determined by preoperative radiological examinations; (3) metastatic disease was limited to the lungs, or extrapulmonary distant metastasis(es) was controlled or controllable if present; (4) loco-regional control of the primary RCC was achieved or achievable; and (5) good overall general conditions and adequate respiratory function to tolerate lung resection were present. Histopathological evaluation of the lung resected specimens revealed RCC metastases in all patients. Repeat lung resections were also performed if the patient met the criteria for first lung resection. Type of resection was selected according to the size and location of the recurrent lung metastases. Lesser resection was preferably selected as long as a curative resection was possible. Clinical information was obtained from the medical records in our hospital. The median time interval between primary nephrectomy and lung resection was 4.1 years (range, 0.2–19.7). The mean age at the time of first pulmonary resection was 62 years (range, 38–78). Eight patients underwent resection for extrapulmonary metastases, and one patient underwent simultaneous resection of both metastatic RCC to the lung and to the thyroid gland. Patient characteristics are summarised in Table 1. The disease-free interval (DFI) was defined as the time from nephrectomy to the diagnosis of the first metastatic pulmonary lesion. DFI-2 was defined as the time from the first pulmonary metastasectomy to the diagnosis of recurrent pulmonary metastasis. Complete resection was defined as follows: no additional extrapulmonary sites of metastatic disease or already resected if present, no loco-regional recurrence or no macroscopic tumour tissue is left behind at lung resection.

Follow-up was generally based on chest X-ray or chest and abdominal computed tomography (CT), physical examination and blood chemistry performed every 6–12 months after the first pulmonary metastasectomy. The follow-up information was obtained from the medical records in our hospital, letters from the general practitioner or from the death certificates of the Registry Office. Patients or their families were contacted by phone if necessary. The overall survival was the main end point defined as the time interval between the date of lung resection and death, or the last follow-up for surviving patients.

Statistical analysis was performed using StatView 5.0 software (SAS Institute, Berkley, CA, USA) and Dr SPSS II software (SPSS Japan, Tokyo, Japan). Overall survival was analysed by the Kaplan–Meier method using the date of pulmonary resection as the starting point. The significance of differences between subgroups was calculated using the log-rank test. Multivariate analysis of prognostic factors was performed using the Cox multivariate proportional hazard model with backward elimination method. A p value less than 0.05 was considered statistically significant. Data are expressed as mean ± SD or median values.

Table 1. Patient characteristics and clinicopathological features of resected lungs.

Characteristics	No. of patients
Sex	
Male	38
Female	10
Age (years)	
Mean	62
Range	38–78
Pathologic stage of primary RCC[a]	
I	1
II	20
III	8
IV	6
Unknown	13
Histopathological grading of primary RCC	
I	16
II	30
III	2
History of resection of extrapulmonary metastases of RCC	
Yes	8
No	40
Time interval between primary nephrectomy and lung resection (years)	
<1	6
1–2	8
2–5	14
≥6	19
No. of resected metastases	
1	29
2	6
3	4
≥4	9
Site of metastasis	
Unilateral	36
Bilateral	12
Largest size of metastatic tumour (cm)	
<3	38
≥3	10
Type of resection	
Sublobar resection	40
Lobectomy	8
Hilar or mediastinal lymph node metastasis	
Yes	5
No	43
Completeness of resection	
Complete resection	43
Incomplete resection	5

[a] Stage of disease was defined according to the 1997 update of tumour–node–metastasis (TNM) criteria established by UICC.

3. Results

There was no operative mortality for the first lung resection. Complete resection was performed in 43 of the 48 (90%) patients. The reasons for incomplete resections were as follows: unresectable multiple lung metastases was observed at surgery in one patient, pleuritis carcinomatosa was observed at surgery in one patient and unresectable hilar

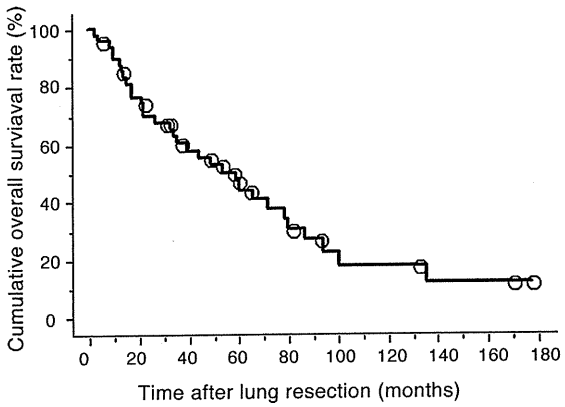

Fig. 1. Overall survival rate of 48 patients. The cumulative 3-, 5-, and 10-year survival rates were 60%, 47%, and 18%, respectively.

or mediastinal lymph node metastases were observed at surgery in three patients. Sublobar resection (wide-wedge resection or segmentectomy) was performed in 40 patients and lobectomy in eight. Twenty-nine patients had solitary metastasis and 19 patients had multiple metastasis. Table 1 summarises the clinicopathological features of patients who underwent lung resection.

To date, 34 of 48 patients have developed recurrence. The initial site of recurrence after lung resection was the lung in 12 patients, while four showed lung metastases and mediastinal lymph node metastases and 18 had extrapulmonary distant metastases.

The time interval between lung resection and death, or latest follow-up in the present series, ranged from 3 to 177 months (median, 39). The cumulative 3-, 5- and 10-year survival rates were 60%, 47% and 18%, respectively (Fig. 1). The following factors were selected for univariate analysis of survival: sex, age, pathological stage of the primary RCC according to tumour–node–metastasis (TNM) classification, histopathological grading of primary RCC, history of resection of extrapulmonary metastases of RCC, DFI, number of lung metastases, location of the metastases (unilateral or bilateral), diameter of the largest resected lung metastatic tumour, type of resection (lobectomy or sublobar resection), presence of hilar or mediastinal lymph node metastasis and completeness of resection. The results of univariate analysis are shown in Table 2. Significant relationships ($p < 0.05$) were found between the following factors and survival: DFI (<2 vs ≥2 years), number of resected metastases (solitary vs multiple) and completeness of resection (complete vs incomplete). The 5-year survival rate of patients with DFI of ≥2 years was 58%, while that of patients with DFI <2 years was 26%. The 5-year survival rate of patients with solitary metastasis was 55%, while that of patients with multiple metastases was 37%. The 5-year survival rate of patients who underwent complete resection was 50%, while that of patients who underwent incomplete resection was 20%.

Table 2. Results of univariate analysis.

Factors	p value
Sex	NS
Age (<60 years vs ≥60 years)	NS
Pathologic stage of primary RCC (I, II vs III, IV)	NS
Histopathological grading of primary RCC (I vs II, III)	NS
History of resection of extrapulmonary metastases (yes vs no)	NS
DFI (<2 years vs ≥2 years)	0.009
No. of resected metastases (solitary vs multiple)	0.045
Localisation of metastasis (unilateral vs bilateral)	NS
Largest size of metastases (<3 cm vs ≥3 cm)	NS
Type of resection (sublobar resection vs lobectomy)	NS
Hilar or mediastinal lymph node metastasis (yes vs no)	NS
Completeness of resection (complete vs incomplete)	0.034

NS: not significant; DFI: disease-free interval; and RCC: renal cell carcinoma.

Table 3. Results of multivariate analysis.

Variable	p value	Risk ratio	95% Confidence interval
DFI: <2 years	0.01	2.77	1.31–5.87
Completeness of resection: incomplete	0.04	2.78	1.03–7.48

Multivariate analysis was performed using the same factors selected for univariate analysis described above. Table 3 lists the results of multivariate analysis. DFI and completeness of resection were identified as the independent and significant determinants of prognosis. The survival curves according to DFI and completeness of resection are shown in Figs. 2 and 3.

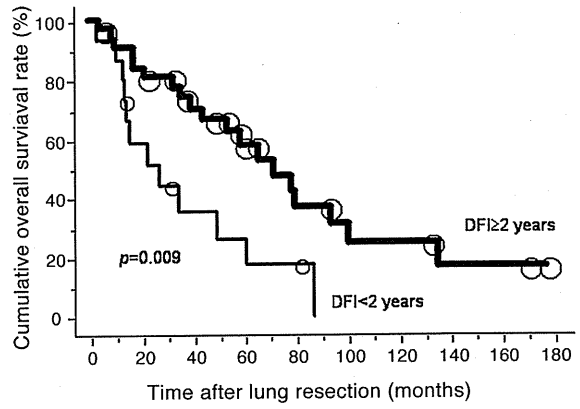

Fig. 2. Survival rates according to disease-free interval (DFI) (<2 and ≥2 years).

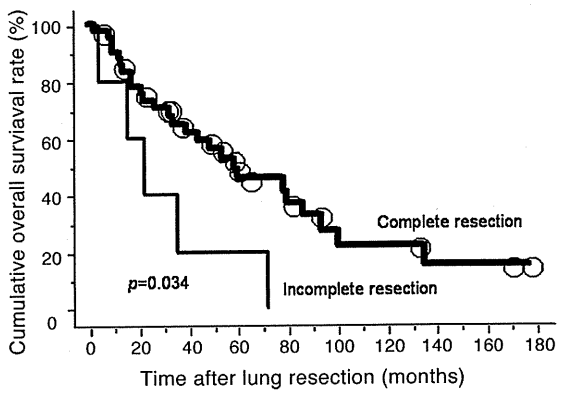

Fig. 3. Survival rates according to completeness of resection (complete and incomplete).

Table 4. Details of patients who developed subsequent pulmonary metastases after first lung resection.

Case	Age/sex	Solitary or multiple	DFI (month)	DFI-2 (month)	Treatment for second relapse/reason	Outcome/survival after first pulmonary metastasectomy (month)
1	44/M	Multiple	12	26	Repeat resection	DOD/49
2	53/M	Multiple	14	8	Repeat resection and chemotherapy	DOD/86
3	57/M	Solitary	29	21	Repeat resection	DOD/78
4	76/F	Solitary	48	5	Repeat resection and chemotherapy	DOD/17
5	56/M	Solitary	60	58	Repeat resection and chemotherapy	DOD/72
6	65/F	Solitary	77	60	Repeat resection	DOD/136
7	61/F	Multiple	79	85	Repeat resection	NED/92
8	62/M	Solitary	99	111	Repeat resection	NED/133
9	77/F	Solitary	18	6	Chemotherapy/unresectable due to respiratory function	DOD/14
10	62/M	Multiple	50	2	Chemotherapy/unresectable due to respiratory function	DOD/94
11	70/M	Multiple	99	17	Chemotherapy/patient refused repeat resection	DOD/80
12	71/M	Multiple	120	5	Chemotherapy/unresectable due to old age	DOD/44

DFI: disease-free interval (time from nephrectomy to the initial diagnosis of metastatic pulmonary tumour); DFI-2: disease-free interval-2 (time from first pulmonary metastasectomy to the diagnosis of recurrent pulmonary metastasis); DOD: died of disease; and NED: no evidence of disease.

Eight of 12 patients, who had lung metastases after the first lung resection, underwent repeat lung resections. All repeat lung resections were complete resections. Details of patients who developed subsequent lung metastases after the first lung resection are shown in Table 4.

Of eight patients, who underwent repeat resection, five underwent wide-wedge resections for the first and second time (cases 1, 3, 5, 6 and 8). One patient underwent a wide-wedge resection for the first time and a completion lobectomy for the second time (case 4). One patient underwent a wide-wedge resection for the first time and a segmentectomy for the second time (case 7). One patient underwent third resection (case 2). The types of resection of case 2 included segmentectomies for the first and second time, and a wide-wedge resection for the third time. No major operative morbidity or mortality was observed for repeat lung resections. Respiratory dysfunction also was not observed postoperatively in this cohort. Adjuvant chemotherapy was administered in three patients (cases 2, 4 and 5). Three of the eight patients, who underwent second lung resection, underwent third lung resection for pulmonary metastases (cases 2, 5 and 6). So far, two of these patients (cases 7 and 8) remain alive without any evidence of disease. Both these patients have the longest DFI and longest DFI-2. The number of metastases (solitary vs multiple) does not seem to be associated with long-term survival.

4. Discussion

In our hospital, 780 pulmonary metastasectomies have been performed for various diseases, such as colorectal cancer, soft-tissue sarcoma and hepatocellular carcinoma, according to the general eligibility criteria described above in Section 2, and good surgical outcome has been reported. In the present study, we analysed pulmonary metastasectomy from RCC according to the general eligibility criteria in our hospital. The overall 5-year survival rate was 47% and that for patients with complete resection it was 50%. Table 5 provides a comparison of the outcomes of studies that have investigated patients undergoing surgical resection of pulmonary metastases from RCC [7,12–24]. The overall 5-year survival rates in previous reports ranged from 21% to 60%, while the 5-year survival rate for patients with complete

Table 5. Comparison of surgical outcome of studies on patients undergoing surgical resection of pulmonary metastasis from RCC.

Author	Year	No. of pts	Patients with complete resection		5-year survival rate (%)		Prognostic factors
			Number	%	Overall survival	For complete resection	
Morrow	1980	30	NA	NA	24	NA	None
Jett	1983	44	31	70	27	NA	DFI, size of metastases
Dernevik	1985	33	NA	NA	21	NA	DFI
Pogrebniak	1992	23	15	65	60	NA	None
Cerfolio	1994	147	96	65	NA	36	DFI, no. of metastases
Fourquier	1997	50	NA	NA	44	NA	None
Kavolius	1998	50	NA	NA	30	54	Complete resection, DFI, age
Friedel	1999	93	77	83	NA	39	DFI, no. of metastases
Piltz	2002	105	105	86	25	40	Complete resection, no. of metastases, size of metastases
Pfannschmidt	2002	191	149	78	37	42	Complete resection, DFI, no. of metastases, LN metastases
Hofmann	2005	64	31	57	33	40	Complete resection, DFI, No. of metastases
Murthy	2005	92	63	68	31	42	Complete resection, size of metastases, no. of LN metastases, decreased preoperative FEV1
Marulli	2006	59	54	92	53	NA	Age
Assouad	2007	65	54	83	34	37	Size of metastases, LN metastases
Present series	2010	48	43	90	47	50	Complete resection, DFI, no. of metastases

NA: not available; DFI; disease-free interval; LN: lymph node; and FEV1: 1-second forced expiratory volume.

resection ranged from 36% to 54%. Our results demonstrated a higher rate of complete resection (90%) and favourable outcome.

Univariate analysis showed that the number of resected metastases correlated with good prognosis. Patients with solitary metastases survived significantly longer than patients with multiple metastases. This result is in agreement with those of previous studies on pulmonary metastasectomy for RCC [16,18,21].

Our study identified DFI of ≥2 years and complete resection as significant prognostic factors by multivariate analysis. The 5-year survival rate of patients who underwent complete resection was 50%, while that of patients who underwent incomplete resection was 20%. Several investigators have indicated that completeness of resection is a prognostic factor for survival [7,19–22]. Considered together, these results indicate that incomplete resection has no obvious benefits for patients with metastatic RCC to the lung. The result that DFI of ≥2 years is a significant prognostic factor is consistent with the results of previous studies that patients with a longer DFI have significantly higher probability of survival [13,14,16,18,20,21].

No major operative morbidity or mortality was observed for repeat lung resections, and respiratory dysfunction also was not observed postoperatively. It is speculated that repeat lung resection for metastatic RCC is a safe procedure that provides satisfactory patient outcomes. To our knowledge, there are no reports on the prognostic factors for a second pulmonary resection for recurrent RCC in the lung. Our data demonstrated that patients with longer DFI tend to have longer survival. This finding is compatible with the results of multivariate analysis. The number of metastases (solitary vs multiple) did not seem to be associated with survival. Patients with longer DFI-2 who underwent repeat resections tended to have longer survival. In fact, two patients with long survival time (≥92 months) with no evidence of disease (cases 7 and 8) had long DFI and DFI-2. However, a longer follow-up period is needed to determine the true outcome in the long-term survivors. Interestingly, DFI-2 is reported to be a prognostic factor after repeat resection for recurrent pulmonary metastases of other types of malignancies. Kandioler et al. [8] reported the prognostic factors in 35 patients after repeat resection for recurrent pulmonary metastases of malignant tumours including epithelial carcinomas (mainly colon and breast cancers) ($n = 20$), osteosarcomas ($n = 10$) and sarcomas ($n = 5$). The prognosis of patients with longer DFI-2 (>40 months) was significantly better than that of patients with shorter DFI-2. The number of metastases or nature of primary tumour (i.e., epithelial cancer, osteosarcoma and sarcoma) did not correlate with survival.

This study had some limitations. The analysis was of patients treated over several decades with changing radiologic modalities. Although we have selection criteria described in Section 2 in this article, the assessment of extrapulmonary metastasis is widely different. Extrapulmonary metastasis might be underestimated in patients in the early period. Recently, F18-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) was introduced in our hospital for hilar and mediastinal lymph node staging in patients with metastatic lung tumours. Future data collection using FDG-PET/CT is needed to investigate the value of this additional preoperative information in patients who undergo pulmonary metastasectomy.

5. Conclusions

Surgical resection of pulmonary metastases from RCC provides favourable outcome in selected patients. Multivariate analysis identified DFI and completeness of resection as significant prognostic factors for survival after pulmonary metastasectomy. Repeat lung resection for metastatic RCC is a safe procedure that provides satisfactory patient outcomes.

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THE ANNALS OF THORACIC SURGERY

Left Innominate Venous Aneurysm Presenting as an Anterior Mediastinal Mass

Mio Sakai, Ryu Kanzaki, Takenori Kozuka, Masahiko Higashiyama, Yasuhiko Tomita, Ken Kodama and Katsuyuki Nakanishi

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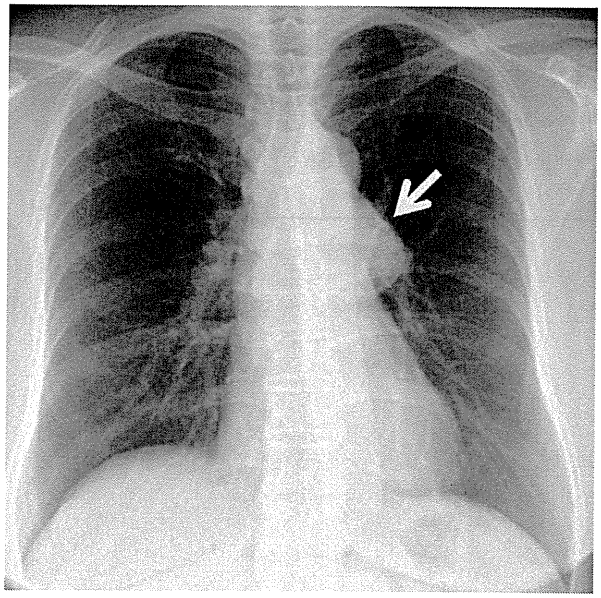

Fig 1.

A 48-year-old woman was referred to our institution because of a mediastinal mass that had been incidentally found on a chest roentgenogram performed as a part of medical checkup (Fig 1, *arrow*). During a clinical examination, a smooth anterior mediastinal mass was demonstrated on a contrast-enhanced computed tomographic scan and on magnetic resonance images. A nonenhanced mural nodule was noted (Fig 2, *arrow*). The mural nodule was hyperintense on fat suppressed T1-weighted images and hypointense on T2-weighted images, suggesting a clot. Three-dimensional time-resolved magnetic resonance angiography demonstrated that the mass showed a delayed contrast enhancement compared with the left innominate vein, which was located adjacent to the mass (Figs 3A, 3B, *arrows*).

During the surgery, an aneurysm arising from the leftward end of the left innominate vein was observed. Complete excision of the aneurysm was performed. Opening the

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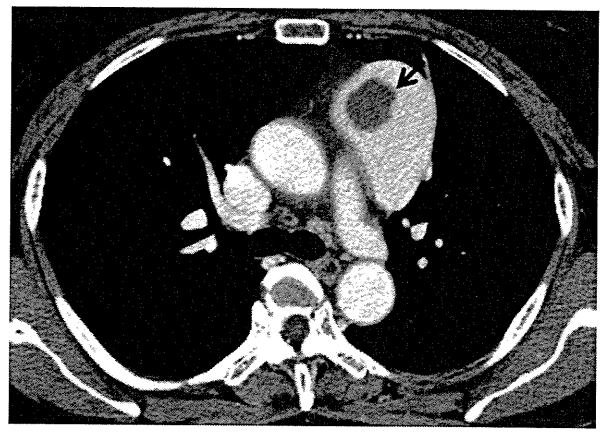

Fig 2.

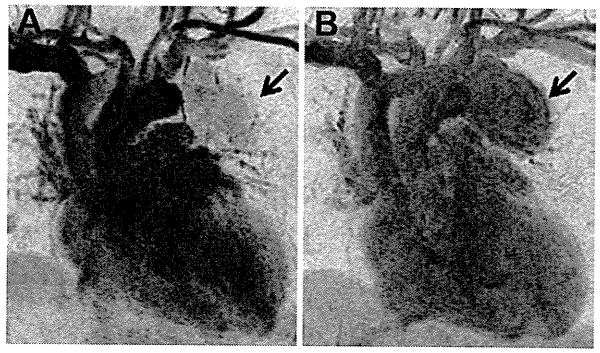

Fig 3.

mass revealed a nodal thrombus, which was believed to be consistent with the mural nodule shown on the computed tomographic scan and magnetic resonance images. Histologic examination demonstrated no evidence of inflammation or degenerative change in the vessel wall. The patient had an uneventful postoperative course.

Aneurysms of the innominate vein are rare. In this case, the preoperative diagnosis was complicated due to the location, the mural nodule, and also the delayed stain of the aneurysm. We attribute the delayed contrast enhancement to a small entry site and slow inflow of venous blood into the large aneurysm.

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Occult mediastinal lymph node metastasis in NSCLC patients diagnosed as clinical N0-1 by preoperative integrated FDG-PET/CT and CT: Risk factors, pattern, and histopathological study

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ABSTRACT

Background: Integrated F18-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is widely used for mediastinal lymph node (MLN) staging in patients with non-small cell lung cancer (NSCLC). However, FDG-PET/CT has certain limitations. Prediction of occult MLN metastasis could allow selection of candidates for preoperative cervical mediastinoscopy or endobronchial ultrasound-guided transbronchial needle aspiration. This study defined risk factors for occult MLN metastasis in patients with NSCLC patients who were diagnosed as clinical N0-1 by preoperative integrated FDG-PET/CT and CT.

Methods: Consecutive patients with NSCLC who underwent staging using integrated FDG-PET/CT as an adjunct to CT prior to lung resection from October 2006 to September 2009 were evaluated retrospectively. The prevalence of MLN metastasis in patients diagnosed as clinical N0-1 was analyzed according to clinicopathological factors such as tumor location, tumor size, histology, and FDG uptake by the primary tumor. Risk factors for occult MLN metastasis were defined by multivariate analysis. Patterns of occult MLN metastasis were also analyzed and the involved MLNs were further examined histopathologically.

Results: The incidence of MLN metastasis was 11% (24 patients of 224). Multivariate analysis identified adenocarcinoma ($P=0.04$), tumors located in upper or middle lobe ($P=0.02$), tumor size >3 cm ($P=0.01$), and SUV_{max} of primary tumor >4.0 g/ml ($P=0.04$) as significant risk factors for MLN metastasis. The pattern of occult MLN metastasis was typical for NSCLC cases. The size of metastatic foci were small, with 68% of foci smaller than 4.0 mm.

Conclusions: The present study demonstrated that adenocarcinoma, tumors located in the upper or middle lobe, tumor size >3 cm, and SUV_{max} of primary tumor >4.0 g/ml are risk factors for occult MLN metastasis in patients with NSCLC who were diagnosed as clinical N0-1 by preoperative integrated FDG-PET/CT and CT. Patients with tumors located in the right upper or middle lobe are considered candidates for cervical mediastinoscopy because the involved metastatic mediastinal lymph nodes are easily accessible by these modalities.

1. Introduction

Lung cancer is the leading cause of cancer-related deaths in the Western world [1]. Despite advances in surgical management, chemoradiotherapy, and early diagnosis, the prognosis for patients with lung cancer remains poor. Accurate staging for non-small cell lung cancer (NSCLC) patients is important for both assessing prognosis and selecting the optimal therapy. Mediastinal lymph node (MLN) staging is particularly critical because survival is improved in patients with stage IIIA disease who undergo chemoradiotherapy followed by surgery, compared to those undergoing with surgery alone [2–4].

Chest computed tomography (CT) and cervical mediastinoscopy have been the gold-standard modalities for MLN staging in NSCLC patients. F18-fluorodeoxyglucose positron emission tomography (FDG-PET) has become increasingly utilized for MLN staging in

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