Review Article

Impact of surgical margin after sublobar resection of lung cancer: a narrative review

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Background and Objective: The use of low-dose computed tomography for screening has improved the detection of early-stage lung cancers. In addition, two large clinical studies have recently reported good outcomes of sublobar resection for early-stage lung cancers, increasing the need for limited resection. However, locoregional recurrence is an important issue in sublobar resection, and R0-resection with sufficient surgical margin is essential to prevent recurrences. This study aimed to investigate the suitable surgical margin distance after sublobar resection of lung cancers with a review of the literature.

Methods: We used the PubMed interface to search the Medline database for retrieving literature related to surgical margin after sublobar resection published between 2003 and 2023.

Key Content and Findings: Overall, 175 papers were found; of them, we investigated the outcomes of 18 selected papers. The correlation between the actual surgical margin distances and recurrences was evaluated in seven articles. All the articles, except one, indicated that an increased margin distance was associated with survival and a lower risk of locoregional recurrence. Further, a surgical margin of 9–15 mm was reported to be sufficient. The correlation between the margin-tumor ratio (M/T) and recurrences was investigated in six articles, most of which demonstrated that the ratio of <1 would be a remarkable predictor of recurrence or poor survival. Although the correlation between surgical margin and spread through air spaces (STAS) was discussed in four articles, their findings remain debatable.

Conclusions: A surgical margin of >10 mm or M/T of ≥1 would be necessary for sublobar resection for STAS-negative early-stage non-small cell lung cancer, although it is difficult to draw a definite conclusion about the appropriate surgical margin because of the characteristics of available literature (mainly retrospective, with different inclusion criteria and surgical margin measurement methods).

Keywords: Surgical margin; sublobar resection; locoregional recurrence; wedge resection; segmentectomy

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Introduction

Lung cancer is recognized as a leading cause of cancer-related death worldwide, and it accounted for nearly 2.2 million cases in 2020 (1). In 1995, the North American Lung Cancer Study Group reported that the overall survival (OS) and recurrence-free survival (RFS) rates were better in the lobectomy group than in the sublobar resection group for early-stage non-small cell lung

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cancer (NSCLC) (tumor diameter ≤3 cm) (2), indicating that sublobar resection should be suggested only for compromised lung cancer patients. Since then, lobectomy has been used as the standard surgical treatment for lung cancer. On the other hand, in 2011, the National Lung Screening Trial reported that compared with single-view posteroanterior chest radiography, the use of low-dose computed tomography (CT) for screening reduced the rate of mortality due to lung cancer (3), thereby improving the detection of early-stage lung cancer. Furthermore, in 2023, two large clinical trials expanded the indications of sublobar resection for early-stage lung cancer. First, the JCOG0802/WJOG4607L study—a multicenter randomized controlled trial conducted in Japan—compared the outcomes of lobectomy and segmentectomy for clinical stage IA NSCLC (tumor diameter ≤2 cm; consolidation-to-tumor ratio >0.5) and demonstrated the superiority and noninferiority of segmentectomy to lobectomy in terms of OS (4). Second, the Cancer and Leukemia Group B (CALGB) 140503 study—a multicenter randomized trial conducted in the United States, Canada, and Australia—compared the outcomes of sublobar resection (wedge resection or segmentectomy) and lobectomy for clinical stage IA NSCLC (tumor diameter ≤2 cm) and demonstrated the noninferiority of sublobar resection to lobar resection in terms of OS and RFS rates (5). Although the results of these trials indicated that compared with lobectomy, sublobar resection is associated with an equivalent or higher survival rate in patients with early-stage lung cancer, they reported that the locoregional recurrence rate was higher with sublobar resection than with lobectomy. In the JCOG0802/WJCOG4607L trial, locoregional recurrences [surgical margin, bronchial stump, hilar/mediastinal lymph nodes (LN), ipsilateral lung, and pleura] were found in 38 (6.9%) cases in the segmentectomy group. This number was significantly higher than that in the lobectomy group [17 (3.1%) cases]. Furthermore, in the CALGB 140503 trial, the rate of locoregional recurrences (lung or hilar LN of the index lobe) was 13.4% in the sublobar resection group, which was slightly higher than that in the lobectomy group (10.0%), although the difference between the two groups was not statistically significant. Accordingly, it can be inferred that a curative R0-resection with sufficient surgical margin would be essential to prevent recurrences, especially locoregional ones.

However, the following questions remain unanswered: How far should the surgical margin distance be obtained? How should the surgical margin be measured? Does the ideal surgical margin depend on tumor size, histology, and CT findings? Therefore, the present study aimed to review the literature related to surgical margin after sublobar pulmonary resection of lung cancer to address the abovementioned clinical questions. We present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-711/rc).

Methods

Regarding the literature search, we used the PubMed interface to search the Medline database from the date of inception to March 11, 2023, for studies in English. The search strategy was designed, and the search was conducted by a researcher with input from the principal investigator of this study. Controlled vocabulary supplemented with keywords was used to search for studies on surgical margin after sublobar pulmonary resection using the following keywords: "margin", "lung neoplasm", "sublobectomy", "segmentectomy", "edge resection", "sublobar", "limited resection", or "recurrence". Eventually, the search yielded 175 articles. Table S1 presents the actual strategy, listing all search terms used and their combination.

The inclusion criteria were as follows: all articles related to the surgical margin; peer-reviewed articles; articles published in the last 20 years; articles in English; full-text articles; and studies involving the human population. Conversely, the exclusion criteria were as follows: papers not related to the surgical margin; nonpeer-reviewed articles, including gray literature (Master's thesis and white papers); unpublished literature, including abstracts and conference abstracts; studies involving individuals aged >20 years; and articles not written in English (*Table 1*).

Surgical margin after sublobar resection of lung cancers

Overall, 175 published articles were retrieved from the initial search. After removing duplicates and eliminating publications according to the eligibility criteria, 18 studies were selected for the analysis (Figure S1).

Measurement of surgical margin

Measurement of the surgical margin distance between the

Table 1 The search strategy summary

Items	Specification
Date of search	11 March 2023
Databases and other sources searched	PubMed
Search terms used	Please see Table S1
Timeframe	2003–2023
Inclusion and exclusion criteria	The inclusion criteria: all articles related to the surgical margin; peer-reviewed articles; articles published in the last 20 years; articles in English; full-text articles; and studies involving the human population
	The exclusion criteria: papers not related to the surgical margin; nonpeer-reviewed articles, including gray literature (Master's thesis and white papers); unpublished literature, including abstracts and conference abstracts; studies involving individuals aged >20 years; and articles not written in English
Selection process	Nagano conducted a literature search and analysis, consulted with all authors, and reached a consensus

tumor edge and resection line is crucial for discussing the significance of the surgical margin after sublobar resection for lung cancer. Notably, a study by Goldstein published in 2003 deliberately described how to measure the surgical margin after wedge resection for adenocarcinoma (6): further, several studies cited Goldstein's criteria. These studies measured the surgical margin distance in three different ways: pleural surface-based margin, gross cut surface, and microscopic margin distances. The pleural surface-based margin distance was defined as the distance between the edge of the palpated tumor and the staple line measured by a ruler placed on the pleural surface. The gross cut margin distance was measured after carefully cutting the staples away from the parenchyma and transecting the tumor. The microscopic distance was calculated with an ocular reticule of pathological slides. Interestingly, the gross cut margin distance (median, 4.0 mm) was 9 mm smaller than the pleural surface-based margin distance (median, 13.0 mm), and the microscopic distance (median, 2.0 mm) was 2 mm smaller than the gross cut margin distance. The mentioned studies did not assess recurrence because lobectomy was performed after wedge resection, but their results indicated that the calculated distances significantly differed between the different measurements. Among the other 17 articles reviewed, 8 articles used the gross cut margin distance and 1 used the pleural surface-based margin distance. Further, in two articles, it was unclear whether the gross cut or pleural surface-based margin was used, and six articles did not mention how the surgical margin was measured in their methods.

Correlation between actual surgical margin distances and recurrences

The determination of the actual surgical margin distance required for sublobar resection is crucial, and seven articles attempted to investigate this important issue (*Table 2*).

Two studies tried to determine the optimal margin cutoff for local RFS. Wolf *et al.* examined 138 patients who underwent wedge resection for NSCLC ≤2 cm and found 33 locoregional or distant recurrences (24%) as well as a significant correlation between increased margin distance (gross cut margin) and reduced risk of recurrence (7). A margin distance of >9 mm was associated with a longer RFS, and a distance of >11 mm was associated with a longer OS. Furthermore, Mohiuddin *et al.* reviewed data from 479 patients who underwent wedge resection for NSCLC of ≤2 cm and reported that an increased margin distance (margin definition is unclear) was associated with a reduced risk of locoregional recurrences (same lobe, draining hilar/mediastinal LN) and that there was no evidence on additional benefit obtained for margins beyond 15 mm (8).

Three other articles set the margin cutoff at 10 mm and analyzed the correlation between surgical margin distance and locoregional recurrence. Sienel *et al.* compared 49 and 150 cases of segmentectomy and lobectomy for stage IA NSCLC, respectively, and demonstrated that the locoregional recurrence rate (same lung, ipsilateral hilar LN) was higher in the segmentectomy group than in the lobectomy group (9). Among 49 patients who underwent segmentectomy, recurrence occurred in 8 (23%) of

Table 2 Correlation between the actual surgical margin distance and recurrence

Author	Year	Study period	Type of surgery: No. of patients	Definition of surgical margin	Inclusion criteria	Margin distance	Definition of locoregional recurrence	Key results for surgical margin
Wolf *et al.* (7)	2017	2000–2005	W: 138	Gross cut	≤2 cm	9 mm, 11 mm	Unknown	A margin distance of >9 mm was associated with the longest recurrence-free survival
								A margin distance of >11 mm was associated with the longest overall survival
Mohiuddin *et al.* (8)	2014	2001–2011	W: 479	Gross cut? Pleural surface?	≤2 cm	15 mm	Same lobe, draining hilar/mediastinal LN	An increased margin distance of ≤15 mm was associated with a lower risk of locoregional recurrence
Sienel *et al.* (9)	2007	1987–2002	S: 49 *vs*. L: 150	Gross cut	Stage IA (TNM ver7)	10 mm	Same lung, ipsilateral hilar/ mediastinal LN	A margin distance of <10 mm tended to be associated with locoregional recurrence of segmentectomy
El-Sherif *et al.* (10)	2007	1997–2004	W + S: 81	Gross cut	Stage IA (TNM ver7)	10 mm	Local: same lobe, ipsilateral hilar LN	A margin distance of <10 mm was associated with a higher local recurrence
							Regional: same lung, ipsilateral mediastinal LN	Wedge resection was a high risk for locoregional recurrence, compared to segmentectomy
Dolan *et al.* (11)	2022	2010–2016	W: 695 *vs*. L: 391 PSM (167 *vs*. 167)	Unknown	Stage I (TNM ver7)	10 mm	Surgical margin, same lung, ipsilateral hilar/mediastinal LN	The locoregional recurrence rate was higher for wedge resection than for lobectomy when the margins were ≤10 mm
Moon *et al.* (12)	2017	2004–2013	W + S: 91	Gross cut	≤3 cm	5 mm	Unknown	The surgical margin did not affect the recurrence of the GGO-predominant tumor, but it affected the recurrence of the solid-predominant tumor
Maurizi *et al.* (13)	2015	2003–2013	W: 182	Unknown	Stage I (TNM ver7)	10 mm, 20 mm	Lung parenchyma, hilar/mediastinal LN	Surgical margin did not influence recurrence or survival rate when R0 was achieved

W, wedge resection; LN, lymph nodes; S, segmentectomy; L, lobectomy; PSM, propensity score matching; GGO, ground-glass opacity.

35 patients with a margin distance of ≤10 mm, whereas no recurrence occurred in 14 patients with a margin distance of >10 mm. El-Sherif *et al.* reviewed data of 81 patients who underwent sublobar resection (wedge resection and segmentectomy) for stage IA NSCLC (10). In their study, 6 (14.6%) of 41 patients with a gross cut margin distance of ≤10 mm had local recurrence (same lobe, ipsilateral hilar LN), and 3 (7.5%) of 40 patients with a margin distance of >10 mm had local recurrence. Interestingly, wedge resection was performed in 34 (61.8%) of 41 patients with a margin distance of ≤10 mm, and all patients with local recurrence in this group underwent wedge resection. Accordingly, El-Sherif *et al.* reported that compared with segmentectomy, wedge resection was a high-risk factor for locoregional recurrence. Furthermore, Dolan *et al.* evaluated survival and recurrence rates between wedge resection and lobectomy for stage I NSCLC by performing a propensity score matching analysis (11). Although the OS rate was equivalent between the two groups, locoregional recurrence (surgical margin, same lung, ipsilateral hilar/ mediastinal LN) was higher in the wedge resection group than in the lobectomy group. Conversely, based on the results of subgroup analysis, the locoregional recurrence rate in patients who underwent wedge resection with a surgical margin (definition not mentioned) of >10 mm was equivalent to that in patients who underwent lobectomy.

Further, Moon *et al.* evaluated the correlation between the actual surgical margin distance and sublobar resection for NSCLC with ground-glass opacity (GGO) (12). Among 91 patients who underwent sublobar resection (wedge resection or segmentectomy) for NSCLC of ≤3 cm, 52 and 39 patients had GGO- and solid-dominant tumors,

respectively. Although the surgical margin distance was not associated with recurrence (local or distant) in GGO-dominant tumors, the margin distance of ≤5 mm was a significant risk factor for recurrence in solid-dominant tumors.

However, only one study reported that there was no significant correlation between surgical margin distance and recurrence or survival rate. This study was conducted by Maurizi *et al.* who evaluated 243 patients with stage I NSCLC who underwent wedge resection and systematic LN dissection because of a functional contraindication to major lung resection; subsequently, they analyzed 182 patients with pathologic stage I and R0 resection. The margin (definition not mentioned) cutoff was set at 10 and 20 mm, and the patients were classified into the following three groups according to the margin distance: <10, 10–20, and >20 mm (13). Locoregional recurrence (lung parenchyma, hilar/mediastinal LN) and distant recurrence were detected in 48 (26.4%) and 20 (11%) patients, respectively. Notably, the abovementioned three groups did not differ in terms of locoregional or distant recurrence or OS.

Correlation between margin-tumor ratio (M/T) and recurrences

In 2004, the concept of M/T was advocated for the first time by Sawabata *et al.*, but their study was not included in the literature search of this review (14). Their multicenter prospective study aimed to determine the optimal size of a malignant negative margin. Further, they enrolled 115 patients with NSCLC who underwent wedge resection and analyzed whether the surgical margin was malignant positive by cytologic and histologic examinations. Among 118 NSCLC lesions, 72 (61%) were malignant negative for the surgical margin by both cytologic and histologic examinations. Further, it was found that all 46 (39%) NSCLC lesions with malignant positive margins had M/T of <1.

Since then, the correlation between M/T and recurrences has been investigated in six articles (*Table 3*). Sawabata *et al.* analyzed the data of 37 patients who underwent wedge resection without additional resection for peripheral NSCLC (15). The maximum and median tumor diameters were 35 and 15 mm, respectively. The surgical margin was measured based on the gross cut margin distance. Among 13 cases with recurrence, 11 had a surgical margin with M/T of <1. Furthermore, the 5-year OS rate was significantly lower in cases with M/T of <1 than in cases with M/T of ≥1. Takahashi *et al.* reviewed data from 32 patients who underwent sublobar resection (wedge resection or segmentectomy) for stage I NSCLC (16). The surgical margin was calculated based on the pleural surface-based margin distance. The number of cases with M/T of ≤1 was 20, and a significant decrease in RFS (locoregional and distant) and OS rates was observed between patients with M/T of <1 and those with M/T of >1. Schuchert *et al.* compared the long-term outcomes between patients undergoing segmentectomy (n=182) and those undergoing lobectomy (n=246) for stage I NSCLC, although the maximum tumor diameter was 7.0 and 11.2 cm for the segmentectomy and lobectomy groups, respectively (17). However, the definition of the surgical margin was unclear. For 182 cases of anatomic segmentectomy, M/T of <1 was a significant predictor of locoregional (same lobe, hilar/mediastinal LN) and distant recurrences. Furthermore, Schuchert *et al.* concluded that lobectomy should be performed if surgical margins are considered insufficient for segmentectomy. In addition, they published a new article in 2017 that analyzed data from >1,000 patients with stage I NSCLC who underwent segmentectomy (n=384) and lobectomy (n=748) (18). In their study, among 227 (20%) cases of recurrences, 65 and 155 were locoregional (same lobe, hilar/mediastinal LN) and distant recurrences, respectively. Further, M/T of <1 was associated with a higher recurrence rate (22.4%) than M/T of ≥1 (16.6%) in all patients, including those who underwent segmentectomy and lobectomy, suggesting that M/T of <1 is a significant predictor of recurrence. Recently, Moon *et al.* published two papers, one of which analyzed the effect of M/T on recurrence according to the histological subtypes of adenocarcinoma (19). They classified 133 patients into four groups: lepidic tumor with M/T of <1, lepidic tumor with M/T of ≥1, non-lepidic tumor with M/T of <1, and non-lepidic tumor with M/T of ≥1. The surgical margin was measured using the gross cut margin method. Among the lepidic predominant tumors, no recurrence (locoregional or distant) was found even when two cases had only a 2-mm margin distance. Conversely, among non-lepidic tumors, in the group with M/T of <1, eight cases had a recurrence, of which seven had locoregional recurrence (same lung/pleura, ipsilateral hilar/mediastinal LN). However, in the group with M/T of ≥1, only one case had locoregional recurrence. The 5-year RFS rate was significantly lower in the non-lepidic tumor group with M/T of <1 (49.9%). Another study investigated the correlation between locoregional

Table 3 Correlation between the M/T and recurrence

Author	Year	Study period	Type of surgery: No. of patients	Definition of surgical margin	Inclusion criteria	Definition of locoregional recurrence	Key results for surgical margin
Sawabata *et al.* (15)	2012	1999–2002	W: 37	Gross cut	Unknown (≤3.5 cm)	Surgical margin, lung, pleura	Many cases of locoregional recurrence occurred in patients with M/T <1
							The 5-year OS was significantly lower for patients with M/T <1 than for those with M/T ≥1
Takahashi *et al.* (16)	2019	2008–2012	W + S: 32	Pleural surface	Stage I (TNM ver7)	Unknown	Patients with M/T ≤1 tended to have low RFS and OS
Schuchert *et al.* (17)	2007	2002–2006	S: 182 *vs*. L: 246	Unknown	Unknown (≤7 cm for S)	Same lobe, hilar/ mediastinal LN	M/T <1 was a significant predictor of distant and locoregional recurrences for segmentectomy
Schuchert *et al.* (18)	2019	Unknown	S: 384 *vs*. L: 748	Unknown	Stage I (TNM ver8)	Same lobe, hilar/ mediastinal LN	M/T <1 was a significant predictor of distant and locoregional recurrences for segmentectomy
Moon *et al.* (19)	2018	2008–2015	W + S: 133	Gross cut	≤2 cm adenocarcinoma	Same lung/pleura, ipsilateral hilar/ mediastinal LN	RFS was not associated with M/T in patients with lepidic-dominant tumors
							M/T <1 was a significant risk factor for recurrence with non-lepidic tumors
Moon *et al.* (20)	2020	2008–2017	W + S: 193	Gross cut	Invasive size ≤2 cm	Surgical margin, pleura, ipsilateral hilar/ mediastinal LN	The margin/invasive component ratio was significantly associated with a higher rate of locoregional recurrence

M/T, margin-tumor ratio; W, wedge resection; OS, overall survival; S, segmentectomy; TNM, tumor-node-metastasis; RFS, recurrence-free survival; L, lobectomy; LN, lymph nodes.

recurrence and the margin/invasive component ratio (20). This study included 193 patients who underwent sublobar resection (wedge resection or segmentectomy) for tumors with an invasive size of ≤2 cm. The surgical margin was measured using the gross cut margin method. The results of the study indicated that seven patients had locoregional recurrences (surgical margin, pleura, ipsilateral hilar/ mediastinal LN). Interestingly, the 5-year RFS rate was significantly lower in the group with a margin/invasive component ratio of <1 than in the group with the ratio of ≥1, but M/T was not a significant risk factor for recurrence.

Correlation between surgical margin and spread through air spaces (STAS)

Only a few articles have discussed the correlation between surgical margin and STAS, and the results remain controversial (*Table 4*). Gross *et al.* aimed to determine whether STAS could be detected in additional resected specimens even after sublobar resection (nine cases of wedge resection and one case of segmentectomy) with a negative surgical margin (definition unknown) in the first surgery (24). These 10 cases were found to be STAS-positive according to the findings of the first resected sample. Although all cases had a negative surgical margin (1–18 mm), M/T was <1 in all specimens. Thus, additional resections were performed to secure an additional margin in all cases, with all additional resected specimens containing STAS. Masai *et al.* analyzed data from 508 patients who underwent sublobar resection (wedge resection and segmentectomy) for NSCLC (21). Although the inclusion criteria of their study were unknown, the maximum tumor diameter was found to be 4.5 cm. The surgical margin measurement method (gross cut or pleural surface-based) was not described in detail. They set the margin cutoff at 10 mm, and their multivariate analysis revealed that the presence of STAS and a surgical margin of <10 mm were independent risk factors for local (surgical margin)

Table 4 Correlation between the surgical margin and STAS

Author	Year	Study period	Type of surgery: No. of patients	Definition of surgical margin	Inclusion criteria	Surgical margin	Definition of locoregional recurrence	Key results for surgical margin
Masai, *et al.* (21)	2017	2004–2013	W + S: 580	Gross cut? Pleural surface?	Unknown (≤4.5 cm)	10 mm	Local: surgical margin Regional: same lung/ pleura, ipsilateral hilar/ mediastinal LN	The presence of STAS and tumor margins <10 mm were significant risk factors for local recurrence for sublobar resection
Eguchi, *et al.* (22)	2019	1995–2014	W + S: 527 *vs.* L: 970 PSM (349 *vs.* 349)	Gross cut	Stage IA (TNM ver7)	M/T	Local: surgical margin, same lobe	In STAS-negative tumors, locoregional recurrences occurred in patients with M/T <1
							Regional: same lung, ipsilateral hilar/ mediastinal LN	In STAS-positive tumors, locoregional recurrences occurred regardless of M/T
Kagimoto, *et al.* (23)	2021	2011–2020	S: 107 *vs*. L: 186 PSM (75 *vs.* 75)	Unknown	Stage IA (TNM ver8) STAS-positive	M/T	Surgical margin, same lung, ipsilateral hilar/ mediastinal LN	The locoregional and distant recurrence rates were not different between the lobectomy and segmentectomy groups The margin/invasive component ratio was <1 in all segmentectomy recurrences

STAS, spread through air spaces; W, wedge resection; S, segmentectomy; LN, lymph nodes; L, lobectomy; PSM, propensity score matching; TNM, tumor-node-metastasis; M/T, margin-tumor ratio.

recurrence in sublobar resection. Eguchi *et al.* reviewed data from 1,497 patients with stage IA NSCLC, of whom 527 and 970 underwent sublobar resection and lobectomy, respectively (22). In their study, propensity score matching revealed that among patients with STAS-negative tumors, locoregional recurrences occurred only in those with M/T of <1. Conversely, among patients with STAS-positive tumors, these recurrences occurred irrespective of M/T. Moreover, they showed that patients with STAS who underwent sublobar resection had a higher risk of recurrence and lung cancer-specific death than those who underwent lobectomy. Contrarily, Kagimoto *et al.* insisted that among patients with STAS-positive tumors, the locoregional (surgical margin, same lung, ipsilateral hilar/mediastinal LN) and distant recurrence rates were not different between those who underwent lobectomy and those who underwent segmentectomy (23). They compared patients undergoing segmentectomy (107 cases) and those undergoing lobectomy (186 cases) for stage IA STAS-positive NSCLC by performing a propensity score matching analysis. After matching, the rates of local, locoregional, and distant recurrence were not significantly different between the two groups. Furthermore, 5 out of 107 cases of segmentectomy had recurrence, and the margin/invasive component ratio was found to be <1. The abovementioned articles suggest that M/T of <1 or surgical margin of <10 mm is a significant risk factor for recurrence or survival in STAS-negative cases, but it is still uncertain whether these criteria regarding surgical margin in STAS-positive tumors are sufficient.

Discussion

This paper reviewed 18 articles that discussed surgical margin distance after sublobar resection of lung cancers. Most of these articles suggested that the surgical margin distance is significantly related to postoperative recurrence and overall survival rates. However, it is unclear how far the surgical margin distance should be obtained depending on the distance measurement method, tumor size, tumor characteristics (with or without STAS), and type of surgery.

We believe that a gross cut margin distance of 10 mm may be a good parameter to prevent recurrences. Although only one article reported that the surgical margin distance may not be related to recurrence or survival rate, the other six articles reported that a certain amount of

margin distance should be secured in sublobar resection. Notably, the actual surgical margin distance associated with recurrence was found to be 5, 9, 10, and 15 mm in one, one, three, and one articles, respectively. Further, more than half of the articles measured the surgical margin using the gross cut margin distance. Therefore, the gross cut margin of 10 mm may be one of the standard cutoffs in sublobar resection for lung cancers.

Notably, M/T of 1 measured by gross cut may be a good indicator to prevent recurrences. Among six articles discussing the correlation between M/T and recurrences, five indicated that M/T of <1 is associated with both locoregional and distant recurrences, whereas one suggested the importance of the margin/invasive component ratio. The gross cut margin was used to measure the surgical margin distance in three articles; thus, the gross cut margin with M/T of >1 could be recommended in sublobar resection for lung cancers.

We reckon that appropriate surgical margin distance required in wedge resection and segmentectomy might be the same. Several papers selected in this review showed that which type of surgery, wedge resection or segmentectomy, was not a significant risk factor for recurrence (12,19,20). In addition, other papers suggested that a surgical margin of >10 mm or M/T of >1 might be necessary to prevent recurrence regardless of wedge resection (7,11,15) or segmentectomy (9,17,18). On the other hand, a few studies cautioned that insufficient surgical margin were seen more frequently in wedge resection than in segmentectomy, leading to locoregional recurrence (10,12). Thus, segmentectomy or lobectomy should be performed when a surgical margin distance obtained in wedge resection is considered to be inappropriate.

To date, how far the surgical margin should be obtained for STAS-positive lung cancers is unclear. Four articles that discussed the correlation between surgical margin and recurrences in lung cancer reported different results. M/T of <1 or margin distance of <10 mm may be associated with a poor prognosis in sublobar resection for STAS-positive lung cancers; however, whether these cutoffs would be sufficient for this type of cancer remains debatable. In addition, preoperative or intraoperative diagnosis of STAS is challenging. Cao *et al.* examined 111 preoperative percutaneous transthoracic needle biopsy specimens and subsequent resection specimens, showing that only six biopsy specimens were suspected to be STAS-positive among 36 lung adenocarcinoma with STAS confirmed by the subsequent resection specimens (25). Kameda *et al.* reported that STAS could be identified in frozen sections intraoperatively with a sensitivity and specificity of 71% and 92%, respectively (26). At present, therefore, definitive diagnosis of STAS should be done in the postoperative pathological findings, and completion lobectomy should be taken into consideration for patients with STAS.

This review analyzing the surgical margin required in sublobar resection for NSCLC has several limitations. First, most of the studies included in the review were retrospective and conducted at a single institution. In addition, inclusion criteria, such as tumor size, tumor type (with or without GGO), and surgical procedure (wedge resection and/or segmentectomy), varied among studies. These factors make it difficult to draw a definite conclusion. Second, the reviewed articles provided different definitions of surgical margin and locoregional recurrence. Correct measurement of the surgical margin distance is considered essential for analyzing the correlation between the margin and recurrence, but surprisingly, some articles did not mention how the authors calculated the surgical margin. Finally, some studies included hilar/mediastinal LNs or different lung lobes at locoregional sites, whereas others restricted locoregional sites to the surgical margin and the same lung. This difference would have greatly influenced the results of the correlation between surgical margin and locoregional recurrences.

We believe that the measurement of the surgical margin should be precisely described in studies, and in the future, it would be essential to reach a consensus on the definition of the surgical margin. Additionally, further prospective studies with accurate measurements of the surgical margin distance and precise inclusion criteria are warranted to establish a clear cutoff of the surgical margin distance in sublobar resection for lung cancers.

Conclusions

The present literature review suggests that a surgical margin of >10 mm or M/T of >1 may be essential to prevent recurrence (particularly locoregional) in sublobar resection for STAS-negative early-stage NSCLC. However, it would be difficult to draw a definitive conclusion about the appropriate surgical margin for sublobar resection because almost all analyzed articles had a retrospective design, and these articles had different measurement methods to assess surgical margin, definition of locoregional recurrence, tumor size, and type of surgery. In the future, more prospective studies with the accurate measurement of

surgical margin and precise inclusion criteria are warranted.

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Footnote

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Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-711/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 The detailed search strategy

No.	Search terms
#1	lung neoplasm [Mesh Term]
#2	margin [All Fields]
#3	recurrence [All Fields]
#4	sublobectomy [Title/Abstract]
#5	segmentectomy [Title/Abstract]
#6	wedge [Title/Abstract]
#7	sublobar [Title/Abstract]
#8	limited resection [Title/Abstract]
#9	#4 OR #5 OR #6 OR #7 OR #8
#10	#1 AND #2 AND #3 AND #9

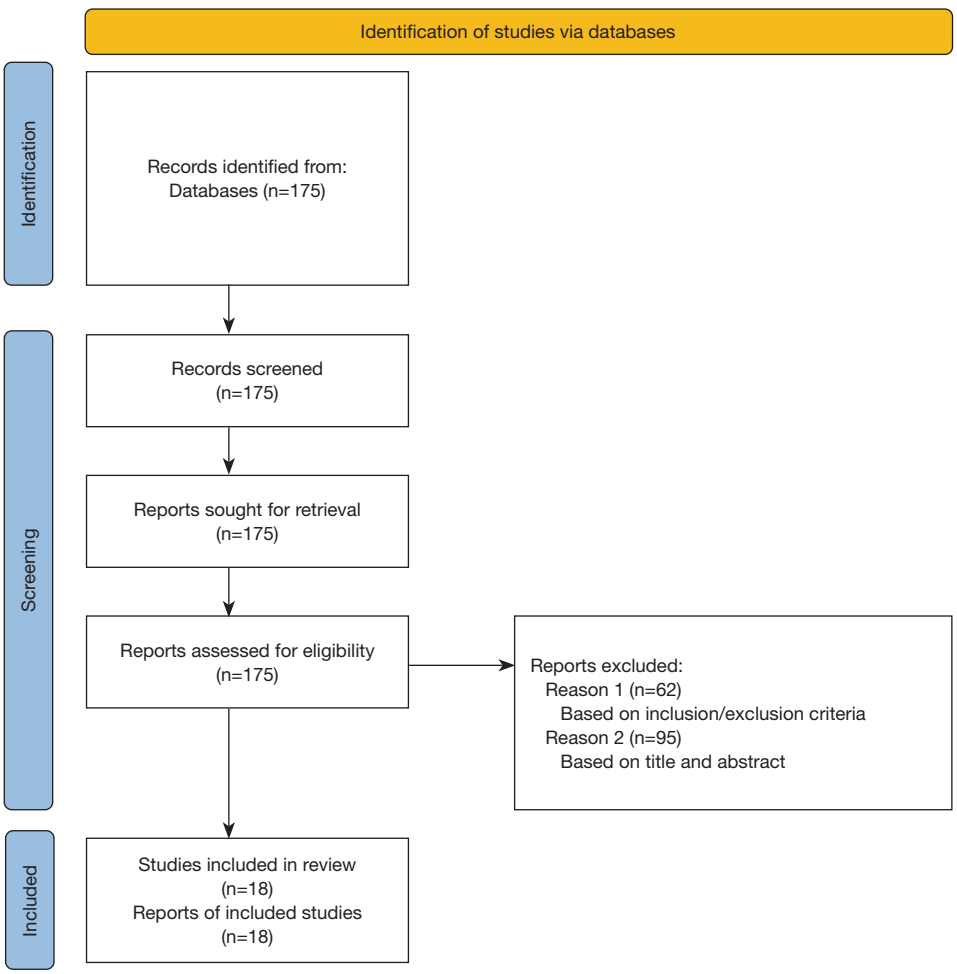

Figure S1 Flowchart of the study selection process.

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