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CERVICAL SPINE

Anterior Cervical Fusion Assessment Using Reconstructed Computed Tomographic Scans

Surgical Confirmation of 254 Segments

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Study Design. Retrospective study developing diagnostic criteria.

Objective. To validate 2 computed tomography–based findings, extragraft bone bridging (ExGBB) and intragraft bone bridging (InGBB), as diagnostic criteria for anterior cervical fusion using subsequent surgical confirmation and to demonstrate the different diagnostic accuracy on the basis of the graft material used.

Summary of Background Data. The accuracy and the methodology for evaluating bone bridging on computed tomographic scans to determine anterior cervical fusion status have not been validated or standardized.

Methods. One hundred ten patients with 254 surgically explored segments along with reconstructed computed tomographic scans were included. Bone bridging at each cervical level was assessed for ExGBB and InGBB. ExGBB was defined as complete cortical bridging at any peripheral margins (anterior, posterior, left, or right) of the operated disc space, outside of the graft. InGBB was defined as cortical or trabecular bridging within the confines of the graft only. ExGBB and InGBB were serially evaluated on reformatted coronal and sagittal views by 3 independent raters. The reliabilities and validities correlated with surgical exploration were evaluated.

Results. Surgical exploration revealed 123 fused and 131 pseudarthrosis segments. The reliability of 3 raters showed near perfect agreement for ExGBB and substantial agreement for InGBB. ExGBB also had higher validity for all raters than did InGBB. The autocortical graft group had the highest accuracy for both InGBB and ExGBB, with both values being nearly identical. The allograft group had the next highest validity values. For the cage group, InGBB had the lowest specificity (53.2%) and positive predictive value (35.5%), whereas ExGBB had 100% sensitivity and negative predictive value.

Conclusion. ExGBB seems to be a far more reliable and accurate to determine anterior cervical fusion. The diagnostic criteria using bone bridging should be different based on the intradiscal materials. With cages in particular, InGBB seems unreliable and ExGBB is necessary to determine anterior cervical fusion.

Key words: anterior cervical arthrodesis, pseudoarthrosis, CT scan, reliability, fusion assessment.

Level of Evidence: 2

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The radiographical fusion rate is one of the most commonly used and important indices for comparing the surgical results of various kinds of anterior cervical fusion surgical procedures. Computed tomography is commonly used to evaluate the fusion status in cases suggestive of pseudarthrosis.[1–3] The Food and Drug Administration defines bone fusion as the presence of bone bridging the fusion area without any lucencies.[4] A few reports have tried to provide detailed definitions of bone bridging after intervertebral fusion surgical procedure.[5–8] However, very limited number of studies of the cervical spine[9,10] have investigated the accuracy of bone bridging on computed tomographic (CT) scans as diagnostic criteria for fusion using surgical exploration as the reference standard. Furthermore, the criterion of bone bridging has still not been validated or standardized.

In addition, most studies have focused only on the juncture between graft and host for evaluating bone bridging. Bone formation in outside of intradiscal graft would provide important information about fusion status according to what kinds of intradiscal materials used. No previous studies, however, have assessed extragraft bone formation when evaluating anterior cervical fusion status, nor have any studies considered whether different computed tomography–based radiographical fusion criteria may be necessary for different

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types of intradiscal devices. For example, it is thought that some metal cages can hinder the evaluation of bone bridging from CT scans.[7]

We developed 2 computed tomography–based fusion criteria, extragraft bone bridging (ExGBB) and intragraft bone bridging (InGBB), to assess anterior cervical fusion status using multiaxial reconstructed CT scans. The purpose of this study was to evaluate the accuracy of these 2 computed tomography–based findings as diagnostic criteria using subsequent intraoperative confirmation. In addition, we sought to demonstrate the differences of the accuracy on the basis of the type of intradiscal graft used, including autocortical graft, allograft, and synthetic cages.

MATERIALS AND METHODS

Subjects

The study was approved by the institutional review board. We retrospectively investigated all consecutive patients who required anterior or posterior exploration of previous anterior cervical arthrodesis of any level(s) ranging from C2–C3 to C7–T1 from April 2012 to April 2004. The medical records were reviewed for age at revision surgery, sex, cervical level, the type of revision surgery, results of surgical exploration, and duration from index surgery to time of surgical exploration. To be included in this study, the patients must have had preoperative thin cut multiaxial reconstructed CT scan available on a computer working station using PACS (Picture Archiving and Communication System; Siemens Magic Software, Germany) obtained just before exploration and be at least 1 year postoperative from their index anterior cervical arthrodesis. The patients with a CT scan unavailable on PACS and who underwent surgery because of pathological infectious or traumatic conditions were excluded. The surgical levels with concomitant posterior fusion surgeries, equal to or greater than two-level corpectomy, and vague description of fusion status at each level on operation records were also excluded. One hundred ten patients with 254 cervical operated segments were included in the study. Among them, 87 (anterior: 35, posterior: 52) patients underwent exploration because of suspicion of pseudoarthrotic segment(s) and the remaining 23 (anterior: 13, posterior 10) patients underwent operation because of clinical adjacent segment pathology. All revision operations were performed at a single institution by a single surgeon.

Definitions of ExGBB and InGBB

We divided bone bridging into 2 categories: ExGBB and InGBB. In evaluating CT scan, first, 3 planes were set at each level as follows: The axial plane was set parallel to the disc space on the coronal and sagittal views. The sagittal plane was set perpendicular to the disc space on the coronal view and the posterior margin of the vertebra on the axial view. The coronal plane was set perpendicular to the disc space on the sagittal view and parallel to the posterior margin of the vertebra on the axial view (Figure 1). The sagittal and coronal views were then serially examined for ExGBB and InGBB at each level. ExGBB was defined as any peripheral bone bridging of cortical density with no lucent lines crossing the peripheral margins of the operated disc space outside of the graft or cage at each cervical segment, and the peripheral cortical margins were evaluated at the anterior, posterior margin (on sagittal views), left, and right margins (on coronal views). At least 1 of these margins had to have

Figure 1. A 43-year-old male who underwent anterior cervical fusion at C45 and C56 levels using autograft. The sagittal view **(A)** was set perpendicular to the disc space on coronal view **(B)** and the posterior margin of the vertebra (black line) on the axial view **(C)**. Coronal view was set perpendicular to the disc space on sagittal view and parallel to the posterior margin of the vertebra on axial view. At the C45 level, sagittal and coronal views show anterior, posterior, and left peripheral cortical margins (arrows) and cancellous and cortical (dotted arrow) bone bridging within the graft. At the C56 level, there are no ExGBB and InGBB.

peripheral cortical margin to be categorized as fusion. InGBB was defined as any cortical or trabecular bone bridging with no lucent lines within the confines of the graft or cage (Figure 1). To be defined as ExGBB and InGBB, the bone bridging had to be present at both the cranial and caudal endplates of each cervical segment with no lucent lines and needed to be present in both the coronal and sagittal views simultaneously (Figure 2). In the 20 patients with a previous 1-level corpectomy, each InGBB was evaluated at the cranial endplate for above level and the caudal endplate for below level abutting the graft. In evaluating ExGBB, it is important to distinguish peripheral cortical margin from bone spurs. Bone spurs usually have a direction of radial outgrowth from the disc space with discontinuity of cortical density, whereas peripheral cortical margin is nearly parallel to the margins of adjacent vertebral bodies.

Independent Reviewers

Three spine surgeons with 2, 5, and 7 years of experience participated independently and had no information about the results of surgical exploration. Each cervical segment was evaluated for ExGBB and InGBB at 2 different time points that were at least 3 weeks apart. The inter- and intraobserver reliability and the validity of ExGBB and InGBB as diagnostic criteria for fusion correlated with intraoperative findings were evaluated.

Surgical Exploration

For anterior exploration, the determination of fusion status was made by high-powered microscope inspection of the fusion mass, which required removal of all soft tissues and inspection for any fissures in the bone by burring off 1 to 2 mm of the ventral cortical bone after removal of any existing anterior plate. If there was still doubt after this maneuver, we placed Caspar distractor pins cranial and caudal to the cleft and distracted and compressed while inspecting for any motion. Posteriorly, we inspected the facet joints under the highest power microscope visualization while prying the spinous processes apart with a small Cobb elevator. Solidly fused patients were those in whom the facets had bridging bone overlying either joint (mature fusion) or the joints had no motion. Pseudarthrosis had obvious motion in the facets joints when the same maneuver was applied. In some cases, the fusion status was indeterminate using the aforementioned techniques, because there was equivocal motion in one or both joints. If it was still unclear, we called these "indeterminable" and did not include these levels in our evaluation.

Statistics

For all continuous variables, we used Shapiro-Wilk tests to assess the normality of the data. Because none of the variables were normally distributed, the data were analyzed with nonparametric tests, including the Mann-Whitney *U* test, Kruskal-Wallis test, and Bonferroni correction for *post hoc* tests. Descriptive variables were analyzed with χ^2 tests or Fisher exact tests, as appropriate. Results were expressed as the mean (95% confidence interval) or absolute number. Reliability was assessed with Cohen κ value (95% confidence interval), and the level of agreement for the κ value was determined as per Landis and Koch.[11]

RESULTS

Demographic Data

Operative confirmation revealed that there were 123 fused segments and 131 pseudarthrotic segments. The pseudarthrotic segments were a shorter duration from the index operation ($P < 0.001$) (Table 1). Regarding the graft materials used, excluding 2 segments in which a combination of cage and allograft was used in 1 disc space, pseudarthrotic segments for the autograft and allograft groups had a longer duration from index surgery than those in the cage group ($P = 0.021$), but there were no differences for the fused segments (Table 2).

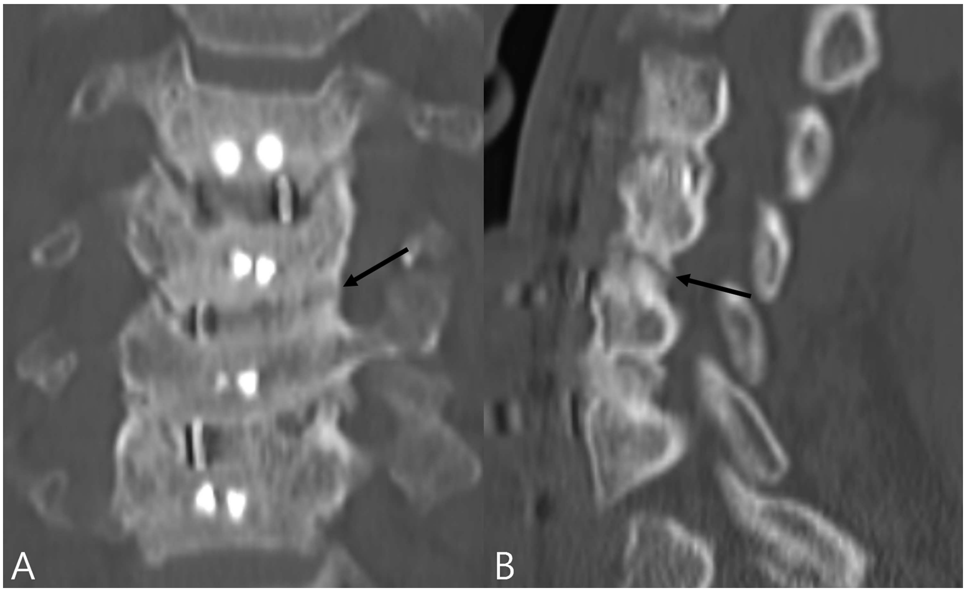


Figure 2. Although the arrow on coronal view (**A**) shows suspicious left peripheral cortical margin (arrow), the sagittal view (**B**) demonstrates incomplete peripheral cortical bone bridging (arrow). The segment was proved to be pseudarthrosis in surgical exploration.

TABLE 1. Demographic Data (the Values Are Expressed as Mean [95% Confidence Interval] or Absolute Number)

	Fused Segments (123 Segments/69 Patients)	Pseudoarthrotic Segments (131 Segments/88 Patients)
Age at revision surgery	52.53 (51.12–53.93)	51.44 (49.67–53.22)
Male:female ratio (no. of patients)	52:71	55:76
Cervical level C23/C34/C45/C56/C67/C71 (no. of segments)	1/13/29/46/30/4	0/8/19/51/46/7
No. of anterior/posterior revision surgery	54 segments in 30 patients/69 segments in 39 patients	37 segments in 28 patients/94 segments in 60 patients
No. of anterior/posterior revision surgery due to adjacent segment pathology	29 segments in 13 patients/23 segments in 10 patients	
Duration from index surgery (month)*	56.32 (49.21–63.42)	42.74 (35.41–50.07)

*$P < 0.05$.

The types of cages used included polyetheretherketone cages in 45 levels, metal cages in 12 cases (threaded cage: 5 cases; mesh cage: 4 cases; and other: 3 cases), and ceramic cages in 2 levels.

Reliability of ExGBB and InGBB

The intraobserver reliability of the 3 raters was significantly higher for ExGBB (range: 0.905–0.921) than for InGBB (range: 0.666–0.680). Likewise, the interobserver reliability of the 3 raters was higher for ExGBB (range: 0.862–0.925) than for InGBB (range: 0.609–0.669). All observer reliabilities for ExGBB were nearly perfect in agreement, whereas their reliabilities for InGBB were substantial. In ExGBB, the anterior peripheral cortical margin had the lowest intra- and interobserver reliabilities with ratings of substantial or moderate compared with nearly perfect or substantial in other margins. ExGBB also showed a nearly perfect agreement (0.907) with the results of surgical exploration whereas InGBB showed a substantial agreement (0.663) (Table 3).

Validity of ExGBB and InGBB

For all observers, validity values correlated with surgical exploration were higher for ExGBB than for InGBB. ExGBB showed that sensitivity and negative predictive value (NPV) were more than 98%. For both ExGBB and InGBB, specificity and positive predictive value (PPV) were lower than sensitivity and NPV (Table 4).

Validity According to the Type of Graft Material Used

The autocortical graft group had the highest validity values for fusion criteria in both ExGBB and InGBB, and both values were very similar. Of note, specificity and PPV for fusion criteria of ExGBB were 100% for the autocortical graft group. The allograft group had the next highest validity values, but the values for InGBB were lower than those for ExGBB. For the cage group, the validity values for ExGBB were also higher than those for InGBB, and the differences between the 2 measurements were the greatest of the 3 groups. Of note, the specificity and PPV of InGBB were 53.2% and 35.5%,

TABLE 2. Demographic Comparisons According to Graft Materials Used (the Values Are Expressed as Mean [95% Confidence Interval] or Absolute Number)

	Autograft Group (n = 32) (Fused: 20, Pseudo: 12)	Allograft Group (n = 161) (Fused: 88, Pseudo: 73)	Cages Group (n = 59) (Fused: 13, Pseudo: 46)	*P*
Age at surgery	50.59 (48.22–52.97)	52.64 (51.13–54.14)	50.88 (48.50–53.27)	0.458
Male:female ratio (no. of patients)	11/21	70/90	26/33	0.611
No. of cervical levels C23/C34/C45/C56/C67/C71	0/3/9/12/7/1	1/10/29/62/51/8	0/8/10/23/16/2	0.779
Duration from index surgery (mo)				
In Pseudoarthrotic segments	62.25 (28.69–95.81)	48.62 (37.28–59.95)	28.33 (22.62–34.03)	0.021
In fused segments	50.79 (28.31–73.27)	58.80 (50.52–67.07)	52.08 (30.04–74.11)	0.241

TABLE 3. Intra- and Inter-Rater Reliabilities for ExGBB and InGBB (Reliability Was Expressed as Cohen κ Value [95% Confidence Interval] for Each Rater)

	ExGBB	Anterior PCM	Posterior PCM	Right PCM	Left PCM	InGBB
Intrareliability of rater A	0.921 (0.875–0.971)	0.633 (0.523–0.704)	0.860 (0.794–0.918)	0.822 (0.752–0.893)	0.838 (0.777–0.913)	0.680 (0.599–0.784)
Intrareliability of rater B	0.913 (0.864–0.965)	0.694 (0.602–0.779)	0.904 (0.851–0.957)	0.869 (0.806–0.929)	0.822 (0.757–0.899)	0.683 (0.588–0.767)
Intrareliability of rater C	0.905 (0.853–0.957)	0.720 (0.633–0.805)	0.895 (0.840–0.951)	0.839 (0.784–0.918)	0.817 (0.766–0.906)	0.666 (0.581–0.767)
Inter-reliability of A and B	0.925 (0.892–0.958)	0.732 (0.679–0.797)	0.858 (0.816–0.905)	0.821 (0.747–873)	0.814 (0.768–0.868)	0.609 (0.540–0.678)
Inter-reliability of A and C	0.882 (0.844–0.925)	0.609 (0.549–0.686)	0.805 (0.745–0.858)	0.807 (0.762–0.864)	0.827 (0.779–0.877)	0.669 (0.608–0.737)
Inter-reliability of B and C	0.862 (0.820–0.908)	0.575 (0.504–0.647)	0.795 (0.742–848)	0.797 (0.746–851)	0.764 (0.715–0.827)	0.619 (0.556–0.692)
Agreement with surgical confirmation in all raters	0.907 (0.885–927)	0.552 (0.512–0.588)	0.802 (0.773–0.833)	0.798 (0.767–0.827)	0.799 (0.767–0.828)	0.663 (0.556–0.634)

ExGBB indicates extragraft bone bridging; PCM, peripheral cortical margin; InGBB, intragraft bone bridging.

respectively, whereas the sensitivity and NPV of ExGBB were each 100%. If metal cages (n = 12), which could be one of reasons of inherently difficulty to identify intragraft bone bridging on CT scan, were excluded in cages group, sensitivity and NPV were increased to 95% and 97.4%, respectively, but specificity and PPV of InGBB were still too low and ExGBB had 100% sensitivity and NPV (Figure 3).

DISCUSSION

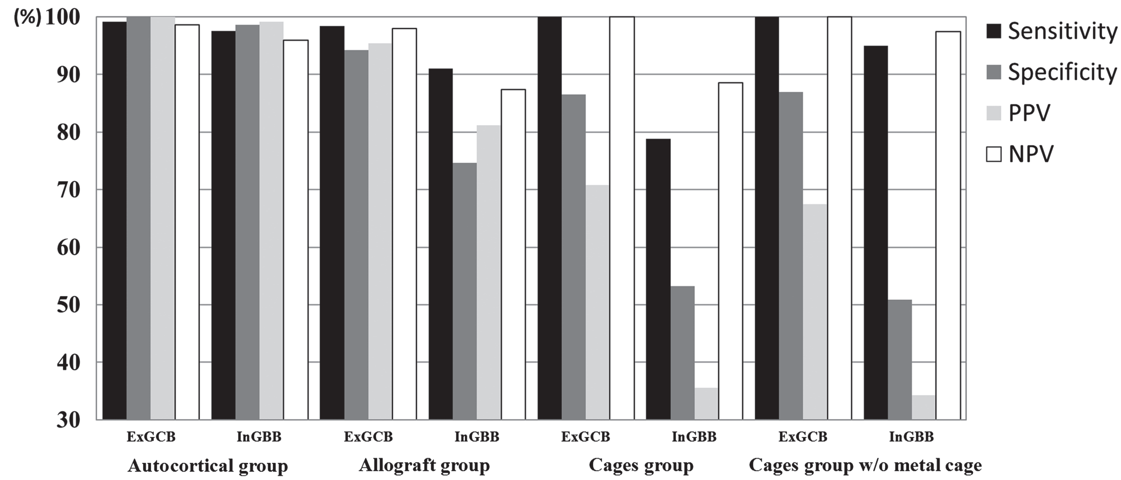
In this study, we used surgical exploration to evaluate the accuracy of ExGBB and InGBB on reconstructed CT scans in 254 cervical segments and found that ExGBB was significantly more accurate reliability and validity than InGBB to determine anterior cervical fusion status. Most studies[1–3,9,10] define fusion as the presence of bony trabeculation across the fusion level and lack of bony lucency at the graft/vertebral body junction, similar to InGBB in our study. However, detailed descriptions of bone bridging, such as the density and location of the bone bridge, are lacking. Indeed, the term bone bridging is basically descriptive in nature and is thus subject to interpretation, so it is no surprise that achieving high inter- or intraobserver reliability has been difficult. In contrast, the presence of ExGBB is an all-or-none phenomenon and not nearly as subject to interpretive error.

New bone formation outside of the graft occurs only in spinal motion segments that are adequately stabilized; therefore, it represents a reliable sign of fusion. On the contrary, with InGBB, compressive forces can result in the false appearance of bone bridging, and a well-opposed graft, even that has not undergone resorption, may seem to be bridged to the host bone. In lumbar interbody fusion, Burkus *et al*[12] described 5 zones of new bone formation outside of the intradiscal device and suggested that osteoinduction was more likely to begin within the ligaments at margin of disc space before progressing to the scar-filled intervertebral space. To our knowledge, no studies have validated this concept for either cervical or lumbar interbody fusions. Two studies have correlated the results of surgical exploration with anterior cervical pseudarthroses. Buchowski *et al*[10] reported a mean κ value of 0.81 between CT scans and surgical confirmation in 14 patients. We obtained a κ value of 0.907 for the ExGBB and 0.663 for the InGBB. On the basis of these results, it is possible that the

TABLE 4. Results of Performance Characteristics for Each Rater (%)

	Rater A		Rater B		Rater C		Raters (A + B + C)	
	ExGBB	InGBB	ExGBB	InGBB	ExGBB	InGBB	ExGBB	InGBB
Sensitivity	**99.1**	91.8	**98.3**	90.2	**98.7**	89.8	**98.7**	90.6
Specificity	**95.4**	67.9	**93.5**	64.1	**87.4**	75.9	**92.1**	69.3
PPV	**95.3**	72.9	**93.4**	70.2	**88.0**	77.8	**92.1**	73.5
NPV	**99.2**	89.8	**98.3**	87.5	**98.7**	88.8	**98.7**	88.7

ExGBB indicates extragraft bone bridging; InGBB, intragraft bone bridging; PPV, positive predictive value; NPV, negative predictive value.



		Sensitivity	Specificity	PPV	NPV
Autograft group (Fused: 20 seg. Psuedo : 12 seg.)	ExGBB	99.1	100	100	98.6
	InGBB	97.5	98.6	99.1	95.9
Allograft group (Fused: 88 seg. Psuedo : 73 seg.)	ExGBB	98.4	94.2	95.4	98
	InGBB	91	74.6	81.2	87.4
Cages group (Fused: 13 seg. Psuedo : 46 seg.)	ExGBB	100	86.5	70.8	100
	InGBB	78.8	53.2	35.5	88.5
Cages group w/o metal cages (Fused: 10 seg. Psuedo : 37 seg.)	ExGBB	100	86.9	67.4	100
	InGBB	95	50.9	34.3	97.4

Figure 3. Performance characteristics of ExGBB and InGBB according to graft materials used. PPV indicates positive predictive value; NPV, negative predictive value; ExGBB, extragraft bone bridging; InGBB, intragraft bone bridging.

raters in the aforementioned study[10] assessed bone bridging in the extragraft to determine fusion on CT scans. Ghiselli *et al*[9] found that CT scans had a sensitivity of 69.2%, specificity of 100%, PPV of 100%, and NPV of 73% for diagnosing pseudoarthrosis in 24 cervical levels. However, both studies were limited by small sample sizes, which may have affected to get the exact validity values.

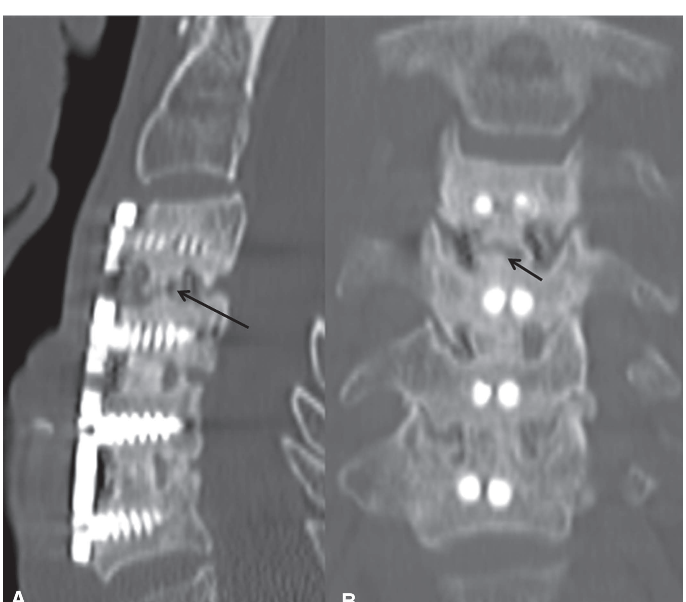


Figure 4. The patient underwent 3 levels of anterior cervical fusion surgery with synthetic cages 28 months ago. The C34 level shows a cleft (arrow) in the cage and well-incorporated intragraft bone bridging at C45 and C56 levels on sagittal (**A**) and coronal (**B**) views. Note that there were no ExGBB at all 3 levels. Surgical exploration posteriorly revealed pseudarthroses at all 3 levels.

We found that the validity values for ExGBB and InGBB varied according to the graft material used. The autocortical graft group had the highest validity values, with no significant differences between ExGBB and InGBB. The allograft group had the next highest validity values, and these values were higher for ExGBB than for InGBB. Therefore, InGBB was most accurate for autograft, followed by allograft. When cages were used, InGBB had the lowest validity of 3 groups. In particular, the PPV of InGBB was an essentially useless 35.5% and the specificity was only 53.2%, demonstrating high false-positive rate for diagnosing fusion, whereas both the sensitivity and the NPV of ExGBB were 100%. In case that metal cages were excluded from the analysis because of inherent difficult interpretation of InGBB, the specificity and PPV of InGBB were still too low and ExGBB also had 100% sensitivity and NPV (Figure 3). These results suggest that ExGBB is a necessary finding, and InGBB could provide little value for determining anterior cervical fusion in metal cages and all cages group, outlining another important utility of the ExGBB (Figure 4). Although most cages contain a central void to facilitate bone bridging with the endplate of the host, allograft seems to have greater potential for biological fusion than do synthetic cages, because the cortical structural bone in allograft can supply the fusion bed. Synthetic devices that are composed of various kinds of metal or polyetheretherketone can act as structural spacers, but these devices have very limited or no capacity for direct bony union with the host vertebral endplates. However, immune-based inflammatory responses to allograft can also interrupt the bone-healing process and eventually lead to fusion failure or graft failure,[13] which may be a reason that the validity of InGBB differed between the autocortical graft and allograft groups.

Our study is not without limitations. First, this was a retrospective radiological study, so we did not have data showing serial changes in InGBB and ExGBB over time. Such results would require a prospective study using serial CT scans. However, there are inherent limitations to this approach given the radiation risks and the cost to patients.[14] Second, the 3 different intradiscal material groups that we evaluated differed significantly in the duration from the index operation to the time of pseudarthrosis diagnosis, although not for the fused segments. However, all of our patients were greater than 1 year postoperative at the time of evaluation, and the mean duration from index operation of cage group showed that the shortest period was 28.33 months. Because radiological fusion generally occurs by 1 year after cervical interbody fusion surgery,[9,10] it seems unlikely that selection bias affected our validity tests of different graft materials. Finally, we did not have exact data of the kinds of materials augmenting the void of the synthetic cages, so our results cannot demonstrate the differences of augmented graft materials in especially polyetheretherketone cages.

This retrospective study on the correlation of ExGBB and InGBB with surgical exploration has important implications for determination of anterior cervical fusion. First, our results indicate that peripheral bone formation in the extragraft could provide significant information on fusion status. In particular, ExGBB at the peripheral disc space seems to be a very reliable and accurate CT finding. In addition, our study suggests the diagnostic criteria for fusion using CT-based bone bridging should be different according to intradiscal materials. In recent years, the use of allograft and cages for anterior cervical fusion has increased, and our results indicate that the CT-based fusion criteria for these materials should focus on extragraft bone bridging, especially in cages, for which ExGBB could be considered a necessary finding. Our results also call into question previously published values for the anterior radiographical fusion rate, because previous studies[1–3,15–18] have reported using the same criterion, bone bridging similar to our InGBB, although various types of cervical intervertebral devices were used.

➢ Key Points

- ❑ We developed 2 CT-based fusion criteria, extragraft bone bridging (ExGBB) and intragraft bone bridging (InGBB) and evaluated the accuracy as diagnostic criteria for anterior cervical fusion using subsequent intraoperative confirmation.
- ❑ Bone formation in the ExGBB could provide significant information on fusion status and seems to be a very reliable and accurate CT finding.
- ❑ The patterns of bone bridging as diagnostic criteria for fusion could be different according to autocortical graft, allograft, and synthetic cages.
- ❑ The Allograft or cage group should focus on ExGBB, especially in cages, for which ExGBB should be considered a necessary finding, whereas InGBB is unreliable to determine anterior cervical fusion status.

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