developed principally for the detection of colon polyps, and few studies have focused on the detection of ECCs, including flat lesions. In recent years, detection of colon cancers in their early stages, especially lesions of the flat type, was considered to be important in Japan and Western countries. Therefore, evaluation of a CAD protocol in terms of the clinical utility for the detecting early lesions, particularly those of invasive cancer, would be valuable.

The results of this study include 100% sensitivity of CAD for protruding lesions and low sensitivity (69.2%) for flat lesions. Previous investigations reported poor performance of both CTC[22–25] and CAD[26–28] in detecting flat lesions, and our study confirmed these results. The conventional CAD programs were developed mainly for detecting protruding polyps. The four lesions that were not detected by CAD in this study were all flat, suggesting the need for improved CAD diagnostic performance for flat lesions. With conventional CAD, lesions are recognized on the basis of the sphericity of the object protruding from the colonic lumen. In this study, we used the sphericity setting that is effective in diagnosing colon polyps with well-balanced sensitivity and low false-positive rates.[29] The diagnostic performance for flat lesions may be improved by modification of the presently used sphericity setting.

In this study, only one reader demonstrated increased sensitivity when using CAD, whereas the other two showed decreased sensitivity. However, the difference in sensitivity was not significant. Previous studies reported the effectiveness of CAD in detecting polyps, but our study did not prove its effectiveness in detecting ECCs. Moreover, in the ROC analysis, all three readers demonstrated inferior diagnostic performance with CAD, and there was a statistically significant difference. Although the sensitivity of CAD for the detection of ECCs (86.7%) was relatively high, an average of 4.0 ECCs were considered "nonactionable,"[30] which indicated that the lesion was identified correctly by CAD but was not recognized correctly as a lesion by the reader. Therefore, we believe that the clinical utility of CAD can be increased by familiarizing the readers with the use of CAD.

CAD had an average false-positive number of 17.1, which might contribute to the inferior diagnostic performance. Fenton et al.[31] reported that CAD increased the number of false-positive diagnoses on mammograms, leading to increased recall and biopsy rates. Therefore, reducing CAD false-positive rates would be required for improving the diagnostic performance.

All three readers showed fair agreement in their CRs for the detection of ECCs with and without CAD, indicating a possible influence of the readers' experience with CTC image reading. Mang et al.,[20] in a study on image reading by two expert radiologists and two nonexperts, reported that the sensitivity for detecting colon polyps was increased with CAD, with the increase being significant for the two nonexperts. In our study, reader A showed beneficial effects from using CAD for seven segments with a lesion, suggesting the usefulness of CAD for nonexperts. However, reader A also showed detrimental effects of CAD for 7 segments with a lesion and for 20 segments without lesions. These results suggest that nonexperts could receive some benefit from CAD, but their insufficient experience in the reading of CTC might affect their diagnostic performance.[32–34] As Halligan et al.[21] mentioned, the improvement in diagnostic accuracy by using CAD is insufficient to recommend that CAD can substitute for adequate training for readers who are relatively inexperienced.

Our study has potential limitations. Only a small number of patients were included. Although the number of samples for the ROC study was not so small (30 positive and 150 negative samples), each of the six colonic segments, which were divided from one case, was considered to be clustered in terms of statistical issues. For example, the reader's attention for the detection of a lesion might be diverted when he or she found lesions in the same patient. Because ROC analysis assumed that each sample was independent from others, it was considered to be a bias to use clustered data in the ROC study.

There was a 1-week interval between the two readings without and with CAD. Generally, the interval of 1 week for two readings is relatively small if the first reading can provide additional information to readers at the second reading. However, in the observer performance study for evaluating CAD, it was demonstrated that two independent and sequential readings without and with CAD were thought to be comparable in terms of the radiologists' performance obtained by the ROC study.[35] Because the first reading without CAD did not provide any additional information for the second reading, we believe that the short length of the intervals between the two readings caused no bias in this study.

We used conventional ROC analysis in this observer study, rather than free-response ROC analyses,[36] because we wanted to the minimize the radiologists' tasks in the observer study. In addition, ROC analysis can provide reliable estimates of the statistical significance of differences between two conditions (i.e., without and with the CAD output) when multiple readers were employed in a study.[13] However, it should be noted that this observer study involved several limitations that were well understood to be limitations of conventional ROC analysis.[37] The scoring of true-positive responses on each image by

radiologists did not take into account the location of nodules when the ROC curves were estimated, so some false-positive responses in actual ECC cases could be counted as true-positive responses. Furthermore, radiologists were allowed to indicate only one CR on each segment, so additional false-positive responses and/or true-positive responses might have been obtained if radiologists were allowed to indicate two or more lesions in one segment. Although almost all observer performance studies that employ ROC analysis have been done under these limitations, their results are generally considered useful.

Conclusion

The present CAD programs do not contribute to improved diagnostic accuracy for the detection of ECCs on CTC. The present CAD analysis algorithm demonstrated an inferior performance in detecting flat-type lesions compared to that for protruding lesions. Further investigation is required to clarify the specific features of flat lesions that would improve the performance of the CAD algorithm. Moreover, the reader's experience in diagnostic CTC reading would be considered in the evaluation of the clinical utility of CAD for detecting ECCs.

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References

1. Halligan S, Altman DG, Taylor SA, Mallett S, Deeks JJ, Bartram CI, et al. CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed minimum data set for study level reporting. Radiology 2005;237:893–904.
2. Sosna J, Morrin MM, Kruskal JB, Lavin PT, Rosen MP, Raptopoulos V. CT colonography of colorectal polyps: a metaanalysis. AJR Am J Roentgenol 2003;181:1593–8.
3. Bielen D, Kiss G. Computer-aided detection for CT colonography: update 2007. Abdom Imaging 2007;32:571–81.
4. Bogoni L, Cathier P, Dundar M, Jerebko A, Lakare S, Liang J, et al. Computer-aided detection (CAD) for CT colonography: a tool to address a growing need. Br J Radiol 2005;78(Spec. No. 1):S57–62.
5. Summers RM, Jerebko AK, Franaszek M, Malley JD, Johnson CD. Colonic polyps: complementary role of computer-aided detection in CT colonography. Radiology 2002;225:391–9.
6. Soetikno R, Friedland S, Kaltenbach T, Chayama K, Tanaka S. Nonpolypoid (flat and depressed) colorectal neoplasms. Gastroenterology 2006;130:566–76.
7. Saitoh Y, Waxman I, West AB, Popnikolov NK, Gatalica Z, Watari J, et al. Prevalence and distinctive biologic features of flat colorectal adenomas in a North American population. Gastroenterology 2001;120:1657–65.
8. Rembacken BJ, Fujii T, Cairns A, Dixon MF, Yoshida S, Chalmers DM, et al. Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. Lancet 2000;355:1211–4.
9. Park SH, Lee SS, Choi EK, Kim SY, Yang S-K, Kim JH, et al. Flat colorectal neoplasms: definition, importance, and visualization on CT colonography. AJR Am J Roentgenol 2007;188:953–9.
10. Japanese Society for Cancer of the Colon and Rectum. General rules for clinical and pathological studies on cancer of the colon, rectum, and anus. 7th edition. Tokyo: Kanehara; 2006 (in Japanese).
11. Metz CE, Herman BA, Shen JH. Maximum likelihood estimation of receiver operating (ROC) curves from continuously distributed data. Stat Med 1998;17:1033–53.
12. Fleiss, JL. Statistical methods for rates and proportions. 2nd edition. New York: Wiley; 1981. p. 38–46.
13. Dorfman DD, Berbaum KS, Metz CE. ROC rating analysis: generalization to the population of readers and cases with the jackknife method. Invest Radiol 1992;27:723–31.
14. Fenlon HM, Nunes DP, Schroy PC III, Barish MA, Clarke PD, Ferrucci JT. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. N Engl J Med 1999;341:1496–503.
15. Yee J, Akerkar GA, Hung RK, Steinauer-Gebauer AM, Wall SD, McQuaid KR. Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. Radiology 2001;219:685–92.
16. Pineau BC, Paskett ED, Chen GJ, Espeland MA, Phillips K, Han JP, et al. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. Gastroenterology 2003;125:304–10.
17. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 2003;349:2191–200.
18. Nicholson FB, Barro JL, Bartram CI, Dehmeshki J, Halligan S, Taylor S, et al. The role of CT colonography in colorectal cancer screening. Am J Gastroenterol 2005;100:2315–23.
19. Bond JH. Progress in refining virtual colonoscopy for colorectal cancer screening. Gastroenterology 2005;129:2103–6.
20. Mang T, Peloschek P, Plank C, Maier A, Graser A, Weber M, et al. Effect of computer-aided detection as a second reader in multidetector-row CT colonography. Eur Radiol 2007;17:2598–607.
21. Halligan S, Altman DG, Mallett S, Taylor SA, Burling D, Roddie M, et al. Computed tomographic colonography: assessment of radiologist performance with and without computer-aided detection. Gastroenterology 2006;131:1690–9.
22. Fidler JL, Johnson CD, MacCarty RL, Welch TJ, Hara AK, Harmsen WS. Detection of flat lesions in the colon with CT colonography. Abdom Imaging 2002;27:292–300.
23. Jensch S, van Gelder RE, Florie J, Thomassen-de Graaf MA, Lobé JV, Bossuyt PM, et al. Performance of radiographers in the evaluation of CT colonographic images. AJR Am J Roentgenol 2007;188:W249–55.
24. European Society of Gastrointestinal and Abdominal Radiology CT Colonography Group Investigators. Effect of directed

training on reader performance for CT colonography: multicenter study. Radiology 2007;242:152–61.
25. Park SH, Ha HK, Kim MJ, Kim KW, Kim AY, Yang DH, et al. False-negative results at multi-detector row CT colonography: multivariate analysis of causes for missed lesions. Radiology 2005;235:495–502.
26. Kim SH, Lee JM, Lee JG, Kim JH, Lefere PA, Han JK, et al. Computer-aided detection of colonic polyps at CT colonography using a Hessian matrix-based algorithm: preliminary study. AJR Am J Roentgenol 2007;189:41–51.
27. Summers RM, Yao J, Pickhardt PJ, Franaszek M, Bitter I, Brickman D, et al. Computed tomographic virtual colonoscopy computer-aided polyp detection in a screening population. Gastroenterology 2005;129:1832–44.
28. Graser A, Kolligs FT, Mang T, Schaefer C, Geisbüsch S, Reiser MF, et al. Computer-aided detection in CT colonography: initial clinical experience using a prototype system. Eur Radiol 2007;10:2608–15.
29. Dehmeshki J, Halligan S, Taylor SA, Roddie ME, McQuillan J, Honeyfield L, et al. Computer assisted detection software for CT colonography: effect of sphericity filter on performance characteristics for patients with and without fecal tagging. Eur Radiol 2007;17:662–8.
30. Shiraishi J, Abe H, Engelmann R, Doi K. Effect of a high sensitivity in a computerized scheme for detecting extremely subtle solitary pulmonary nodules in chest radiographs: observer performance study. Acad Radiol 2003;10:1302–11.
31. Fenton JJ, Taplin SH, Carney PA, Abraham L, Sickles EA, D'Orsi C, et al. Influence of computer-aided detection on performance of screening mammography. N Engl J Med 2007; 356:1399–409.
32. Taylor SA, Halligan S, Burling D, Morley S, Bassett P, Atkin W, et al. CT colonography: effect of experience and training on reader performance. Eur Radiol 2004;14:1025–33.
33. Newcombe RG. Improved confidence intervals for the difference between binomial proportions based on paired data. Stat Med 1998;17:2635–50.
34. Soto JA, Barish MA, Yee J. Reader training in CT colonography: how much is enough? Radiology 2005;237:26–7.
35. Kobayashi T, Xu XW, MacMahon H, Metz CE, Doi K. Effect of a computer-aided diagnosis scheme on radiologists' performance in detection of lung nodules on radiographs. Radiology 1996;199:843–8.
36. Chakraborty DP, Winter LH. Free-response methodology: alternate analysis and a new observer-performance experiment. Radiology 1990;174:873–81.
37. Metz CE. Some practical issues of experimental design and data analysis in radiological ROC studies. Invest Radiol 1989;24:234–45.

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CLINICAL INVESTIGATION

Transcatheter Arterial Chemoembolization (TACE) with Lipiodol to Treat Hepatocellular Carcinoma: Survey Results from the TACE Study Group of Japan

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Abstract The purpose of this study was to retrospectively clarify the current status in Japan of TACE using Lipiodol together with anticancer agents to treat hepatocellular carcinoma (HCC). We retrospectively surveyed 4,659 (average annual total) procedures for HCC over the years 2002–2004 at 17 institutions included in the TACE Study Group of Japan. The survey included six questions that were related mainly to TACE and Lipiodol for HCC treatment. The most frequently applied among the 4,659 procedures at the 17 institutions were TACE (2,310; 50%) and local ablation (1,395; 30%). Five of the institutions applied 201–300 procedures and 4 applied 101–200. Lipiodol was used in "all procedures" and in "90% or more" at seven and nine institutions, respectively. Almost all institutions applied 4–6 (mean, 5) ml of Lipiodol during TACE to treat tumors 5 cm in diameter. In conclusion, this survey clarified that TACE using Lipiodol and anticancer agents is a popular option for HCC treatment in Japan.

Keywords Hepatocellular carcinoma · Transcatheter arterial chemoembolization · Lipiodol · Survey results · Japan

Introduction

The rate of hepatocellular carcinoma (HCC) is increasing and transcatheter arterial chemoembolization (TACE) seems to be becoming more important as a treatment strategy [1, 2]. Although much information about TACE

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for treating HCC has been published [1–36], we consider that to understand the current status of TACE for HCC would be valuable in Japan, where TACE has been applied for more than 20 years [3–22]. We also consider that the concomitant use of iodinated oil (Lipiodol; Lipiodol Ultra-Fluide; Guerbet Co.) for more than 20 years [3–23] should be reviewed [24–26, 32–36]. Although the efficacy of Lipiodol for hepatic TACE has been generally recognized for more than two decades, and segmental or subsegmental TACE using Lipiodol is considered a more effective and less invasive tool for treating localized HCC [9–17], Lipiodol (distributed by Terumo Co. in Japan) has not yet been approved for this application in Japan and other countries. We thus believe that urgent effort is required to obtain official permission from the Pharmaceuticals and Medical Devices Agency (PMDA) of the Japanese Ministry of Health, Labour and Welfare to apply Lipiodol in this manner, based on incontrovertible evidence of expansive usage and value. Therefore, we organized the TACE Study Group in Japan to retrospectively study the issue using a questionnaire at 17 institutions where TACE is frequently applied. We intended to gain fundamental data about TACE and other treatment options for patients with HCC that would reflect the actual use of Lipiodol in clinical practice and its benefits. Our findings should facilitate understanding of the current status of HCC therapy in Japan and establish a foothold for regulatory approval of Lipiodol not only in Japan, but also in other countries.

Materials and Methods

The TACE Study Group distributed questionnaires to 20 institutions throughout Japan and 17 (85%) of them responded regarding 4,774 procedures for HCC including 2,264 TACE (average total per year) during the years 2002–2004. We analyzed the replies to six questions (Q1–Q6) regarding TACE and Lipiodol for the treatment of HCC.

Q1 Annual approximate total of HCC procedures during the years 2002–2004 at the institution.

When 100 procedures were displayed as one average annual frequency unit for convenience in data comparisons, the replies were classified as number of procedures per year per institution as follows: 1, ≤100; 2, 101–200; 3, 201–300; 4, 301–400; 5, 401–500 and 6, ≥501.

Q2 Annual number of individual therapies selected for HCC treatment.

a, Surgery; b, local ablation comprising PEIT (percutaneous ethanol injection therapy), PMCT (percutaneous microwave coagulation therapy), RFA (radiofrequency ablation); c, TACE; d, TACI (transcatheter arterial chemoinfusion therapy); e, CAIC (continuous arterial infusion chemotherapy); f, Cx (systemic chemotherapy); g, RT (radiotherapy).

Q3 Rate of use of Lipiodol in TACE.

Q4 When Lipiodol was not used, reasons why, and methods of TACE.

Q5 Rate of use of Lipiodol in TACI.

Q6 Volume of Lipiodol applied during TACE to treat tumors 5 cm in diameter (clinical stage I).

a, 3–4 ml; b, 4–5 ml; c, 5–6 ml; d, 6–7 ml; e, Other ( ) ml.

Results

Replies (R1–R6) to the questions (Q1–Q6) were as follows.

R1 Four institutions each applied 101–200 and 201–300 procedures per year; three applied ≤100, one applied 401–500 per year, two applied 301–400 per year, and one applied 501 or more per year.

R2 Table 1 reports the annual total of HCC treatments and annual numbers (rate) of the top four individual therapies at 17 institutions. Of the treatments applied at the 17 institutions, the most frequent was TACE (2,264 of 4,774; 47%), followed by local ablation (1,443; 30%), TACI (898; 19%), and resection (341; 9%). The mean annual total of procedures was 281 at 17 institutes. The mean rates of each procedure at these institutions were as follows: TACE, 47%; ablation, 30%; and TACI, 19%.

The total average frequency of TACI in addition to TACE, which treats cancer using a catheter inserted into the hepatic artery, accounted for approximately 66% of the total HCC treatments at 17 institutes.

R3 Regarding Lipiodol in TACE under the premise that Lipiodol is used to prepare a miscible liquid of anticancer drugs (usually Lipiodol emulsion is mixed with anticancer and nonionic contrast agents), seven and nine institutions replied that Lipiodol was used in "all procedures" and in "90% or more," respectively. One institution claimed to

Table 1 Annual total of HCC treatments and annual number (rate) of the top four individual therapies at 17 institutions

Institute	Total therapies/yr	Resections/yr	Ablations/yr	TACE/yr	TACI/yr
Total 17	4,774	391 (8%)	1,443 (30%)	2,264 (47%)	898 (19%)
Mean of 17	281	23 (8%)	85 (30%)	133 (47%)	53 (19%)

Note: TACI, transcatheter arterial chemoinfusion therapy

use "80% or more," but the exact rate was 89%. When the rate of Lipiodol use in TACE at all institutions was calculated simply from all reported TACE over 3 years at 17 institutions, the ratio reached 6,328 of a total of 6,740 TACE (94%) procedures.

R4 Except for the 7 institutions (41%) that used Lipiodol in all TACE procedures, 5 of the 10 institutions that did not use Lipiodol for some TACE procedures replied that Lipiodol might impair hepatic function and 3 replied that they were considering other options. One respondent indicated that TACE did not include Lipiodol at their institution because the therapeutic effect was sometimes limited. Six institutions replied that only gelatin sponge particles are used with anticancer drugs in TACE when Lipiodol is not used.

R5 The rates of Lipiodol use in TACI varied. Although six institutions (35%) used Lipiodol in more than 80% of TACI procedures and four institutions (24%) used it in 40–80%, three institutions (18%) used it in only 20–40 procedures and four institutions (24%) did not use Lipiodol in TACI at all.

R6 The volume of Lipiodol used in TACE to treat tumors 5 cm in diameter in the absence of obviously disrupted liver function (clinical stage I) was 5–6 ml (c) at eight institutions (47%), 6–7 ml (d) at five (29%), 4–5 ml (b) at three (18%), and 3–4 ml (a) at one. The average volume (dose) of Lipiodol applied during TACE for HCC 5 cm in diameter (clinical stage I) essentially reflected the tumor volume as indicated by the diameter (cm) at many of the institutions.

Figure 1 shows an example of a HCC measuring 38 × 45 mm with typical CT patterns that was treated by subsegmental TACE for S5 using 4 ml (6 ml of Lipiodol emulsion) of Lipiodol mixed with 30 mg of doxorubicin (dissolved in 2 ml of nonionic contrast medium and saline) followed by injection with gelatin sponge particles.

Discussion

The rate of HCC is increasing worldwide including in Japan [1, 2]. As HCC frequently presents as multiple lesions, invades surrounding tissues, and is usually accompanied by liver dysfunction, indications for resection or local ablation are restricted even now when earlier stages of HCC are being increasingly diagnosed owing to advances in imaging technology. In addition, multiple lesions frequently recur not only after surgery but also after ablation therapy such as radiofrequency ablation. Therefore, TACE is an important option for HCC treatment and the procedure involves the use of iodized oil (Lipiodol) all over the world.

The efficacy of TACE using Lipiodol for HCC has remained controversial despite evaluations, long-term discussions, and various randomized trials. Whereas some randomized control study findings have questioned the utility of TACE [25–27], more recent reports, also including some randomized studies [24, 30–32], have recognized the value of TACE using Lipiodol [5–23, 33–36]. The most important factors in choosing TACE are to obtain favorable therapeutic effects and to reduce adverse side effects. Thus, the dose of Lipiodol mixed with anticancer drugs should be individually adapted to the tumor size, number of tumors, and hepatic function of each patient. However, the dose of Lipiodol in most randomized control studies was uniform and not adapted to individual needs [25, 26, 31, 33, 36]. We believe that these studies missed the effect of TACE because the doses of Lipiodol and anticancer agents were not optimized, and furthermore, TACE was not repeated before recurrence was diagnosed by imaging, including CT, after the first TACE. However, TACE using Lipiodol is gradually becoming recognized worldwide and randomized control studies seem unnecessary since TACE already seems proven to confer a significant benefit on HCC [2, 24, 30–32].

The present retrospective study clarifies the current status of TACE including the use of Lipiodol for the treatment of HCC at representative institutions that participated in the TACE Study Group in Japan. The results obtained from 17 nationwide institutions showed that although the approximate annual total of HCC procedures over the past 3 years differs at each facility, several hundred HCC procedures per year are performed at the midsize to large leading institutions and >200 treatments are performed annually at more than half of all surveyed institutions. Thus, TACE accounts for 50–60% of all HCC procedures at institutions involved in the TACE Study Group of Japan. Focal radiofrequency ablation therapy is becoming widely prevalent in Japan for localized small HCC lesions. However, TACE has also become a popular strategy for such tumors owing to the use of microcatheters and Lipiodol mixed with anticancer agents, as well as gelatin sponge particles, which are popular for segmental or subsegmental Lipiodol TACE. The excellent effects of segmental or subsegmental Lipiodol TACE in terms of the absence of damage to surrounding normal hepatic tissue have already been proven by histopathological and clinical findings [9–14, 21]. Chemoembolization using Lipiodol combined with percutaneous radiofrequency thermal ablation therapy is becoming another treatment option for HCC, as a larger sphere of ablation can be induced [20]. Repeated TACE with Lipiodol for the recurrence with various collateral pathways is also very useful and important to positively impact the survival of patients with HCC [22]. Therefore, the results of this survey and of most published studies indicate that TACE is an indispensable therapeutic tool that is frequently applied worldwide to treat various types of HCC [2, 4–24, 28–36].

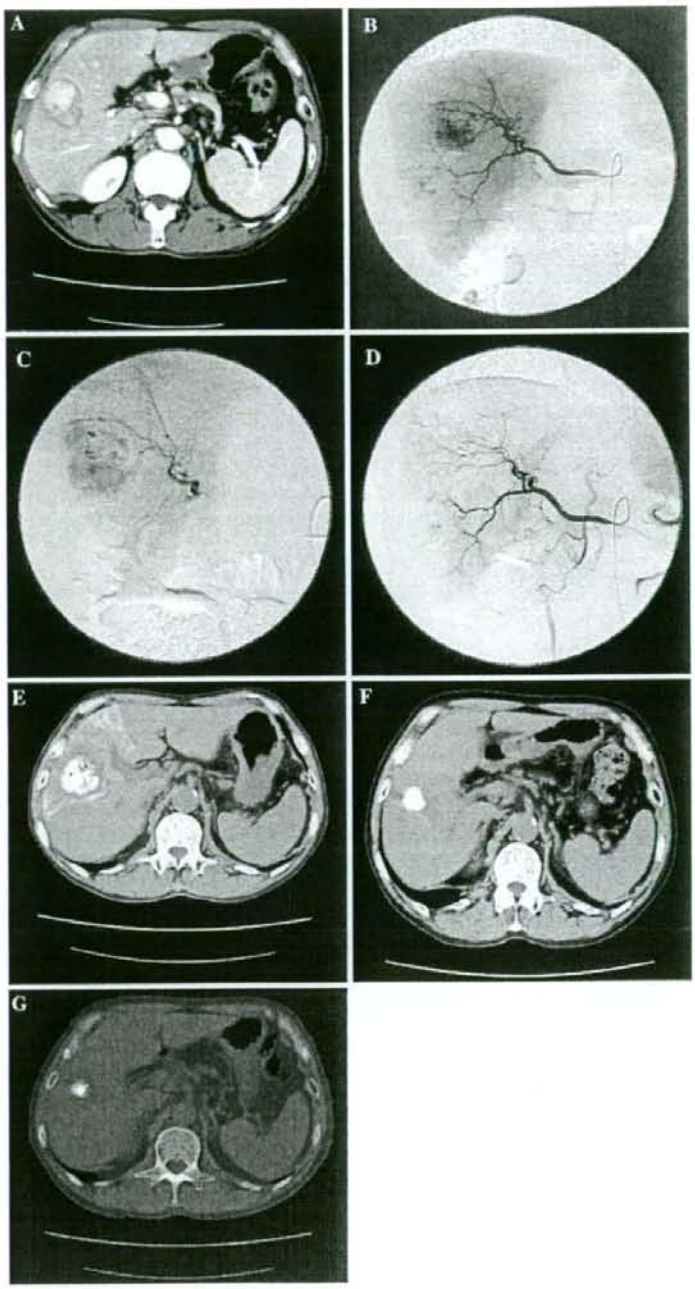

Fig. 1 Hepatocellular carcinoma 38 × 45 mm in diameter showing typical CT profiles and treated with subsegmental TACE using Lipiodol. Subsegmental TACE was performed using 4 ml of Lipiodol (6 ml of Lipiodol emulsion) mixed with 30 mg of doxorubicin in 2 ml of nonionic contrast medium and saline, followed by injection of gelatin sponge particles. (**A**) CT shows hypervascular HCC in S5. (**B**) Hepatic angiogram also demonstrates hypervascular HCC in S5. (**C**) Superselective hepatic angiogram via the anterior-inferior branch (A5) shows hypervascular tumor in S5. (**D**) Hepatic angiogram after subsegmental TACE for S5 shows disappearance of tumor vessels and visualization of surrounding hepatic arteries. (**E**) CT 1 week after subsegmental TACE: Lipiodol is visualized in the embolized S5 area, as well as in the tumor. (**F**) CT 1 year after subsegmental TACE shows homogeneous tumor accumulation of Lipiodol. (**G**) Two years after subsegmental TACE, CT shows dense accumulation of Lipiodol and tumor shrinkage. This tumor did not recur

The efficacy of Lipiodol in TACE for HCC has been recognized by several investigators worldwide [4–24, 28–36], whereas only a few articles indicate contrary findings [25–27]. Although the rate of TACE for HCC differs slightly among institutions, this survey shows that >90% of HCCs treated by TACE included Lipiodol. However, although Lipiodol is generally used as a useful carrier of anticancer agents in Japan and elsewhere, it is not legally permitted for hepatic TACE in Japan. Legal permission to use Lipiodol must be based on clear evidence of expansive usage and value. Therefore, we retrospectively surveyed 17 leading Japanese institutions to generate some fundamental data about the use of hepatic TACE with Lipiodol for treating HCC. Seven institutes used Lipiodol in all TACE procedures, nine used Lipiodol in >90% of them, and one used it in >80%, indicating that Lipiodol/TACE is widely perceived as beneficial.

Under the premise that Lipiodol is used in miscible solutions of anticancer drugs, seven and nine institutions replied that Lipiodol was used in "all" and in "90% or more" of procedures, respectively. One institution replied that Lipiodol was used in "80% or more" of procedures, but the actual frequency was almost 90%.

Although Lipiodol is used in about 40% of all TACE procedures, it is not used at about 60% of institutions in <10% of TACE procedures. This is due to potential impairment of hepatic function among patients with poor liver function or a huge HCC that would require a large volume of Lipiodol. Therefore, TACE is occasionally performed with a reduced amount of Lipiodol mixed with anticancer agents, or a first TACE might use only gelatin sponge particles without Lipiodol and anticancer agents for HCC >10 cm in diameter. A second TACE might include a small volume of Lipiodol mixed with anticancer agent after the tumor has been reduced. When only gelatin sponge particles are used in TACE, some institutions nevertheless essentially agreed that TACE can include Lipiodol mixed with an anticancer agent.

This variable use of Lipiodol in TACI indicates that HCC treatment policies differ among institutions. The total frequency of transcatheter arterial therapy (total of TACE and TACI continuous arterial infusion therapy), which treats cancer using a catheter inserted into the hepatic artery, accounted for 60% of the total HCC procedures. The most frequently applied was TACE, followed by local ablation and TACI. These methods accounted for approximately 90% of all HCC therapies. The average volume of Lipiodol used for TACE for HCCs 5 cm in diameter was almost 5 ml, which reflected the tumor volume and was verified in this survey. Our basic criteria regarding the dose of Lipiodol used for TACE state that that average dose (ml) is roughly equal to the tumor diameter (cm). This is reflected in the tumor volume shown in Fig. 1. We already proposed criteria to select the dose of injected Lipiodol for each patient based on tumor size [9–12, 14, 16]. These criteria have generally been agreed on and are applied in Japan. Therefore, we believe that the survey responses regarding the Lipiodol dose were quite uniform.

A recent article describing the mechanism of action of chemoembolization using Lipiodol in Japan helps to elucidate and support the present study [37].

A prospective cohort study of transarterial chemoembolization for unresectable hepatocellular carcinoma in 8,510 patients has been reported [38]. However, the focus of the contents of registration and the questionnaire of that report is completely different from that in the present study.

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References

1. El-Serag HB (2002) Hepatocellular carcinoma: an epidemiologic view. J Clin Gastroenterol 35(Suppl):72–78
2. Brown BD, Geschwind JF, Soulen MC, et al. (2006) Society of interventional radiology position statement on chemoembolization of hepatic malignancies. J Vasc Interv Radiol 17:217–223
3. Kanematsu T, Inokuchi K, Sugimachi K, et al. (1984) Selective effects of lipiodolized antitumor agents. J Surg Oncol 25:218–226
4. Ohishi H, Uchida H, Yoshimura H, et al. (1985) Hepatocellular carcinoma detected by iodized oil. Radiology 154:25–29
5. Sasaki Y, Imaoka S, Kasugai H, et al. (1987) A new approach to chemoembolization therapy for hepatoma using ethiodized oil, cisplatin, and gelatin sponge. Cancer 60:1194–1203
6. Ohishi H, Yoshimura H, Uchida H, et al. (1989) Transcatheter arterial embolization using iodized oil (Lipiodol) mixed with an anticancer drug for the treatment of hepatocellular carcinoma. Cancer Chemother Pharmacol 23(Suppl):S33–S36
7. Nakamura H, Hashimoto T, Oi H, et al. (1989) Transcatheter oily chemoembolization of hepatocellular carcinoma. Radiology 170:783–786
8. Konno T (1990) Targeting cancer chemotherapeutic agents by use of lipiodol contrast medium. Cancer 66:1897–1903
9. Uchida H, Ohishi H, Matsuo N, et al. (1990) Transcatheter hepatic segmental arterial embolization using lipiodol mixed with an anticancer drug and gelfoam particle for hepatocellular carcinoma. CardioVasc Interv Radiol 13:140–145
10. Uchida H, Matsuo N, Sakaguchi H, et al. (1993) Segmental embolotherapy for hepatic cancer: key to success. CardioVasc Interv Radiol 16:67–71
11. Uchida H, Matsuo N, Nishimine K, et al. (1993) Transcatheter arterial embolization for hepatoma with Lipiodol. Hepatic arterial and segmental use. Semin Interv Radiol 10:19–26
12. Matsuo N, Uchida H, Nishimine K, et al. (1993) Segmental transcatheter hepatic artery chemoembolization with iodized oil for hepatocellular carcinoma: antitumor effect and influence on normal tissue. J Vasc Interv Radiol 4:543–549

13. Matsui O, Kadoya Y, Yoshikawa J, et al. (1993) Small hepatocellular carcinoma: treatment with subsegmental transcatheter arterial embolization. Radiology 188:79–83
14. Nishimine K, Uchida H, Matsuo N, et al. (1994) Segmental transarterial chemoembolization with Lipiodol mixed with anticancer drugs for nonresectable hepatocellular carcinoma: follow-up CT and therapeutic results. Cancer Chemother Pharmacol 33(Suppl):S60–S68
15. Nakao N, Uchida H, Kamino K, et al. (1994) Determination of the optimum dose level of Lipiodol in transcatheter arterial embolization of primary hepatocellular carcinoma based on retrospective multivariate analysis. CardioVasc Interv Radiol 17:76–80
16. Sakaguchi H, Uchida H, Maeda, et al. (1995) Combined transjugular intrahepatic portosystemic shunt and segmental Lipiodol hepatic artery embolization for the treatment of esophagogastric varices and hepatocellular carcinoma in patients with cirrhosis: preliminary report. CardioVasc Interv Radiol 18:9–15
17. Matsuo N, Uchida H, Sakaguchi H, et al. (1997) Optimal lipiodol volume intracatheter arterial chemoembolotherapy for hepatocellular carcinoma: study based on Lipiodol accumulation pattern and histopathological findings. Semin Oncol 24(Suppl 6):61–70
18. Ueno K, Miyazono N, Inoue H, et al. (2000) transcatheter arterial chemoembolization therapy using iodized oil for patients with unresectable hepatocellular carcinoma: evaluation of three kinds of regimens and analysis of prognostic factors. Cancer 88:574–1581
19. Takayasu K, Muramatsu Y, Maeda T, et al. (2001) Targeted transarterial oily chemoembolization for small foci of hepatocellular carcinoma using a unified helical CT and angiography system: analysis of factors affecting local recurrence and survival rates. AJR 176:681–688
20. Higashihara H, Okazaki M (2002) Transcatheter arterial chemoembolization of hepatocellular carcinoma: a Japanese experience. Hepatogastroenterology 49:72–78
21. Yamakado K, Nakatsuka A, Ohmori S, et al. (2002) Radiofrequency ablation combined with chemoembolization in hepatocellular carcinoma: treatment response based on tumor size and morphology. J Vasc Interv Radiol 13:1225–1232
22. Iwamoto S, Sanafuji H, Okuda K (2003) Angiographic subsegmentectomy for the treatment of patients with small hepatocellular carcinoma. Cancer 97:1051–1056
23. Miyayama S, Matsui O, Taki K, et al. (2004) Transcatheter arterial chemoembolization for hepatocellular carcinoma fed by the reconstructed inferior phrenic artery: anatomical and technical analysis. J Vasc Interv Radiol 15:815–823
24. Bronowicki JP, Vetter D, Dumas F, et al. (1994) Transcatheter oily chemoembolization for hepatocellular carcinoma: a 4-year study of 127 French patients. Cancer 74:16–24
25. Groupe d'Etude et de Traitment du Carcinome Hepatocellulaire (1995) A comparison of lipiodol chemoembolization and conservative treatment for unresectable hepatocellular carcinoma. N Engl J Med 332:1256–1261
26. Pelletier G, Ducreux M, Gay F, et al. (1998) Treatment of unresectable hepatocellular carcinoma with lipiodol chemoembolization: a multicenter randomized trial. J Hepatol 27:129–134
27. Bruix J, Llovet JM, Castells A, et al. (1998) Transarterial embolization versus symptomatic treatment in patients with advanced hepatocellular carcinoma: results of a randomized, controlled trial in a single institution. Hepatology 27:1578–1583
28. Solomon B, Soulen MC, Baum RA, et al. (1999) Chemoembolization of hepatocellular carcinoma with cisplatin, doxorubicin, mitomycin-C, Ethiodol, and polyvinyl alcohol: prospective evaluation of response and survival in a U.S. population. J. Vasc Interv Radiol 10:793–798
29. Treviasani F, De Notariis S, Rossi C, et al. (2001) Randomized control trials on chemoembolization for hepatocellular carcinoma: Is there room for new studies? J Clin Gastroenterol 32: 383–389
30. Lo CM, Ngan H, Tso WK, et al. (2002) Randomized controlled trial of transarterial Lipiodol chemoembolization for unresectable hepatocellular carcinoma. Hepatology 35:1164–1171
31. Llovet JM, Real MI, Montana X, et al. (2002) Arterial embolization or chemoembolization versus symptomatic treatment in patients with unresectable hepatocellular carcinoma. Lancet 359: 1734–1739
32. Barone M, Ettorre GC, Ladisa R, et al. (2002) Transcatheter arterial chemoembolization (TACE) in treatment of hepatocellular carcinoma. Hepatogastroenterology 50:183–187
33. Chen MS, Li JQ, Zhang YQ, et al. (2002) High-dose iodized oil transcatheter arterial chemoembolization for patients with large hepatocellular carcinoma. World J Gastroenterol 8:74–78
34. Saccheri S, Lovaria A, Sangiovanni A, et al. (2002) Segmental transcatheter arterial chemoembolization treatment in patients with cirrhosis and inoperable hepatocellular carcinoma. J Vasc Interv Radiol 13:995–999
35. Geshwind JF, Ramsely DE, Choti MA, et al. (2003) Chemoembolization of hepatocellular carcinoma: results of a meta-analysis. Am J Clin Oncol 26:344–349
36. Eurvilaichit C (2004) Outcome of transcatheter oily arterial chemoembolization in patients with hepatocellular carcinoma. Hepatogastroenterology 51:20–24
37. Bonneman B (2006) Lipiodol—mechanism of action for chemoembolization. Jpn IVR 21:64–68
38. Takayasu K, Arii S, Ikai I, et al. (2006) Prospective cohort study of transarterial chemoembolization for unresectable hepatocellular carcinoma in 8510 patients. Gastroenterology 131:461–469

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ORIGINAL ARTICLE

Percutaneous vertebroplasty performed by the isocenter puncture method

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Abstract
Purpose. The aim of this study was to clarify the usefulness of the isocenter puncture (ISOP) method.
Materials and methods. We investigated 73 vertebral bodies that had undergone percutaneous vertebroplasty (PVP) by the ISOP method, 118 vertebral bodies that had undergone the puncture simulation method, and 33 vertebral bodies that had undergone the conventional method. The items to be examined included the success rate (SR) of the median puncture of the vertebral body and the procedure time. The puncture accuracy and fluoroscopy time were also measured for the ISOP method.
Results. The SR was significantly higher and the procedure time significantly shorter when using the ISOP method rather than the conventional method. However, no significant differences were observed between the ISOP method and the puncture simulation method. The errors between the puncture needle tip and the puncture target point in the ISOP method were an average of 1.52, 2.08, and 1.87 mm in each of the horizontal, ventrodorsal, and craniocaudal directions. The fluoroscopy time when operating on one vertebral body was an average of 5.8 min.
Conclusion. The ISOP method is considered to be a useful approach while also reducing the puncture time and the fluoroscopy time.

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Key words ISOP method · Percutaneous vertebroplasty · Unilateral transpedicular approach · Isocenter marker · PVP

Introduction

Percutaneous vertebroplasty (PVP), a rapidly acting treatment for pain caused by a compressed fracture of the vertebral body, is increasingly being used worldwide. PVP is generally performed using a C-arm radiographic system and puncturing the vertebral arch pedicle percutaneously under X-ray fluoroscopy. The puncture approach includes both the unilateral and bilateral transpedicular approaches. The unilateral transpedicular approach is relatively difficult to perform as it requires advancing the tip of a puncture needle to the midline of the vertebral body. Therefore, some institutions use the bilateral transpedicular approach. However, the unilateral transpedicular approach may decrease the number of punctures required during such surgery.[1,2]

We have therefore developed an isocenter puncture (ISOP) method[3], which is a puncture support method for the unilateral transpedicular approach. The ISOP method allows pinpoint targeting and puncturing of a target within the vertebral body under X-ray fluoroscopy.

We herein describe the results of PVP using the ISOP method and compare the findings with those achieved with the puncture simulation method[2] using the puncture angle measured by the preoperative CT examination and those by the conventional puncture method, as a historical control, while also examining the usefulness of the ISOP method.

Materials and methods

This study was approved by the ethics committee at our institution.

ISOP method concept and procedures

The isocenter of the C-arm radiographic system is the center of the radiation field and the center of the C-arm rotation. Therefore, regardless of how the C-arm rotates, the isocenter always remains at the center of the radiation field and the center of the monitor screen. The ISOP method applies this principle, and therefore adjusting the puncture target to the position of the isocenter becomes essential with this method. For this purpose, we created a black dot-like isocenter marker (ICM; Toshiba Medical, Tokyo, Japan), which is constantly illuminated at the center of the fluoroscopic monitor screen (Fig. 1).[2] We set the anterior one-third median site of the vertebral body as a target point.

The procedures of the ISOP method start with positioning the puncture target point at the isocenter. The first step is a frontal view on the fluoroscopic monitor. The examining table is moved as necessary to align it with the median of the vertebral body with the ICM (Fig. 2a). Next, the lateral view is used with the C-arm tilted 90° for guidance. The examining table is moved so that the anterior one-third median site of the vertebral

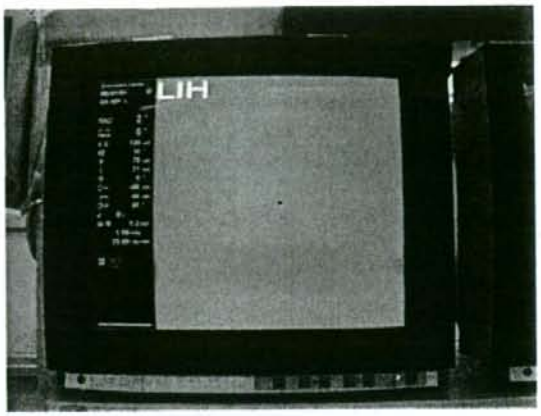

Fig. 1. Isocenter marker (ICM)

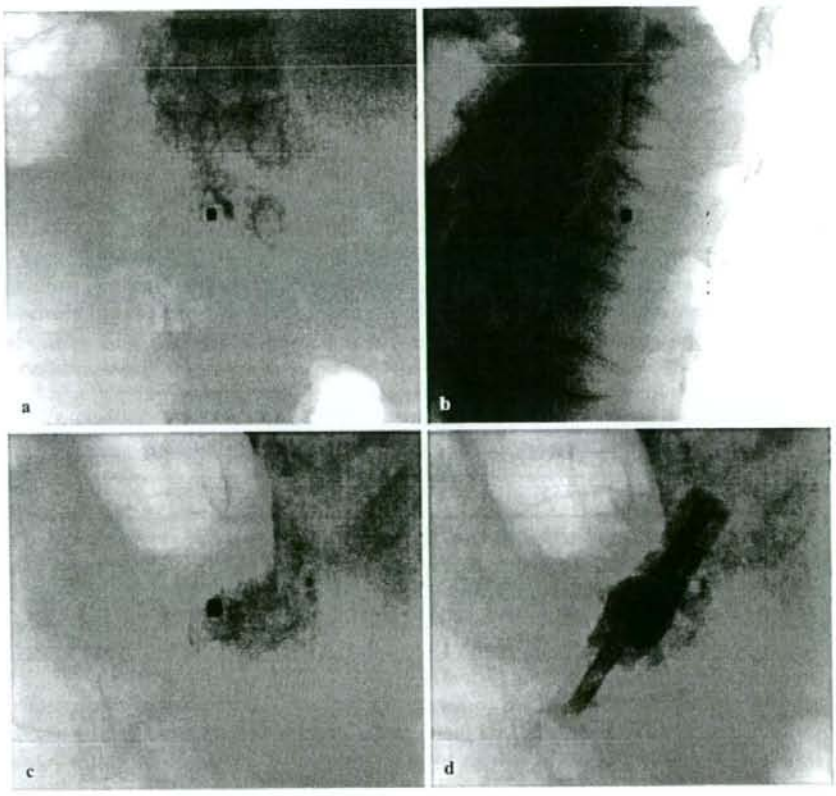

Fig. 2. Positioning. **a** In the frontal view, the ICM is aligned with the median of the vertebral body. **b** In the lateral view, the ICM is aligned with the anterior one-third median site of the vertebral body. **c** The C-arm is moved in a three-dimensional manner so the ICM is aligned with the center of the shadow of the vertebral arch pedicle. **d** The shadow of the puncture needle becomes a *dotted line* and is aligned with the ICM

body is aligned with the ICM (Fig. 2b). After carrying out these steps, the positioning of the isocenter marker in regard to the patient's position is completed. Consequently, regardless of how the C-arm rotates, the puncture target point is now aligned with the ICM at all times.

Next, the direction of the puncture direction is determined by rotating the C-arm in a three-dimensional manner so the ICM overlaps the center of the pediculus arcus vertebral image (Fig. 2c). With this step, the puncture direction is determined under fluoroscopy.

After confirming the cutaneous puncture site on the skin and administering local anesthesia, the puncture is performed while maintaining the puncture direction so the puncture needle overlaps the ICM in a point-like manner under fluoroscopy (Fig. 2d). When the needle reaches a depth of 1–2 cm in the vertebral arch pedicle, and the assistance of the needle is thus no longer required, the monitor is switched to the lateral fluoroscopic image, and the puncture needle is moved forward until the needle tip reaches the ICM (Fig. 3a). When moving the needle forward, a hammer is used as required. After the puncture needle tip has reached the ICM in the lateral image, the monitor is returned to the frontal fluoroscopic image to confirm that the puncture needle tip is aligned with the ICM (Fig. 3b), thereby completing the puncture by the ISOP method.

Materials

A total of 122 patients (224 vertebral bodies) underwent fluoroscopic PVP. They were then divided into three groups. Table 1 represents the characteristics of those groups. The first (group A) comprised 41 patients (73 vertebral bodies) who had undergone PVP by the ISOP method from January 2006 to March 2007. The second group (group B) comprised 58 patients (118 vertebral bodies) who had undergone PVP by the puncture simulation method from September 2004 to January 2006. The third group (group C) comprised 23 patients (33 vertebral bodies) who had undergone PVP without using the ICM from June 2002 to May 2004.

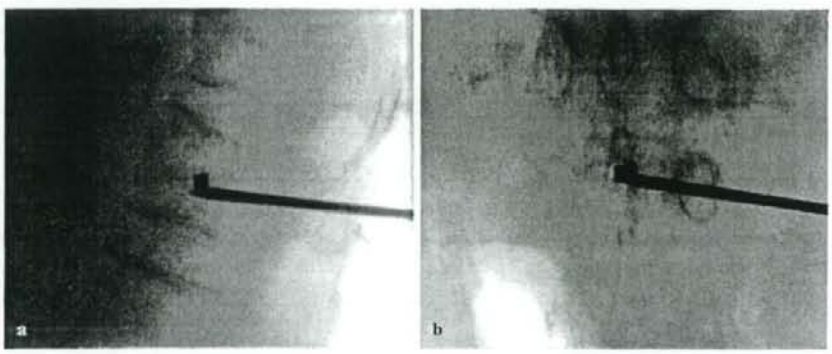

Fig. 3. Verification.
a Lateral view: the puncture needle tip overlaps the ICM.
b Frontal view: the puncture needle tip overlaps the ICM

Table 1. Summary of patients

Characteristic	ISOP method (group A)	Puncture simulation (group B)	Conventional method (group C)
Cases (vertebrae)	41 (73)	58 (118)	23 (33)
Male/female	8/33	11/47	9/14
Age (years), average/range	68.3/37–90	67.2/33–91	73.9/30–87
Location (case)	Th7 (1), Th8 (2), Th10 (3), Th11 (2), Th12 (12), L1 (18), L2 (14), L3 (10), L4 (9), L5 (2)	Th5 (1), Th6 (3), Th7 (2), Th8 (6), Th9 (8), Th10 (4), Th11 (10), Th12 (14), L1 (12), L2 (16), L3 (18), L4 (18), L5 (6)	Th8 (2), Th11 (1), Th12 (4), L1 (4), L2 (6), L3 (4), L4 (5), L5 (7)
Underlying disease (cases/vertebrae)			
Osteoporosis	34/58	45/81	11/15
Bone metastasis	7/15	13/37	11/17
Multiple myeloma			1/1

Methods

For all groups, we measured the success rate of the median puncture of the vertebral body (SR)[1,2] and the time required to perform a needle puncture successfully. The SR was evaluated by three radiologists during the procedure. It was judged by macroscopic evaluation of whether the needle tip reached the median of the vertebral body and by objective evaluation of whether the bone cement was distributed beyond the median of the vertebral body. These evaluations were done by using examples from previous observations of Kim et al.[1] For cases of failure, puncture was performed from the opposite side or from the same side after removing the needle. Fisher's exact test was used to evaluate all groups.

The procedure time for needle puncture was defined from the start of the positioning to puncture completion. The procedure time for needle puncture did not include the time needed to prepare the bone cement or the time needed to inject the cement. For a comparison of the puncture time, Mann-Whitney's U-test was used.

In group A, the puncture error, fluoroscopy time, and adverse events were further examined. Because the puncture target point with the ISOP method is determined by the operator's visual estimation during the procedure, it is not necessarily the anterior one-third median site of the vertebral body. When the patient is moved after the puncture direction is determined, a slight misalignment is likely to occur between the puncture target point and the ICM. Therefore, to evaluate the puncture error in the ISOP method, we verified where the puncture needle tip is located on the image obtained before the cement injection and measured the positional error between the puncture needle tip and the ideal puncture target point. For the error between the puncture needle tip and the ideal puncture target point, we measured the lateral direction of the axis in the frontal view and the craniocaudal direction of the axis in the lateral view.

For the fluoroscopy time during the procedure, the time between the positioning and rotation digital angiography immediately after the procedure was thus measured. The examination of adverse events was based on their presence or absence during the procedure.

A single plane C-arm of Infinix celeve VC (Toshiba Medical) was used for X-ray fluoroscopy. The puncture needle, an osteo-site bone biopsy needle (13 gauge, 15 cm; Cook, Spencer, IN, USA) was used. For injecting the cement preparation, Osteoject (Integra NeuroScience, Plainsboro, NJ, USA) was used. PMMA (polymethylmethacrylate) was the bone cement, which was prepared by mixing 20 g of PMMA with 6 g of sterilized barium sulfate.

Table 2. Success rate ratio

Group	SR	Non-SR	Total
A	72	1	73
B	110	8	118
C	19	14	33
Total	201	23	224

SR, success rate

Results

Success rate of the median puncture of the vertebral body

The success rate (SR) for median puncture of the vertebral body was 98.6% (72/73) in group A, 93.2% (110/118) in group B, and 58% (19/33) in group C (Table 2). No significant differences were observed between groups A and B ($P = 0.15$). When comparing groups A and C, the SR was significantly higher in group A ($P < 0.05$).

In cases where a median puncture could not be successfully performed, either additional punctures were attempted from the opposite side or the same puncture was repeated. In all cases, satisfactory cement distribution to the lateral regions crossing the median was ultimately obtained.

Procedure time

The average procedure time for needle puncture for one vertebral body was 9.3 ± 3.8 min in group A, 11.2 ± 4.6 min in group B, and 30.9 ± 11.2 min in group C. No significant differences between groups A and B were observed regarding the puncture time ($P = 0.22$); however, the time was significantly shorter between groups A and C ($P < 0.01$).

Positional relation between the ideal puncture target point and the puncture needle tip—ISOP method

The average error in the horizontal direction was 1.52 ± 1.31 mm (maximum 5.92 mm), the average error in the ventrodorsal direction was 2.08 ± 1.50 mm (maximum 6.41 mm), and the average error in the craniocaudal direction was 1.87 ± 1.43 mm (maximum 5.81 mm). Figure 4 shows the positional relation between the ideal puncture target point and the puncture needle tip to each axis. As shown in Fig. 4b, we detected a tendency for the puncture needle tip to go slightly deeper toward the abdominal side of the vertebral body.

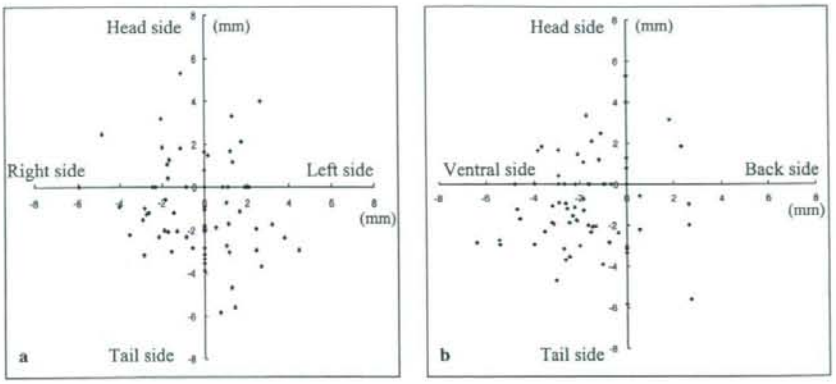

Fig. 4. Positional relation between the puncture needle tip and the puncture target point. **a** frontal view. **b** lateral view

Fluoroscopy time during the procedure—ISOP method

In group A, the average fluoroscopy times during the procedure were 5.8 ± 0.9 min for 23 cases of operating on one vertebral body, 8.97 ± 3.79 min for 8 cases of operating on two vertebral bodies, 9.33 ± 3.79 min for 4 cases of operating on three vertebral bodies, and 11.8 ± 2.83 min for 6 cases of operating on four vertebral bodies.

Adverse events—ISOP method

Two patients in group A had a fever after the procedure. Although the hospitalization period of these patients was extended by approximately 1 week, the symptoms were alleviated by antibiotic administration. No technique-related complications were observed.

Discussion

There have been only a few reported evaluations of PVP procedures, and most of them reported on cement distribution and leakage.[1–8] Many institutions select PVP using the bilateral transpedicular approach, thus expecting an even cement distribution within the vertebral body. Kim et al.[1] noted that if the unilateral transpedicular approach can achieve cement distribution across the median there are no differences in treatment effects compared to the bilateral transpedicular approach. In our examination, it was confirmed that by using the ISOP method the PVP success rate was 98.6%, and that even with the unilateral vertebral transpedicular approach bilateral cement distribution can be achieved if puncture is successfully performed with a target point of the anterior one-third median site of the vertebral body.

In group A, puncture had to be repeated in one case. In this case, it was attributed to body movement after positioning, whereby the ICM was misaligned from the puncture target point during the puncture. In this case, the ISOP method was applied again after removing the puncture needle. Favorable treatment effects were then obtained.

The puncture times were significantly shorter in group A than in group C, suggesting that the ISOP method contributes to a reduction of the puncture time in comparison to the conventional method.

In our hospital, before introducing the ISOP method, PVP had been implemented using the puncture simulation method.[2] With both the ISOP method and the puncture simulation method, there were no significant differences in the SR or the puncture time. Based on the above results, we speculate that no substantial differences exist between the ISOP method and the puncture simulation method. However, the puncture simulation method requires a preoperative CT examination and measurement of the puncture angle. Considering the labor hours and complexity, it is obvious that the ISOP method is a simpler, more useful puncture method.

Puncture accuracy in the ISOP method was an average of 2 mm in each of the horizontal, ventrodorsal, and craniocaudal directions. With this examination, except for case in which a second puncture was required owing to the patient's body movement (group A), the puncture needle tip reached the ICM in all cases, which is thus regarded as high puncture accuracy.

Reports on the amount of exposure and fluoroscopy time in the PVP are scarce.[10–12] Komemushi et al. have performed PVP by using the IVR-CT system and reported that the fluoroscopy time was 6.66 ± 2.45 min.[11] We used only a fluoroscopy device. The average fluoroscopy time for one vertebral body was 5.8 ± 0.9 min,

which was short, on average. In addition, Mehdizade et al. reported that the PVP fluoroscopy time under fluoroscopy was 10–60 min.[10] Compared to these reports, PVP under fluoroscopy by means of the ISOP method is believed to contribute to a significant reduction in the fluoroscopy time.

Conclusion

Compared to the conventional method, the ISOP method is thought to be a useful approach as it improves the PVP completion rate by using the unilateral vertebral arch pedicle approach; it also reduces the puncture time and fluoroscopy time. Thus, we speculate that the ISOP method is a more convenient technique than the puncture simulation method.

References

1. Kim AK, Jensen ME, Dion JE, Schweickert PA, Kaufmann TJ, Kallmes DF. Unilateral transpedicular percutaneous vertebroplasty: initial experience. Radiology 2002;222:737–41.
2. Kobayashi K, Takizawa K, Koyama M, Yoshimatsu M, Sakaino S, Nakajima Y. Unilateral transpedicular percutaneous vertebroplasty using puncture simulation. Radiat Med 2006;24:187–94.
3. Takizawa K, Yoshimatsu M, Nakajima Y, Sakaino S, Yagihashi K, Ogawa Y, et al. Development of a new support method for transpedicular punctures of the vertebral body: the isocenter puncture method. Cardiovasc Intervent Radiol 2007;30:757–60.
4. Koyama M, Takizawa K, Kobayashi K, Sasaka K, Hoshikawa Y, Nakaji S, et al. Initial experience of percutaneous vertebroplasty using single plane C-arm fluoroscopy for guidance. Radiat Med 2005;23:256–60.
5. Jensen ME, Evans AJ, Mathis JM, Kallmes, DF, Cloft HJ, Dion JE. Percutaneous polymethylmethacrylate vertebroplasty in the treatment of osteoporotic vertebral body compression fractures: technical aspects. AJNR Am J Neuroradiol 1997;18:1897–904.
6. Cotton A, Boutry N, Cortet B, Assaker R, Demondion X, Leblond D, et al. Percutaneous vertebroplasty: state of the art. Radiographics 1998;18:311–20.
7. Tohmeh AG, Mathis JM, Fenton DC, Levine AM, Belkoff SM. Biomechanical efficacy of unipedicular versus bipedicular vertebroplasty for the management of osteoporotic compression fractures. Spine 1999;24:1772–6.
8. Deramond H, Depriester C, Galibert P, LeGars D. Percutaneous vertebroplasty with polymethylmethacrylate: technique, indications, and results. Radiol Clin North Am 1998;36:533–46.
9. Do HM, Kim BS, Marcellus ML, Curtis L, Marks MP. Prospective analysis of clinical outcomes after percutaneous vertebroplasty for painful osteoporotic vertebral body fractures. AJNR Am J Neuroradiol 2005;26:1623–8.
10. Mehdizade A, Lovblad KO, Wilhelm KE, Somon T, Wetzel SG, et al. Radiation dose in vertebroplasty. Neuroradiology 2004;46:243–5.
11. Komemushi A, Tanigawa N, Kariya S, Kojima H, Shomura Y, Sawada S. Radiation exposure to operators during vertebroplasty. J Vasc Interv Radiol 2005;16:1327–32.
12. Kallmes DF, O E, Roy SS, Piccolo RG, Marx WF, Lee JK, et al. Radiation dose to the operator during vertebroplasty: prospective comparison of the use of 1-cc syringes versus an injection device. AJNR Am J Neuroradiol 2003;24:1257–60.

ORIGINAL ARTICLE

ACTA RADIOLOGICA

Improvement in Respiratory Function by Percutaneous Vertebroplasty

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Tanigawa N, Kariya S, Kojima H, Komemushi A, Shomura Y, Tokuda T, Ueno Y, Kuwata S, Fujita A, Terada J, Sawada S. Improvement in respiratory function by percutaneous vertebroplasty. Acta Radiol 2008;49:638–643.

Background: Percutaneous vertebroplasty (PVP) improves back pain and corrects spinal misalignment to some extent, and thus may improve respiratory function.

Purpose: To retrospectively investigate changes in respiratory function after PVP.

Material and Methods: 41 patients (mean age 72.0 years, range 59–86 years; 39 women, two men) who had undergone PVP for vertebral compression fractures (37 thoracic vertebral bodies [Th6–Th12] and 50 lumbar vertebral bodies [L1–L5]) caused by osteoporosis visited our hospital for follow-up consultation between January and June 2005. At this follow-up consultation, respiratory function testing, including percent forced vital capacity (FVC%) and percent forced expiratory volume in 1 s (FEV_1%), was performed. We retrospectively compared these values with those taken before PVP using a Wilcoxon signed-rank test.

Results: FVC% was 85.2 ± 30.3% before PVP and 91.5 ± 16.8% at follow-up (mean 10 months after PVP), which represented a significant difference ($P < 0.003$). No significant difference in FEV_1% was detected. Regarding the number of treatment levels, that is, single vertebroplasty versus multiple vertebroplasty, no significant difference in improvement of FVC% was confirmed ($P = 0.1$). FVC% was abnormally low (≤ 79%) before PVP in 16 patients and improved to within normal range postoperatively in six of these patients (38%).

Conclusion: PVP improves preoperatively decreased lung function, but this improvement takes time.

Key words: Osteoporosis; percutaneous vertebroplasty; respiratory function

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Vertebral compression fracture due to osteoporosis causes not only back pain, but also spinal misalignment, particularly kyphosis. Kyphosis of the thoracic spine in turn causes rib cage deformity. In this manner, vertebral compression fracture reduces the activities of daily living (ADL) (1), causes respiratory dysfunction due to rib cage deformity, and increases the prevalence of lung diseases (2, 3).

Mortality rates in osteoporotic women who have been clinically diagnosed with vertebral compression fracture are 15% higher than in those without compression fracture (4). Furthermore, mortality rates are 23–34% higher in osteoporotic women with severe multiple compression fractures or kyphosis than in women without these conditions, and this is primarily related to compromised pulmonary function as a result of thoracic and lumbar vertebral fractures (2).

Percutaneous vertebroplasty (PVP) was first reported in 1987 (5). Since then, PVP has been performed to alleviate pain caused by various types of vertebral compression fracture, and dramatic effectiveness in this regard has led to frequent use (6–9). PVP is also useful for back pain caused by compression fractures due to osteoporosis and has contributed greatly to improvements in ADL (6, 10, 11).

Since PVP improves back pain and corrects spinal misalignment to some extent, we hypothesized that respiratory function might also be

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improved, reducing the incidence of respiratory complications and increasing life expectancy. The present study thus investigated the long-term benefits of PVP with regard to respiratory function.

Material and Methods

Patients

The indication for PVP was back pain caused by vertebral body compression fracture, with pain on percussion of the vertebral spinous process. In cases with multiple compression fractures in which percussion pain of the spinous process was unclear, physical examination was performed using fluoroscopy. Patients with back pain attributed to myelopathy or radiculopathy resulting from stenosis of the vertebral canal or narrowing of the intervertebral foramen were excluded.

This study comprised 41 patients (mean age 72.0 years, range 59–86 years; 39 women, two men) who had vertebral compression fractures caused by osteoporosis and had undergone PVP to treat 37 thoracic vertebral bodies (Th6–Th12) and 50 lumbar vertebral bodies (L1–L5) before respiratory function testing. PVP had been performed to treat one vertebral body in 13 patients, two vertebral bodies in 14 patients, three vertebral bodies in 10 patients, and four vertebral bodies in four patients (Table 1).

These 41 patients had undergone PVP at our institution and visited our hospital for follow-up consultation between January and June 2005; one patient who had undergone PVP at our hospital in the past and visited the outpatient clinic due to a new compression fracture during the study period was excluded. At this follow-up consultation, respiratory function testing was performed in all 41 patients. Mean duration between PVP and respiratory function testing was 10 months (range 1–24 months). Preprocedural pulmonary function was retrospectively reviewed. Our institution does not require institutional review board approval for retrospective reviews.

At our institution, respiratory function testing was performed 1–3 days before PVP in all patients. Values from respiratory function testing were not included in the exclusion criteria. Furthermore, patients who underwent PVP during this study period (January to June 2005) underwent additional respiratory function testing the day after PVP.

PVP procedure

All procedures were performed by either one of the authors (N.T.), who had 7 years' experience in PVP, or by a fellowship trainee under the supervision of N.T. PVP was performed under combined computed tomography (CT) and fluoroscopic guidance (Advantex LCA+ACT; GE Medical Systems, Milwaukee, Wisc., USA). Thirty minutes preoperatively, 10 mg of morphine hydrochloride (Sankyo, Tokyo, Japan), 0.5 mg of atropine sulfate (Tanabe, Osaka, Japan), and 25 mg of hydroxyzine hydrochloride (Pfizer Japan, Tokyo, Japan) was administered intramuscularly. Local anesthesia with 10 ml of 1% lidocaine (AstraZeneca, Osaka, Japan) was performed from the skin to the periosteum of the pedicle using a 22G Cathelin needle (Terumo Europe, Leuven, Belgium) under fluoroscopic guidance. After orientation of the puncture needle was confirmed on CT and aligned with the Cathelin needle, a 13G bone biopsy needle (Osteo-Site Bone Biopsy Needle Murphy M2; Cook, Bloomington, Ind., USA) was advanced into the pedicle of the vertebral arch. A unilateral transpedicular approach was selected for all cases. CT was repeated, and after confirming orientation of the biopsy needle, the visualization modality was changed to lateral fluoroscopy and the bone biopsy needle was advanced to the anterior third of the vertebral body close to the midline.

Intraosseous venography was performed using 1–5 ml of iopamidol (Iopamiron 300; Schering Japan, Osaka, Japan) or 5–20 ml of carbon dioxide to confirm that the needle was not positioned within a direct venous anastomosis to the central or epidural veins. Subsequently, 20 g of methyl methacrylate powder (Osteobond copolymer bone cement; Zimmer, Warsaw, Ind., USA) was mixed with 5 g of barium sulfate powder (Horii Pharmaceutical, Osaka, Japan) that had been sterilized with dry heat to increase opacity. Next, 10 ml of liquid methyl methacrylate monomer was added to the powder, and the mixture was blended to a toothpaste-like consistency, producing polymethyl methacrylate (PMMA). Using 1-ml syringes, PMMA was injected under lateral fluoroscopic guidance. PMMA injection was terminated when adequate filling of the vertebral body was achieved or if leakage occurred. If leakage occurred, the needle was repositioned and additional PMMA was injected to fill the remaining part of the vertebral body. The needle was then removed, and all patients were observed in a supine position for 2 hours.

Pulmonary function testing

Respiratory function was assessed using percent forced vital capacity (FVC%), representing restrictive ventilatory disturbance, and percent forced

Table 1. Measurements of pulmonary function.

Patients No./sex/age (years)	Level	FVC%			FEV_1%		
		Pre-PVP (%)	1 day after (%)	At follow-up (%)	Pre-PVP (%)	1 day after (%)	At follow-up (%)
1/F/71	L1, L2, L3	94.8		90.7	80.7		78.6
2/F/71	T12, L4, L5	126.2		123	79.3		75.9
3/F/64	L1, L2	83.1		79.7	60.7		58.2
4/F/75	L1, L2, L3	109.1		93	85.9		88.5
5/F/75	T12	100		93.2	77.8		76.6
6/F/76	T7	61.9		88.3	66.9		69.4
7/F/75	T8, T9	94.9		93	93.1		88.5
8/F/73	T10, T11	79.9		95.6	74.7		75.5
9/F/65	L1	90.7		99.3	88		85.4
10/F/77	T12	60.2		66.6	84.7		73.7
11/F/85	L2	77.8		107.6	78.4		79.7
12/F/73	T9, T10	87.4		95.6	80.4		75.5
13/F/62	T12, L1, L2	91.9		105.5	86.4		87
14/F/71	L1	75.8	88.4	88.4	43.6	47.3	47.3
15/F/71	L1, L2, L3	104.7	97.9	104.1	80.6	82.5	81.7
16/F/73	T9, T10, T11	119.8	100.1	105.9	73.6	74.6	79.9
17/F/68	T9, T10, T11, T12	98.4	107.6	112.3	92.9	88.3	85.3
18/F/78	T6, T7, T8, T9	63.8	75.9	78.2	73.7	66	62.4
19/F/86	T11, T12	50.4	80.3	56.3	70.9	72	73.9
20/F/66	L2	61.3	63.1	80.5	76.7	77.2	77.8
21/F/71	T12, L1, L3	104.7		106.4	80.3		92.3
22/F/66	T12, L1, L2, L3	112.4		122.4	81.9		79.9
23/F/59	T12, L1	66.7		72.6	77.2		87.9
24/F/72	L3	79.5		103.3	83.8		79.7
25/F/72	L1, L3, L4, L5	58.3		83	78.6		75.1
26/F/70	L4, L5	109.7		124.1	83.1		77.8
27/F/74	T11, T12, L1	91.2		94.2	79.8		84.6
28/F/73	L1	84.9		72.5	85.5		98.6
29/M/76	L2, L3	55.2		59.7	83.7		85.5
30/F/78	L1, L4, L5	99.8		92.1	66.7		71.3
31/M/77	T12	77.5		93.8	82.5		74.6
32/F/76	L1, L3	81.4		93.1	73.5		93.1
33/M/61	L4	98.2		99.8	82.2		82.3
34/F/74	L4, L5	47.2		74	72.1		71.9
35/F/86	T11, T12	50.4	80.3	56.3	70.9	72	73.9
36/F/68	T11, T12	84.7	84.9	94.1	85.6	84.4	74.2
37/F/84	T12, L1	108.6	106.3	100.4	73.1	72.1	76.8
38/F/65	T11	75.8		84.9	48.2		46.8
39/F/72	T11, T12, L1	94.5	69.7	88.7	67.6	62.1	76.2
40/F/64	L1	69.6		71.9	81.5		78.8
41/F/64	L3, L4	110.5	105.9	107.9	72.2	76.3	81.1

FVC%: percent forced vital capacity; FEV_1%: percent forced expiratory volume in 1 s.

expiratory volume in 1 s (FEV_1%), representing obstructive ventilatory disturbance.

FVC and FEV_1 were measured using a spirometer (System 9; Minato Ika, Osaka, Japan) with an online computer. Spirometry was performed at least three times for FEV_1 and FVC, which fulfilled the criteria of the American Thoracic Society (12).

Statistical analysis

In all patients, severity of back pain was assessed using a visual analog scale (VAS) of 0–10, with 0 representing no pain and 10 representing the worst pain imaginable, before PVP and at the time of respiratory function testing.

Subjects were divided into single-vertebroplasty and multiple-vertebroplasty groups. The single-vertebroplasty group consisted of patients in whom one vertebra was treated, while the multiple-vertebroplasty group comprised patients who received treatment for two or more vertebrae. FVC% before and after PVP was compared between these two groups using the Wilcoxon signed-rank test. The Mann-Whitney U test was used to compare the degree of improvement in FVC%.

In addition, to ascertain differences in the efficacy of PVP, the degree of improvement in VAS ([VAS score before PVP] – [VAS score at respiratory function testing]) was compared between groups using the Mann-Whitney U test.

Furthermore, FVC% was divided into the following four grades: <60%, 60–79%, 80–99%, and 100%. Frequency distribution of FVC% was compared before and after PVP.

Subjects were also divided into three groups with respect to treatment level: thoracic group, thoracolumbar group, and lumbar group. Cement injection was performed only on thoracic vertebrae in the thoracic group, on both thoracic and lumbar vertebrae in the thoracolumbar group, and on lumbar vertebrae in the lumbar group. Among these groups, FVC% was compared before PVP and at one time during the follow-up period using the Wilcoxon signed-rank test. In addition, to ascertain differences in the efficacy of PVP among groups, the degree of improvement in VAS ([VAS score before PVP] – [VAS score at respiratory function testing]) was compared among groups using the Mann-Whitney U test.

Results

PVP was successfully performed in all cases. No complications were encountered, and no new shadows in the lung parenchyma, such as cement emboli, were identified on postprocedural chest radiography.

Mean VAS was 7.0 ± 2.3 ($n=41$) before PVP, 1.9 ± 2.4 ($n=12$) the day after PVP, and 1.5 ± 1.4 ($n=41$) at the time of follow-up.

FVC% and FEV_1% before, 1 day after, and at a mean of 10 months after PVP are displayed in Table 2. A significant difference in FVC% was evident between before PVP and a mean of 10 months after PVP ($P<0.003$). However, no significant difference was seen in FEV_1%.

Table 2. Changes in FVC% and FEV_1% for all study patients.

Parameters	FVC%	FEV_1%
Before PVP ($n=41$)	85.2 ± 30.3*	77.0 ± 9.98
1 day after PVP ($n=12$)	88.4 ± 15.1	72.9 ± 10.9
At follow-up ($n=41$)	91.5 ± 16.8*	77.6 ± 10.4

Data are expressed as mean ± standard deviation.
FVC%: percent forced vital capacity; FEV_1%: percent expiratory volume in 1 s; PVP: percutaneous vertebroplasty.
*Statistically significant difference ($P<0.01$).

Single vertebroplasty vs. multiple vertebroplasty

Thirteen patients had single vertebroplasty and 28 multiple. Table 3 shows FVC% before PVP and at follow-up for the single- and multiple-vertebroplasty groups. In both groups, significant differences in FVC% were identified (single-vertebroplasty group, $P=0.02$; multiple-vertebroplasty group, $P=0.05$). However, degree of improvement in FVC% following PVP was 10.5 ± 12.6% for the single group and 4.4 ± 10.6% for the multiple group, with no significant difference observed between the groups ($P=0.1$). Moreover, the degree of improvement in pain following PVP was 5.2 ± 3.1 for the single group and 6.0 ± 2.8 for the multiple group. No significant difference was observed between the groups ($P=0.4$).

Treatment at spinal level

Regarding spinal level, the thoracic group included 19, the thoracolumbar group eight, and the lumbar group 14 patients. Mean FVC% before PVP and 10 months after PVP for the thoracic, thoracolumbar, and lumbar groups are shown in Table 4. Only the thoracic group displayed a significant difference ($P=0.02$).

Degree of improvement in pain following PVP was 4.6 ± 3.1 for the thoracic group, 6.1 ± 2.9 for the thoracolumbar group, and 5.8 ± 2.9 for lumbar group, with no significant difference apparent among these groups.

Changes in frequency distribution of FVC%

Table 5 shows the frequency distribution of FVC% before PVP and FVC% at follow-up (mean follow-up, 10 months). FVC% was abnormally low (=79%) before PVP in 16 patients and normalized postoperatively in six of these patients (38%).

Table 3. Relationship between changes in FVC% and the number of treated vertebral bodies.

	Before PVP	At follow-up	*P* value
Single-vertebroplasty group	77.9 ± 13.0	88.5 ± 12.8	0.02
Multiple-vertebroplasty group	88.6 ± 22.4	92.2 ± 18.4	0.05

Data are expressed as mean FVC% ± standard deviation (%).
FVC%: percent forced vital capacity; FEV_1%: percent expiratory volume in 1 s; PVP: percutaneous vertebroplasty.
P value was obtained by Wilcoxon signed-rank test between before and during follow-up.

Table 4. Relationship between changes in FVC% and treatment level.

	Before PVP	At follow-up	P value
Thoracic vertebrae group	83.8±19.3	90.8±15.7	0.02
Thoracic and lumbar vertebrae group	99.5±17.8	101.1±16.9	0.48
Lumber vertebrae group	78.9±20.3	86.7±17.9	0.06

Data are expressed as mean FVC% ± standard deviation (%).
FVC%: percent forced vital capacity; FEV_1%: percent expiratory volume in 1 s; PVP: percutaneous vertebroplasty.
P value was obtained by Wilcoxon signed-rank test between before and during follow-up.

Changes in FVC% for patients with decreased lung function (FVC% <79)

FVC% for these 16 patients is shown in Table 6. A significant difference in FVC% was observed between before PVP and 1 day after PVP ($P = 0.043$), and between before PVP and 10 months after PVP ($P < 0.001$).

Discussion

In our study, 16 of the 41 patients displayed low FVC%, or decreased lung function, before PVP. In these 16 patients, improvement in ventilatory disturbance was achieved immediately after PVP and was maintained thereafter. Furthermore, in six of the 16 patients (38%), FVC% normalized after PVP. In patients with compression fractures due to osteoporosis, PVP effectively improves back pain (6–9). Costal movements that are restricted before PVP due to back pain subsequently improve after PVP due to alleviation of pain. Furthermore, PVP improves reduced vertebral body height due to compression fracture (13, 14), thereby alleviating local kyphosis (15).

For the entire subject group, FVC% was improved only slightly immediately after PVP, but improved to a greater degree at a mean follow-up of 10 months. This suggests that decreased lung function improves even in patients who do not display defined decreased lung function preoperatively, but this improvement takes time. In other words, PVP eliminates back pain immediately after the procedure. Among patients who displayed decreased lung function preoperatively, reduced pain and greater costal movements directly improved FVC%, and among those who did not exhibit decreased lung function preoperatively, PVP improved back pain and increased daily exercise tolerance, allowing indirect improvements to ventilatory capacity. That is, increased daily exercise works as rehabilitation for thoracic cage movement.

Table 5. Frequency distribution of FVC%.

FVC%	0–59%	60–79%	80–99%	100% or more
Before PVP ($n=41$)	5 (12)	11 (27)	15 (37)	10 (24)
At follow-up ($n=41$)	2 (5)	8 (20)	19 (46)	12 (29)

Data are number of patients. Numbers in parentheses are percentages.
FVC%: percent forced vital capacity; PVP: percutaneous vertebroplasty.

Table 6. Changes in FVC% for patients with decreased lung function.

Parameters	FVC%
Before PVP ($n=16$)	65.7±11.3*#
1 day after PVP ($n=16$)	77.6±9.3*
At follow-up ($n=16$)	80.9±15.5#

Data are expressed as mean value ± standard deviation.
FVC%: percent forced vital capacity; PVP: percutaneous vertebroplasty.
*Statistically significant difference ($P=0.04$).
#Statistically significant difference ($P<0.01$).

No significant differences in degree of pain improvement were seen between the single- and multiple-vertebroplasty groups, and FVC% significantly improved for both groups. These results might be explained by the fact that improvements in decreased lung function primarily resulted from improvements in pain.

The three spinal-level groups displayed no significant differences in degree of pain improvement, and FVC% significantly improved only for the thoracic group. This might be explained by the fact that, as described above, decreased lung function improves when rib cage volume, costal movement, and pain improve, and the impact of these changes was greater for the thoracic group.

Pain improved in all of our patients, so statistical confirmation could not be achieved of whether pain alleviation contributed to improvements in decreased lung function. However, pain, particularly back pain, can easily be considered to restrict costal movement. We are therefore certain that pain alleviation represents one of the factors leading to improvements in decreased lung function.

We used forced vital capacity instead of vital capacity to evaluate restrictive ventilatory disturbance. We consider that back pain due to compression is one of the major factors contributing to the induction of obstructive ventilatory disturbance. However, full inspiration followed by forced