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Research Article

Patient versus anesthesiologist controlled analgesia in cirrhotic patients undergoing percutaneous radiofrequency ablation of hepatic tumors

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KEYWORDS

Controlled analgesia;
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Abstract *Background and aims:* Patients may experience pain during Radiofrequency thermal ablation (RFTA) of hepatic tumors. The aim was to compare the use of fentanyl administered through the patient controlled analgesia (PCA) machine with the same drug given intermittently by the anesthesiologist.

Methods: In this prospective, randomized, double-blind study, eighty cirrhotic patients underwent RFTA of hepatic tumors were enrolled. All patient received midazolam 10 μg/kg and fentanyl 1 μg/kg IV, then 5–10 mL of 2% lidocaine were injected from the skin to the liver capsule along a specified insertion route, then the RFTA electrode was advanced into the tumor. For maintenance of analgesia bolus doses of fentanyl were then administered either by patient himself (PCA group, $n = 40$) with each bolus dose contained 10 μg of fentanyl with a 1 min lock-out time or by the anesthesiologist (ACA group, $n = 40$).

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Results: PCA group received significantly higher doses of fentanyl with a mean value of 53.5 ± 13.5 μg/session, while it was 36.7 ± 13.4 μg/session in the ACA group. Patient satisfaction rates were higher in the PCA than ACA with mean values of 8.32 ± 0.62 and 7.85 ± 0.73, respectively. The mean pain score was statistically lower in the PCA group than the ACA group with mean value 3.37 ± 0.70 and 3.97 ± 0.89, respectively. There was significant difference in the mean values of the demand/ delivered ratio between groups to be 1.47 ± 0.28 and 2.50 ± 0.73 in PCA and ACA groups, respectively.

Conclusion: PCA with fentanyl proved to be a better alternative than ACA in terms of patient comfort and satisfaction.

1. Background

Radiofrequency thermal ablation (RFTA) is a technique in which an electromagnetic energy deposition is used to thermally ablate the hepatic tumor tissue [1,2]. During RFTA treatment, heat energy generated by high-frequency alternating currents targeted at the living tissues causes protein denaturation at a temperature of 60–110 °C through ionic vibration, resulting in coagulative necrosis of the target lesion. In addition, RFTA treatment stimulates the immune system and provides an easy way to achieve in vivo vaccination against tumoral antigens [3]. RFTA is generally indicated for hepatocellular carcinoma (HCC) patients who are not candidates for either liver resection or transplantation [4]. Even with appropriate conscious sedation, patients may experience pain during ablation procedures. Pre-operatively, one of the most common questions asked by those patients is the amount of pain they will experience during the procedure [5].

Patient-controlled analgesia (PCA) is commonly assumed to imply on-demand, intermittent, IV administration of opioids under patient control with or without a continuous background infusion. This technique is based on the use of a sophisticated microprocessor-controlled infusion pump that delivers a preprogrammed dose of opioids when the patient pushes a demand button.

The aim of this work was to compare the analgesic efficacy and side effects of patient versus anesthesiologist controlled analgesia in cirrhotic (child A and B) patients undergoing percutaneous radiofrequency thermal ablation of inoperable hepatic tumors.

2. Patients and methods

This prospective, randomized, double-blinded study was performed in the National Liver Institute – Menofeya University from August 2008 to April 2011. Ethical approval for this study was provided by the Ethical Committee of the anesthesia department, National Liver Institute – Menofeya university. In this work, eighty cirrhotic patients (Child A and B) between 55 and 82 years of age were scheduled for sonographically guided radiofrequency thermal ablation for hepatic tumors. The diagnosis of hepatic tumors was confirmed with the use of a sonographically guided percutaneous needle biopsy, imaging findings of a newly presenting tumor on follow-up, and a characteristic enhancement pattern on contrast-enhanced multiphase helical CT or dynamic contrast-enhanced MRI or both elevated levels of serum tumor markers (α-fetoprotein level > 200 ng/mL) and radiologic findings.

3. Inclusion and exclusion criteria

The inclusion criteria were including: a single nodular HCC not greater than 5 cm in maximum diameter; up to three multinodular HCCs, with each tumor measuring up to 3 cm in maximum diameter; absence of portal venous thrombosis; Child-Pugh classification A or B liver cirrhosis; a prothrombin time ratio > 50% (prothrombin time with international normalized ratio < 1.7); and a platelet count greater than 70,000 cells/mm^3. Patients were excluded from the study if they had any of the following: nodules adjacent to the hepatic hilum due to the risk of thermal injury of the biliary tract; and nodules adjacent to any part of the gastrointestinal tract, [6] history of use of analgesic and/or sedative agents in the past 7 days prior to RF sessions; history of alcohol abuse; a language barrier or mental disorder that would prevent them from understanding how to operate a patient controlled analgesia machine; any degree of encephalopathy, or allergy to any of the study medications.

A list had been created where the numbers from 1 to 80 were randomly assigned to one of the two groups by drawing lots. The patients were put on the list in order of recruitment. Patients were randomized to one of two groups; anesthesiologist-controlled analgesia (group ACA) (n = 40) or patient-controlled analgesia (group PCA) (n = 40). In ACA group patients received their analgesia by the same anesthesiologist throughout the study to eliminate inter-physician variability. All data were recorded by a qualified, independent observer who was blinded to group assignment. Prior to the RFTA procedure, each patient received appropriately detailed instructions regarding proper use of a patient-controlled analgesia device (Master PCA IS – Fesrsenius – France). Specifically, patients were asked to ''push the button'' in response to pain. The RF ablation was performed under real-time ultrasound guidance.

For lesions in the right lobe, an intercostal approach with the patient in the left lateral decubitus position was used, while for lesions in the left lobe, a subcostal or subxiphoid approach was used.

All patients were premeditated by ondasetron 4 mg and after being positioned on the RF table, an electrocardiogram, a non-invasive blood pressure, and a pulse oximeter were applied to each patient. Supplemental oxygen at a flow rate of 4 L/min was administered via nasal cannulae. After recording baseline measurements, all patient received midazolam 10 μg/kg and fentanyl 1 μg/kg IV. After cleaning the skin with iodized alcohol (also used as contact medium), the local anesthesia using 2% lidocaine percutaneously was provided by

injecting 5–10 mL of lidocaine from the skin to the liver capsule along a specified insertion route, then the RFTA electrode was advanced into the tumor (Angio-Dynamics Inc- RITA, model 1500X, USA). For maintenance of analgesia bolus doses of fentanyl were then administered either by patient himself (PCA) group using the PCA delivery system or by the anesthesiologist (ACA) group.

In the PCA group, a standard patient-controlled analgesia pump was loaded with a 20 cm syringe containing 200 μg fentanyl in normal saline made per patient with a concentration of 10 μg fentanyl/ml. Each bolus dose contained 10 μg of fentanyl with a 1 min lock-out time. In the ASA group the anesthesiologist titrated fentanyl doses according to his perception about the patient's comfort while at the same time, patients were given the push button of a patient-controlled analgesia machine that had the same settings as the machine used in group PCA but the syringe was prefilled with normal saline to maintain blinding. The infusion was terminated at the end of the session. RF sessions were began 5 min after administration of the fentanyl/midazolam bolus in both study groups. Rescue analgesia was provided by fentanyl 50 μg IV once, in response to patient request for additional analgesia; or more than 30% increase in the Heart rate or arterial pressure.

Before the procedure, we explained the use of the visual analog scale (VAS) to every single patient. The VAS consists of a 10-cm line which was anchored at one end by a label "no pain, score 0" and at the other end by a label "pain as bad as can be, score 10" [7–9].

4. Measurements

Physiological parameters that included: heart rate, systolic and diastolic blood pressure, respiratory rate and oxygen saturation were all recorded before the RFTA session and every 5 min after its onset. Pain was assessed at baseline, and every 5 min during RFTA using a visual analog scale (VAS) ruler with two anchor points; 0 being no pain, and 10 being the worst pain the patient had ever experienced. The VAS score was considered to be 0 if the patient was asleep at the time of assessment, which was determined by a lack of response to a gentle call of the patient's name by the blinded observer. No attempts were made to wake up those who were asleep to determine their VAS score. At the end of procedure, total dose of fentanyl having been administered, the ratio between the number of total requests (demand) of self-administration to the number of successful attempts (delivery) to were recorded [10].

After arrival to the post RFTA observation area, patients were asked to rate their satisfaction with the analgesic management during the overall surgical experience using a 10-point verbal rating scale. The radiologist, also blinded to group allocation, was asked to the degree of his satisfaction with the patient's tolerance of RFTA using the same method. All adverse events including, but not limited to, respiratory depression (defined as a respiratory rate $\leqslant$10 breaths/min), any episode of oxygen desaturation (oxygen saturation $<$92%), the need for rescue analgesia or even general anesthesia were recorded.

5. Statistical analysis

The statistical power of the matched analysis was computed in a pilot study performed prior to this study (20 cases in each group). It was observed that the visual analog scale (VAS) scores changed clinically and significantly by 70% in the pilot study. Based on the estimates, a sample size that would permit type I error of less than 0.05 and power of 90% was calculated.

Enrollment of 40 patients in each group was found to be sufficient. Statistical analyses were performed using SPSS Ver. 17 software (Statistical Package for Social Sciences for Windows, SPSS Inc., Chicago, IL, USA). The one-way ANOVA was applied to normally distributed data. The pain VAS and satisfaction score were analyzed using a Kruskal–Wallis test. Changes in blood pressures and heart rates among the groups were compared using repeated measures of one-way ANOVA. Parametric summary statistics are presented as mean ± SD. Non-parametric summary statistics are presented as median (interquartile range). Subgroup analysis within the same group was performed with the Pearson chi squared test or Fisher's exact test.

6. Results

Eighty consecutive cirrhotic patients Child A–B whom undergoing radiofrequency thermal ablation of hepatic tumors were recruited into the study. Forty patients were allocated to receive patient controlled analgesia (PCA) while the other forty patients received intermittent anesthesiologist-controlled analgesia (ACA). (Table 1) is showing the patient characteristics, etiology of liver cirrhosis and Child classification of the studied groups. There were no significant differences between the two studied groups in terms of age, weight, etiology of liver cirrhosis and history of previous ablations $p > 0.05$. There were no significant differences between the two groups according to either tumors characteristics or durations of RFTA procedure, $p > 0.05$ (Table 2). Patients used the PCA machine received significantly higher doses of fentanyl with a mean value of 53.5 ± 13.5 μg/session, while it was 36.7 ± 13.4 μg/session in the ACA group with $P < 0.05$ (Fig. 1). Post procedure patient satisfaction rates were higher significantly in the PCA than ACA (Table 3). The mean pain score (VAS) was lower in the PCA group than the ACA group with difference between the means reached statistical significance with $P < 0.05$. There was significant differences in the mean values of the demand/delivered ratio between groups to be 1.47 ± 0.28 and 2.50 ± 0.73 in PCA and ACA groups, respectively (Fig. 2).

7. Discussion

Over the last two decades an increasing number of minimally invasive, local techniques for ablative therapies have been evolved, challenging the role of surgical resection [11]. Radiofrequency ablation (RFTA) in particular, has increasingly been employed with promising results [12,13]. With the new ablation techniques, all hepatic segments can effectively be treated by RFTA [14,15].

Radiofrequency ablation is considered to be a painful procedure, and it attracted a limited interests in the literatures. Traditionally, the purpose has to render this procedure to be safe and tolerable rather than pain free. Also, with similar procedures or during monitored anesthesia care interventions, the level of analgesia and sedation are modulated at the discretion of the anesthesiologist point of view, according to the perceived patient requirements. Currently, it has been suggested

Table 1 Patient characteristics, etiology of liver cirrhosis and Child classification of the studied groups.

	PCA group (n = 40)	ACA group (n = 40)
Age (years)	62.8 ± 6.27	62.3 ± 5.59
Weight (kg)	78.1 ± 4.23	77.7 ± 5.19
Height (cm)	173 ± 5.1	172 ± 5.48
Male/female	31/9	29/11
Etiology of liver cirrhosis		
HCV (%)	33 (82.5)	35 (87.5)
HBV (%)	2 (5)	2 (5)
HCV + HBV (%)	3 (7.5)	2 (5)
Alcoholic (%)	2 (5)	1 (2.5)
Child classification		
Child A (%)	29 (72.5)	27 (67.5)
Child B (%)	11 (27.5)	13 (32.5)
Previous ablation		
Non (%)	31 (77.5)	32 (80)
Yes (%)	9 (22.5)	8 (20)
Co-morbid factors		
Cardiovascular (%)	3 (7.5)	4 (10)
Pulmonary (%)	6 (15)	8 (20)
Diabetes (%)	11 (27.5)	9 (22.5)

PCA: patient-controlled analgesia; ACA: anesthesiologist-controlled analgesia, HCV: hepatitis C virus, HBV: hepatitis B virus. Data presented as mean ± standard deviation or absolute numbers (percentage). All Data Showed no statistical significance ($P > 0.05$).

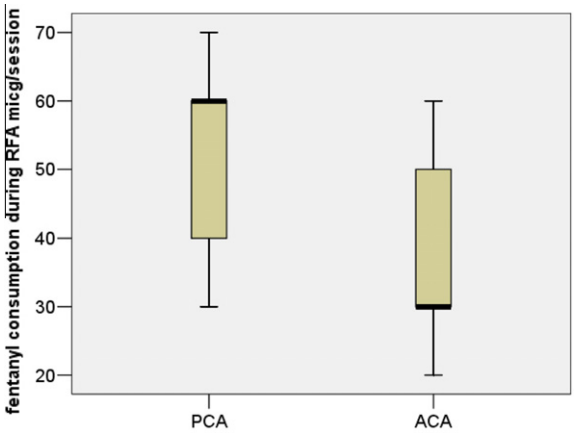

Figure 1 Fentanyl consumption during the radiofrequency ablation in μg/session in the studied groups.

that PCA may be equally or even more effective, and also it has the privilege that it can be adjusted to respond better to the demands of those critical cirrhotic patients and thus improve the quality of pain control [16]. This randomized, double-blind study demonstrated that PCA for RFTA is associated with better pain control compared with ACA. However, this was reached at the expense of higher drug consumption and possibility of complications.

Since that fentanyl and midazolam administered intermittently have been the conventional mode of pain relief in RFTA unit of our institute, we decided to compare the use of fentanyl administered through the PCA machine with the same drug given intermittently by the attending anesthesiologist. However, we chose to retain the use of midazolam in this study because of its excellent sedative and anxiolytic effects but only used a fixed single dose of this drug at the start of the procedure because we believed that excessive amounts of midazolam could potentially inhibit the patient's ability to operate the PCA device. Also it might lead to a bias in the assessment of the memory of the pain felt during the procedure. The qualities of local anesthesia were good in all patients of the two groups. There were no incidences of patients complaints during percutaneous needle insertion after the local lidocaine infiltration.

Pain is considered to be a perception; it is defined as an unpleasant sensory and emotional experience that may be associated with actual or potential tissue damage [17]. There are three major categories of nociceptors—thermal, mechanical, and polymodal. Thermal nociceptors are known to be activated by extreme temperatures (>45 °C or <5 °C). Polymodal nociceptors are triggered by high-intensity mechanical, chemical, or thermal (both hot and cold) stimuli. The three categories of nociceptors are widely distributed in the skin and deep tissues, and nociceptors are believed to work together [17]. The liver is supplied by hepatic nerves that arise from the hepatic plexus and contain both sympathetic and parasympathetic fibers. It is widely accepted that the parenchyma of the liver is insensitive to pain [18,19]. However, pain during the ablation procedures can develop in spite of appropriate conscious sedation techniques [20]. It has been demonstrated that radiofrequency ablation of a tumor in a superficial location or a central tumor close proximity to a big vessel is more likely to produce severe pain during the ablation procedure, however, the level of pain is unpredictable [21–24].

Table 2 Tumors characteristics and duration of RFA procedure.

	PCA group (n = 40)	ACA group (n = 40)
Pre-ablation maximal tumors diameter (cm)	4.3 (0.96)	4.42 (1.10)
Intrahepatic tumors location		
Peripheral near organs (%)	4 (10)	5 (12.5)
Central (%)	29 (72.5)	28 (70)
Close to major vessels (%)	7 (17.5)	7 (17.5)
RFA Session duration (min)	18.77 ± 4.75	17.87 ± 4.70

PCA: patient-controlled analgesia; ACA: anesthesiologist-controlled analgesia, RFA: radiofrequency ablation. Data presented as mean ± standard deviation, or absolute numbers (percentage). All data showed no statistical significance ($P > 0.05$).

Table 3 Physiologic parameters, Pain score, patient-operator satisfaction.

	PCA group (n = 40)	ACA group (n = 40)
Physiologic parameters		
Heart rate (beat/min)	83.5 ± 5.07	82 ± 5.66
Systolic blood pressure (mmHg)	134 ± 10.70	136 ± 9.60
Diastolic blood pressure (mmHg)	84.45 ± 4.20	85 ± 4.76
RR (breath/min)	13.37 ± 0.92	13.7 ± 1.06
Oxygen saturation (%)	99.1 ± 2.34	99.2 ± 2.11
Pain score (VAS) during RFA	3.37 ± 0.70*	3.97 ± 0.89*
Post operative Patient satisfaction (0–10)	8.32 ± 0.62*	7.85 ± 0.73*
Operator satisfaction (0–10)	8.25 ± 0.86	8.07 ± 0.76

PCA: patient-controlled analgesia; ACA: anesthesiologist-controlled analgesia, VAS: visual analog scale, RFA: radiofrequency ablation. Data presented as mean ± standard deviation.
* Statistically significant ($P < 0.05$).

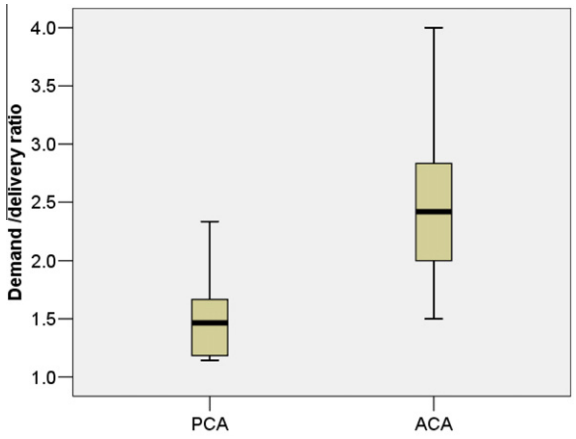

Figure 2 Demand/delivery ratio in the studied groups.

Patient Satisfaction levels were high in both groups, but it was significantly higher in the PCA group (Table 3). Generally, this could be attributed to the fact that the overall patient happiness about the success of the procedure (successful destruction and killing of the tumors according to patient's own words), this concept encourage the patients to overcome the discomfort encountered during the ablation process. Also patients tend to underestimate intra procedure pain since it was inquired about after termination of the procedure not during the ablation process. For that purpose, we monitored (demand/delivered ratio) which is the ratio of analgesic requests to successful deliveries. This ratio was significantly higher in the ACA group denoting large number of unsuccessful attempts was indicative of inadequate pain relief although there was post procedure high satisfaction rate. Another possible reason for the higher satisfaction score in the PCA group is that PCA may enhance patient's satisfaction by giving them a sense of control over an unpleasant stimulus [25]. Observational studies confirm that patients experience high levels of satisfaction when they have a degree of control over their own analgesia and, if given the option, would preferentially use patient controlled machines again [26].

Similar researches showed, that the risk factors related to severity of pain during RFTA included larger tumors, multiple ablations during the same session, and a increased in the duration of ablation. Larger hepatic tumors are usually treated with multiple ablations, and also requiring longer duration of ablation [27]. In agreement with these findings, previous reports described that multiple thermal ablations increase the likelihood of complications [28,21]. Patients who did not experience RFTA procedure for tumors reported a higher VAS during the procedure than patients with previous ablation. This observation may be explained by the reduction of unpleasantness for pain with training, even though the intensity remains at an undiminished level [18]. Dissatisfaction or emotional stress may be reduced in patients with recurrent lesions who have already experienced the RFTA procedure, as the patient reports a lower VAS.

In conclusion, during radiofrequency thermal ablation, PCA with fentanyl proved to be a better alternative than anesthesiologist – controlled technique in terms of patient comfort and satisfaction. However, despite high satisfaction rates, many patients still feel the need for more analgesia during the procedure. Future multi-center trials comparing several analgesic techniques during percutaneous radiofrequency thermal ablation should be conducted to refine analgesia needed for such procedures.

References

[1] Callstrom MR, Charboneau JW. Technologies for ablation of hepatocellular carcinoma. Gastroenterology 2008;134:1831–5.
[2] Cheung TT, Ng KK, Chok KS, Chan SC, Poon RT, Lo CM, Fan ST. Combined resection and radiofrequency ablation for multifocal hepatocellular carcinoma: prognosis and outcomes. World J Gastroenterol 2010;16:3056–62.
[3] Gravante G, Sconocchia G, Ong SL, Dennison AR, Lloyd DM. Immunoregulatory effects of liver ablation therapies for the treatment of primary and metastatic liver malignancies. Liver Int 2009;29:18–24.
[4] Kudo M. Radiofrequency ablation for hepatocellular carcinoma: updated review in 2010. Oncology 2010;78:113–24.
[5] Nalini Vadivelu, Sukanya Mitra, Deepak Narayan. Recent advances in postoperative pain management. Yale J Biol Med 2010;83:11–25.
[6] Crocetti L, de Baere T, Lencioni R. Quality improvement guidelines for radiofrequency ablation of liver tumours. Cardiovasc Intervent Radiol 2010;33:11–7.
[7] Bodian CA, Freedman G, Hossain S, Eisenkraft JB, Beilin Y. The visual analog scale for pain: clinical significance in postoperative patients. Anesthesiology 2001;95:1356–61.
[8] Carlsson AM. Assessment of chronic pain I. Aspects of the reliability and validity of the visual analogue scale. Pain 1983;16:87–101.

[9] Katz J, Melzack R. Measurement of pain. Surg Clin North Am 1999;79:231–52.
[10] McCoy EP, Furness G, Wright PM. Patient-controlled analgesia with and without background infusion. Analgesia assessed using the demand: delivery ratio. Anaesthesia 1993;48:256–60.
[11] Beland M, Mueller PR, Gervais DA. Thermal ablation in interventional oncology. Semin Roentgenol 2007;42:175–90.
[12] Chen MS, Li JQ, Zheng Y, Guo RP, Liang HH, Zhang YQ, et al. A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma. Ann Surg 2006;243:321–8.
[13] Kim SW, Rhim H, Park M, Kim H, Kim YS, Choi D, Lim HK. Percutaneous radiofrequency ablation of hepatocellular carcinomas adjacent to the gallbladder with internally cooled electrodes: assessment of safety and therapeutic efficacy. Kor J Radiol 2009;10:366–76.
[14] Kang TW, Rhim H, Kim EY, Kim YS, Choi D, Lee WJ, Lim HK. Percutaneous radiofrequency ablation for the hepatocellular carcinoma abutting the diaphragm: assessment of safety and therapeutic efficacy. Kor J Radiol 2009;10:34–42.
[15] Abitabile P, Hartl U, Lange J, Maurer CA. Radiofrequency ablation permits an effective treatment for colorectal liver metastasis. Eur J Surg Oncol 2007;33:67–71.
[16] Bright E, Roseveare C, Dalgleish D, Kimble J, Elliott J, Shepherd H. Patient-controlled sedation for colonoscopy: a randomized trial comparing patient-controlled administration of propofol and alfentanil with physician-administered midazolam and pethidine. Endoscopy 2003;35:683–7.
[17] Kandel ER, Schwartz JH, Jessell TM. Principles of neural science, vols. 442–444, 4th ed. New York, NY: McGraw-Hill; 2000. p. 473–7.
[18] Zigmond MJ, Landis SC, Squire LR, editors. Fundamental neuroscience. Academic Press; 1999. p. 762–9.
[19] Cervero F. Sensory innervation of the viscera: peripheral basis of visceral pain. Physiol Rev 1994;74:95–138.
[20] Goldberg SN, Grassi CJ, Cardella JF, et al. Image guided tumor ablation: standardization of terminology and reporting criteria. Radiology 2005;235:728–39.
[21] Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN. Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. Radiology 2003;226:441–51.
[22] Rhim H. Complications of radiofrequency ablation in hepatocellular carcinoma. Abdom Imaging 2005;30:409–18.
[23] Lim HK. Radiofrequency thermal ablation of hepatocellular carcinomas. Kor J Radiol 2000;1:175–84.
[24] Wah TM, Arellano RS, Gervais DA, et al. Image guided percutaneous radiofrequency ablation and incidence of post-radiofrequency ablation syndrome: prospective survey. Radiology 2005;237:1097–102.
[25] Bavisha KA, Elias M, Paris S, et al. Comparison of patient controlled and operator-controlled conscious sedation for restorative dentistry. Eur J Anaesthesiol 2004;21:284–8.
[26] Rudkin GE, Osborne GA, Finn BP, et al. Intra-operative patient controlled sedation. Comparison of patient-controlled propofol with patient-controlled midazolam. Anaesthesia 1992;47:376–81.
[27] Sanghee Lee, Hyunchul Rhim, Young-Sun Kim, Dongil Choi, Won Jae Lee, Lim Hyo K, Shin Byungseop. Percutaneous radiofrequency ablation of hepatocellular carcinomas: factors related to intraprocedural and postprocedural pain. AJR 2009;192:1064–70.
[28] Vogl TJ, Straub R, Eichler K, Woitaschek D, Mack MG. Malignant liver tumors treated with MR imaging- guided laser-induced thermotherapy: experience with complications in 899 patients (2520 lesions). Radiology 2002;225:367–77.