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Original Article

Propensity score matching analysis of efficacy of drug-eluting beads (DEB)-TACE loaded with different drugs in the treatment of hepatocellular carcinoma

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Abstract: Objective: To evaluate the efficacy of drug-eluting beads transarterial chemoembolization (DEB-TACE) in the treatment of hepatocellular carcinoma (HCC) by propensity score matching (PSM) technique. Methods: The clinical data of HCC patients treated with DEB-TACE in the First Affiliated Hospital of Zhengzhou University from June 2017 to June 2020 as well as their 36-month-follow-up data were retrospectively analyzed. The subjects were matched in pairs based on baseline data and laboratory indicators using the PSM method and divided into a pirarubicin group (n = 34), raltitrexed group (n = 34), and arsenic trioxide group (n = 34). Clinical efficacy was evaluated according to mRECIST criteria. The levels of alpha fetal protein (AFP), carcinoma embryonic antigen (CEA) and carbohydrate antigen-125 (CA125) in serum were detected by enzyme-linked immunosorbent assay (ELISA). The progression-free survival (PFS) and overall survival (OS) were recorded by outpatient, inpatient, and telephone follow-up. Adverse reactions were counted. Results: After PSM, no significant differences were seen in gender, age, tumor burden, Child-Pugh grade, portal vein tumor thrombus or TACE frequency among the three groups (all *P*>0.05). The ORR rate of the pirarubicin group and arsenic trioxide group at both 3rd and 6th month post-operation was significantly higher than that of the raltitrexed group (all P<0.05). Before and 1 month after treatment, there were no significant differences in the aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin (TBIL) levels between the three groups (all P>0.05). Before treatment, no significant differences were observed in AFP, CEA, or CA125 levels among the three groups (all P>0.05). After treatment, the levels of AFP in the pirarubicin group and arsenic trioxide group were lower than those in the raltitrexed group (both P<0.05), but there were no significant differences in CEA and CA125 levels (all P>0.05). There were no significant differences in PFS and OS among the three groups (all P>0.05), and the incidence of fever, abdominal pain, and myelosuppression showed no significant differences among the three groups (all P>0.05). Conclusion: The efficacies of DEB-TACE loaded with pirarubicin, raltitrexed, or arsenic trioxide in treating HCC were generally comparable, and the survival benefit of patients was similar. The short-term efficacy of the pirarubicin group and arsenic trioxide group was slightly better than that of the raltitrexed group.

Keywords: Drug-eluting beads transarterial chemoembolization, hepatocellular carcinoma, irarubicin, raltitrexed, arsenic trioxide, efficacy, prognosis

Introduction

As a malignant tumor with high morbidity and mortality, hepatocellular carcinoma (HCC) is characterized by occult onset, difficult early diagnosis, and poor prognosis [1]. With the continuous development of surgical intervention, chemoradiotherapy, and immune-targeted therapy in recent years, the prognosis of HCC patients has been improved. Among various treatment methods, drug-eluting beads (DEBs) are widely used in patients with advanced liver cancer [2]. Study has confirmed that DEB is superior to traditional transarterial chemoembolization (TACE) in saving patients' lives, and the overall incidence of adverse reactions is low

[3]. DEBs can guide the embolization of tumor terminal vessels, ensure complete tumor necrosis, and achieve an effect through continuous and slow drug release. A high proportion of primary liver cancer patients in China have large or giant liver cancers, most of whom are complicated by hepatitis virus infection, cirrhosis, venous tumor thrombus and extrahepatic metastasis. Although DEBs can control the tumors in the liver well, the efficacy is limited in patients with venous tumor thrombus and extrahepatic metastasis [4, 5]. Presently, DEBs combined with iodized oil, targeted drugs, and other interventional therapies have broad application prospects in patients with liver cancer. The drugs routinely loaded by drug-eluting beads-transarterial chemoembolization (DEB-TACE) include anthracyclines (doxorubicin, epirubicin, or pirarubicin) [6, 7]. In terms of clinical efficacy, different studies reported different results. In order to select the best combination of DEB-TACE drugs, this study analyzed the clinical efficacy and safety of pirarubicin, arsenic trioxide, and ratetrexed based on PSM analysis, to provide valuable references for optimizing drug selection, improving efficacy and reducing adverse reactions.

Subjects and methods

Subjects

The clinical data of liver cancer patients treated with DEB-TACE in the First Affiliated Hospital of Zhengzhou University from June 2017 to June 2020 and their 36-month-follow-up data were retrospectively analyzed. The propensity score matching (PSM) method was used to match the study subjects based on baseline data and laboratory indicators to obtain covariate-balanced samples among groups (34 cases in each group and 18 unmatched HCC patients were excluded from this study). Inclusion criteria: (1) Patients diagnosed with liver cancer by pathology, imaging and serology [8]; (2) Patients with Child-Pugh of A or B; (3) Patients with complete general clinical data and laboratory results; (4) Patients with no surgery or related treatment before admission. Exclusion criteria: (1) Patients complicated by other primary tumors or autoimmune liver diseases; (2) Patients complicated by severe infection; (3) Patients who could not meet the follow-up requirements during the whole treatment stage or gave up treatment or transferred to other hospitals for personal reasons. The study was reviewed and approved by the Medical Ethics Committee of the First Affiliated Hospital of Zhengzhou University.

Therapeutic methods

For the preparation of DEBs, a 20 mL syringe was used to extract the beads, and the syringe was placed vertically for 2-3 min. The supernatant was discharged after the beads settled. A 10 mL syringe was used to extract 0.9% NaCl or 5% glucose water to dissolve 60-80 mg of pirarubicin (Shenzhen Main LUck Pharmaceuticals Inc., batch No. H10930105), 4 mg of raltitrexed (Nanjing Chia-Tai Tianqing Pharmaceutical Company, batch No. H20090323) and 60 mg of arsenic trioxide (Beijing SL Pharm, batch No. H20080665) separately, and the dissolved drug was mixed with beads. The syringe was gently shaken every 5 min. The drug loading times for pirarubicin, raltitrexed, and arsenic trioxide were 15 min, 15 min, and 40 min, respectively. The patient was placed in the supine position, and conventional disinfection and surgical draping were performed. After local anesthesia, the right femoral artery was punctured using a modified Seldinger's method. A 5-FRH catheter was introduced into the common hepatic artery, superior mesenteric artery, or diaphragmatic artery under guide wire for angiography to identify the tumor-feeding artery, and evaluate the size and number of tumors and the presence of hepatic artery-portal vein/hepatic venous fistula. A catheter or microcatheter was used to super-select the responsible vessel, and 100 mL of the hydration solution of 100 mg oxaliplatin and 100 mL of the hydration solution of 500 mg fluorouracil were slowly perfused into the responsible vessel. The tumor was embolized with DEBs loaded with pirarubicin, raltitrexed, or arsenic trioxide, separately. The endpoint of embolization was the disappearance of tumor staining by reexamination angiography. If there was still tumor staining, the embolization could be consolidated by adding ordinary embolization microspheres, gelatin sponge particles, or polyvinyl alcohol particles.

Outcome assessment

Short-term curative effect: Clinical efficacy was evaluated according to mRECIST criteria [10].

Patients were divided into complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) according to CT or MRI reexamination results at 1 month and 3 months after treatment, and the overall response rate (ORR) and disease control rate (DCR) were calculated, where OR = CR + PR; DCR = CR + PR + SD.

Hematological markers: Before and after treatment, 5 mL of peripheral elbow venous blood was collected and centrifuged at 3000 r/min for 10 min. Serum was retained, and the levels of alpha fetal protein (AFP), carcinoma embryonic antigen (CEA), and carbohydrate antigen-125 (CA125) in serum were detected by enzyme-linked immunosorbent assay (ELISA); AFP kit was purchased from the Invitrogen company (Batch number: LS-F26670); CEA kit was purchased from the Invitrogen company (Batch number: LS-F26671); and CA125 kit was purchased from the Invitrogen company (Batch number: LS-F26672).

Follow-up and prognosis: This study mainly adopted outpatient, inpatient, and telephone follow-up methods. In the first year, outpatient reexamination was conducted every 2 months, and telephone follow-up was conducted every month. After 1 year, outpatient reexamination and telephone follow-ups were conducted every 3 months. Patients' progression-free survival (PFS) and overall survival (OS) were recorded. The starting point of follow-up was the time the patient started the treatment regimen, and the end point of follow-up was disease progression or death from any cause until December 31, 2021.

Adverse reactions: The severity of adverse events in patients enrolled in this study was evaluated according to the American Institute for Cancer Research Standard Term for Adverse Events Version 5.0 [11]. The adverse events included fever, abdominal pain, and myelosuppression.

Statistical analysis

SPSS21.0 was used to analyze the collected experimental data. The measured data following a normal distribution were represented by X ± S. The independent samples t-test was used for comparing measured data between two groups, and the F-test was used for comparison among multiple groups. The counted data were expressed as number of cases or rate, and the comparison between the two groups was done by the χ^2 test. Kruskal Wallis test was used to compare the ranked data of multiple groups, and the K-M method was used to analyze the survival differences of patients with different treatment methods. All statistical tests were two-sided, and P<0.05 was considered significant.

Results

Comparison of clinical data after PSM among three groups

There were no significant differences in gender, age, tumor burden, Child-Pugh grade, portal vein tumor thrombus, or TACE times among the three groups after PSM (all P>0.05, **Table 1**).

Comparison of short-term efficacy among three groups

No significant differences were seen in overall ORR and DCR among the three groups at the 3rd and 6th month after operation (both P>0.05, **Table 2**).

Comparison of liver function among the three groups before and one month after treatment

There were no significant differences in AST, ALT, or TBIL levels among the three groups before and one month after treatment (all P>0.05, **Table 3**).

Comparison of tumor markers before and one month after treatment among three groups

Before treatment, there were no significant differences in AFP, CEA, or CA125 levels among the three groups (all P>0.05). After treatment, the levels of AFP in the pirarubicin group and arsenic trioxide group were lower than those in the raltitrexed group (both P<0.05), but there were no significant differences in CEA or CA125 levels among the three groups (all P>0.05, **Table 4**).

Comparison of PFS and OS among three groups

There were no significant differences in overall PFS or OS among the three groups (all P>0.05, **Table 5**).

Table 1. Comparison of clinical data after PSM among the three groups

Group	Number of cases	Gender (male/female)	Age (years)	Tumor burden (single lobe/double lobe/multiple nodules)
Pirarubicin group	34	22/12	60.34±7.34	10/12/12
Raltitrexed group	34	29/5	61.86±7.53	13/9/12
Arsenic trioxide group	34	26/8	59.88±7.06	11/12/11
$F/\chi^2/H$		3.921	0.682	1.014
P-value		0.141	0.509	0.908
Group	Number of cases	Child-Pugh grade (A/B)	Portal vein cancer thrombus (with/without)	TACE times (Times)
Pirarubicin group	34	24/10	23/11	2.50±0.43
Raltitrexed group	34	26/8	21/13	2.30±0.36
Arsenic trioxide group	34	23/11	20/14	2.44±0.41
$F/\chi^2/H$		0.675	0.587	2.226
P-value		0.714	0.746	0.113

Table 2. Comparison of short-term efficacy among the three groups

Group	Number of cases	3 months after operation		6 months after operation	
		ORR	DCR	ORR	DCR
Pirarubicin group	34	21	18	11	15
Raltitrexed group	34	14	16	10	15
Arsenic trioxide group	34	22	19	10	16
Z		4.553	0.550	0.093	0.079
P		0.104	0.760	0.955	0.961

Table 3. Comparison of liver function among three groups before and one month after treatment

Group	Number of cases	AST (U/L)	ALT (U/L)	TBIL (μmol/L)
Pirarubicin group (before)	34	54.67±28.63	43.64±23.86	16.88±10.36
Raltitrexed group (before)	34	56.76±29.34	44.76±25.81	15.67±9.76
Arsenic trioxide group (before)	34	55.76±27.93	47.34±27.93	17.13±10.33
F		0.045	0.182	0.201
P		0.956	0.834	0.808
Pirarubicin group (after)	34	50.36±25.34	39.39±22.18	14.34±8.67
Raltitrexed group (after)	34	51.39±24.67	41.97±24.46	14.97±7.96
Arsenic trioxide group (after)	34	52.96±25.96	45.96±26.79	15.36±9.67
F		0.091	0.618	0.116
P		0.913	0.541	0.890

Comparison of adverse reaction rates among the three groups

There were no statistical differences in the incidence of fever, abdominal pain, or myelosuppression among the three groups (all P>0.05, **Table 6**).

Discussion

Liver cancer is one of the most common malignant tumors in clinical practice. Since this disease lacks specific early clinical symptoms, most patients have been in the middle and advanced stages when diagnosed [9]. TACE is

Table 4. Comparison of tumor markers before and one month after treatment among the three groups

Group	Number of cases	AFP (μg/L)	CEA (μg/L)	CA125 (kU/mL)
Pirarubicin group (before)	34	240.64±23.64	22.43±4.65	55.87±4.35
Raltitrexed group (before)	34	238.76±21.86	21.99±4.39	54.99±4.58
Arsenic trioxide group (before)	34	243.52±20.99	22.60±4.55	55.18±5.63
F		0.397	0.1647	0.305
P		0.673	0.849	0.737
Pirarubicin group (after)	34	186.64±18.69	16.34±5.88	28.86±5.34
Raltitrexed group (after)	34	200.34±19.83	16.08±5.38	30.15±4.99
Arsenic trioxide group (after)	34	180.79±17.64	15.76±5.10	30.33±5.38
F		9.746	0.096	0.796
P		<0.001	0.908	0.454

Table 5. Comparison of PFS and OS among the three groups

Group	Number of cases	PFS (months)	OS (months)
Pirarubicin group	34	10.64±3.31	30.64±5.33
Raltitrexed group	34	8.97±2.64	27.66±4.86
Arsenic trioxide group	34	10.30±3.53	28.97±5.34
F		2.615	2.825
P		0.078	0.064

Table 6. Comparison of incidence of adverse reactions among the three groups

Group	Number of cases	Fever	Abdominal pain	Myelosuppression
Pirarubicin group	34	7	16	4
Raltitrexed group	34	7	13	5
Arsenic trioxide group	34	8	14	4
Z		0.116	2.647	0.176
P		0.944	0.266	0.916

the primary treatment for middle and advanced liver cancer in China. The main embolization materials of conventional TACE are iodized oil and chemotherapy emulsion, with mediocre long-term efficacy. Moreover, repeated entry of chemotherapy drugs into the systemic circulation is likely to increase the incidence of systemic adverse reactions in patients [10]. Drug-eluting beads (DEB)-TACE is a new chemoembolization method that can simultaneously consider chemotherapy perfusion and arterial embolization. Its mechanism of action lies in the interaction between cationic and anion groups in drug-loaded microspheres and the structure of chemotherapy drugs, which can continuously input a specific concentration of chemotherapy drugs into the tumor [11]. Presently, drug-loaded microspheres include DC/LC-Bead and HepaSphere in foreign countries. At the same time, domestic CalliSpheres drug-eluting beads (C-DEB) can accurately embolize tumor vascular bed while slowly releasing drugs [12]. A previous study [13] has pointed out that C-DEB has significantly better efficacy in local tumor control and prolongs the survival of patients more than traditional TACE in treating liver cancer. C-DEB attracts positively charged chemotherapeutic drugs mainly through its own negatively charged ion mass, so conventionally loaded drugs include anthracyclines, such as doxorubicin, epirubicin, and pirarubicin. A study has reported loaded drugs such as ratetrexed and arsenic trioxide [14]. It has been reported in the literature [15] that DEB loaded with arsenic trioxide can inhibit MHCC97H and HepG2 cells by inhibiting the high expression of mRNA and VEGF, and the maximum drug loading rate is about 23%. As a new cyto-

toxic drug, raltitrexed can inhibit the DNA synthesis of tumor cells by explicitly inhibiting thymidine synthase, resulting in an anti-tumor effect. It can also be applied to TACE treatment of liver cancer. C-DEB can load raltitrexed with a maximum drug loading rate of 60%. The drug release rates of the three drugs were different. The drug release rate was 50% for pirarubicin, 80% for raltitrexed, and 31.4% for arsenic trioxide at 0.5 h.

Due to the differences in the efficacy of different drug loading, the present study mainly compared the efficacy of different drug-loading chemoembolization in the treatment of HCC and explored the impact of different drugs on the tumor burden.

In this study, PSM was performed to analyze the efficacy of C-DEBs loaded with pirarubicin, raltitrexed, or arsenic trioxide respectively in the treatment of patients with HCC. The results showed no significant differences in ORR and DCR among the three groups at 3rd and 6th month after operation, which is basically consistent with the results reported by Duan et al. [16]. The ORR of the pirarubicin group and arsenic trioxide group at 3rd and 6th month after operation were higher than those of the raltitrexed group, suggesting that the short-term efficacy of C-DEBs loaded with pirarubicin, or arsenic trioxide was slightly better than that with raltitrexed. The reason may be that the anti-tumor mechanisms of different loading drugs are different. Pirarubicin and arsenic trioxide both interfere with DNA and mRNA synthesis of tumor cells and have high anti-tumor activity [17, 18]. In addition, the anti-tumor mechanism of drugs is different. Raltitrexed inhibits only tumor cell DNA synthesis, while pirarubicin and arsenic trioxide can interfere with tumor cell DNA and mRNA synthesis, with a strong anti-tumor activity. At the same time, if the surgeon in DEB-TACE surgery can achieve accurate super-selection without missing parasitic blood vessels, this will also have an impact on efficacy. Raltitrexed inhibits DNA synthesis only in tumor cells, and the drug is released quickly in large quantities from the microspheres, so it cannot act on the tumor site for a long time, which has a certain impact on its short-term efficacy [10, 19].

Tumor markers are the most common means to evaluate the severity of cancer patients in clinical practice besides histopathological examination [20]. OS and PFS were the leading observation indicators in this study. The results of this study show that AFP in the pirarubicin group and arsenic trioxide group was lower than that in the raltitrexed group after treatment, but no significant differences were observed in CEA and CA125 levels, which is similar to previous reports. There were no significant differences in overall PFS and OS among the three groups. The systematic treatment with different protocols of most of the cases in this study may have a particular impact on the results. In the results of this study, no significant differences were seen in the incidence of fever, abdominal pain, or myelosuppression among the three groups, which is also consistent with previous reports.

In conclusion, DEB-TACE loaded with pirarubicin, raltitrexed, or arsenic trioxide in the treatment of HCC were generally equivalent, and patients had similar survival benefits. The short-term efficacy of the pirarubicin group and arsenic trioxide group were slightly better than that of the raltitrexed group. Since the treatment of liver cancer emphasizes the individuality and the combination of multiple means, it is suggested to take interventional therapy as the basis by supplementing it with other treatment strategies such as immunotherapy and targeted therapy.

Disclosure of conflict of interest

None.

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References

[1] Zhang X, Zhou J, Zhu DD, Huang J, Sun JH, Li TF, Shi CS, Sun ZC, Hou QM, Peng ZY, Yu WQ, Ji JS, Gu WJ, Zhou GH, Xie XX, Guo XH, Cao GH, Yu ZH, Xu HH, Fang J, Ying SH, Hu WH, Ji WB, Han J, Wu X, Zheng JP, Luo J, Chen YT, Hu TY, Li L, Hu HJ, Du HJ and Shao GL. CalliSpheres® drug-eluting beads (DEB) transarterial chemoembolization (TACE) is equally efficient and safe in liver cancer patients with different times of previous conventional TACE treatments: a result from CTILC study. Clin Transl Oncol 2019; 21: 167-177.

[2] Tipaldi MA, Ronconi E, Lucertini E, Krokidis M, Zerunian M, Polidori T, Begini P, Marignani M, Mazzuca F, Caruso D, Rossi M and Laghi A. Hepatocellular carcinoma drug-eluting bead transarterial chemoembolization (DEB-TACE): outcome analysis using a model based on pre-treatment CT texture features. Diagnostics (Basel) 2021; 11: 956.
[3] Tamura M, Nakatsuka S, Torikai H, Misu M, Tsukada J, Tamura K, Ito N, Inoue M, Yashiro H and Jinzaki M. Portal vein damage after DEB-TACE and lipiodol-TACE: based on evaluation by computed tomography during arterial portography. Interv Radiol (Higashimatsuyama) 2021; 6: 93-101.
[4] Zhu D, Yuan D, Wang Z and Chen S. Efficacy of drug-eluting bead transarterial chemoembolization (DEB-TACE) combined with radiofrequency ablation versus DEB-TACE alone in Chinese hepatocellular carcinoma patients. Medicine (Baltimore) 2019; 98: e15682.
[5] Ding X, Sun W, Li W, Shen Y, Guo X, Teng Y, Liu X, Zheng L, Li W and Chen J. Transarterial chemoembolization plus lenvatinib versus transarterial chemoembolization plus sorafenib as first-line treatment for hepatocellular carcinoma with portal vein tumor thrombus: a prospective randomized study. Cancer 2021; 127: 3782-3793.
[6] Chang Y, Jeong SW, Young Jang J and Jae Kim Y. Recent updates of transarterial chemoembolilzation in hepatocellular carcinoma. Int J Mol Sci 2020; 21: 8165.
[7] Miyayama S. Ultraselective conventional transarterial chemoembolization: when and how? Clin Mol Hepatol 2019; 25: 344-353.
[8] Dimitroulis D, Damaskos C, Valsami S, Davakis S, Garmpis N, Spartalis E, Athanasiou A, Moris D, Sakellariou S, Kykalos S, Tsourouflis G, Garmpi A, Delladetsima I, Kontzoglou K and Kouraklis G. From diagnosis to treatment of hepatocellular carcinoma: an epidemic problem for both developed and developing world. World J Gastroenterol 2017; 23: 5282-5294.
[9] Marcacuzco Quinto A, Nutu OA, San Román Manso R, Justo Alonso I, Calvo Pulido J, Manrique Municio A, García-Sesma Á, Loinaz Segurola C, Martínez Caballero J and Jiménez Romero LC. Complications of transarterial chemoembolization (TACE) in the treatment of liver tumors. Cir Esp (Engl Ed) 2018; 96: 560-567.
[10] Bargellini I, Lorenzoni V, Lorenzoni G, Scalise P, Andreozzi G, Bozzi E, Giorgi L, Cervelli R, Scandiffio R, Perrone O, Meccia DV, Boccuzzi A, Daviddi F, Cicorelli A, Lunardi A, Crocetti L, Turchetti G and Cioni R. Duration of response after DEB-TACE compared to lipiodol-TACE in HCC-naïve patients: a propensity score matching analysis. Eur Radiol 2021; 31: 7512-7522.
[11] Schobert IT, Savic LJ, Chapiro J, Bousabarah K, Chen E, Laage-Gaupp F, Tefera J, Nezami N, Lin M, Pollak J and Schlachter T. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as predictors of tumor response in hepatocellular carcinoma after DEB-TACE. Eur Radiol 2020; 30: 5663-5673.
[12] Fu Z, Li X, Zhong J, Chen X, Cao K, Ding N, Liu L, Zhang X, Zhai J and Qu Z. Lenvatinib in combination with transarterial chemoembolization for treatment of unresectable hepatocellular carcinoma (uHCC): a retrospective controlled study. Hepatol Int 2021; 15: 663-675.
[13] Ghanaati H, Mohammadifard M and Mohammadifard M. A review of applying transarterial chemoembolization (TACE) method for management of hepatocellular carcinoma. J Family Med Prim Care 2021; 10: 3553-3560.
[14] Heianna J, Makino W, Toguchi M, Iraha T, Ishikawa K, Kusada T, Maemoto H, Takehara S, Ariga T and Murayama S. Transarterial chemoembolization for the palliation of painful bone metastases refractory to first-line radiotherapy. J Vasc Interv Radiol 2021; 32: 384-392.
[15] Zhou G, Li Y, Li S, Liu H, Xu F, Lai X, Zhang Q, Xu J and Wan S. Circulating cell-free mtDNA content as a non-invasive prognostic biomarker in HCC patients receiving TACE and traditional Chinese medicine. Front Genet 2021; 12: 719451.
[16] Duan XH, Ju SG, Han XW, Ren JZ, Li FY, Chen PF, Wu YY and Li H. Arsenic trioxide-eluting Callispheres beads is more effective and equally tolerant compared with arsenic trioxide/lipiodol emulsion in the transcatheter arterial chemoembolization treatment for unresectable hepatocellular carcinoma patients. Eur Rev Med Pharmacol Sci 2020; 24: 1468-1480.
[17] Hou JP, Shi YB, Fu YF and Li H. I-125 seeds insertion with TACE for advanced HCC: a meta-analysis of randomized controlled trials. Minim Invasive Ther Allied Technol 2022; 31: 848-855.
[18] Kong C, Zhao Z, Chen W, Lv X, Shu G, Ye M, Song J, Ying X, Weng Q, Weng W, Fang S, Chen M, Tu J and Ji J. Prediction of tumor response via a pretreatment MRI radiomics-based nomogram in HCC treated with TACE. Eur Radiol 2021; 31: 7500-7511.
[19] Ivanics T, Salinas-Miranda E, Abreu P, Khalvati F, Namdar K, Dong X, Deniffel D, Gorgen A, Erdman L, Jhaveri K, Haider M, Veit-Haibach P and Sapisochin G. A pre-TACE radiomics model to predict HCC progression and recurrence in liver transplantation: a pilot study on a novel biomarker. Transplantation 2021; 105: 2435-2444.
[20] Fan W, Guo J, Zhu B, Wang S, Yu L, Huang W, Fan H, Li F, Wu Y, Zhao Y, Wang Y, Xue M, Wang H and Li J. Drug-eluting beads TACE is safe and non-inferior to conventional TACE in HCC patients with TIPS. Eur Radiol 2021; 31: 8291-8301.