# Drug-eluting Bead transarterial chemoembolization in patients with renal carcinoma

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**Research**

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## Abstract

# Background

This study aimed to investigate the efficacy,safety and outcomes of patients with renal carcinoma treated by transarterial chemoembolization using drug eluting beads.

# Methods

Between 2017 and 2020,37 patients(mean age:70.2 years(33–92 years)) with renal carcinoma were enrolled in this study who were treated by transarterial chemoembolization(TACE)using pirarubicin-loaded beads.Clinical response was evaluated according to modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria.The occurrence of adverse reactions was used to assess safety.Overall survival(OS), progression-free survival(PFS) were also calculated based on Kaplan–Meier method.

# Results

All patients were treated with drug-eluting Bead transarterial chemoembolization(DEB-TACE) loaded with pirarubicin using CalliSpheres beads.The objective response rate(ORR) and disease control rate(DCR) were 75.7% and 91.9% respectively at 1 month after DEB-TACE.The median PFS was 13.2 months (95% CI:5.9–20.5 months), and the median OS was 23.6 months (95% CI:18.5–28.7 months).Among the 37 patients,12 had flank pain,5 had fever,5 had nausea and vomiting and 4 had hypertension.There were no serious adverse events.

# Conclusion

DEB-TACE is a safe and feasible treatment for patients with renal carcinoma.

## Background

Renal carcinoma is one of the most common malignancies,it ranks ninth among the most common malignancies in men and 14th among women[1].Surgical approaches are the most common treatment for the early stage patients,but about 30% of patients have metastatic disease at presentation,and metastasis was found during surgery in 40 percent of patients[2].So Surgical treatments are not suitable for patients who have large unresectable or metastatic tumours,and those who do not want to undergo traditional surgery.Along with the development of treatment,the potential role of catheter-guided transarterial embolization(TAE) has been brought to renewed attention[3].For example, catheter-guided, renal artery embolization has become a safe and accepted treatment for renal trauma and renal angiomyolipoma[4].However,the role of TAE in the treatment of renal carcinoma is not well understood.Transarterial chemoembolization with drug-eluting beads kills tumor cells via the slow release

of chemotherapy drugs after embolization of the tumor area.As a new embolization material,the safety and efficacy of drug-eluting beads in the treatment of hepatocellular carcinoma have been well demonstrated[5–6].In this study,we evaluate the feasibility,safety,and cytoreductive effect of transarterial chemoembolization on renal carcinoma,using drug-eluting beads saturated with pirarubicin.

# Patients And Methods

## Patients

A total of 37 patients with renal carcinoma who received transarterial chemoembolization with drug-eluting beads at Affiliated Hospital of Jining Medical University between January 2017 and January 2020.Inclusion criteria were:(1)Unresectable or refused to receive surgery;(2)Eastern Cooperative Oncology Group(ECOG)performance status≤2;(3)No contraindication to chemoembolization.Exclusion criteria were:(1)Allergic to contrast medium and pirarubicin;(2)Glomerular fifiltration rate<45mL/min; (3)Coagulation abnormalities that were difficult to correct.

This study was approved by the Ethical Committee of Affiliated Hospital of Jining Medical University and followed the Declaration of Helsinki principles. All patients signed the informed consents.

## Methods

A 5-F sheath was placed in the right femoral artery by Seldinger technique after disinfection and local anesthesia.Under DSA fluoroscopy,Cobra catheter was guided to the affected renal artery via the guidewire and angiography was performed,so as to determine the location of the lesion and blood supply. Then,the microcatheter was used to select the target vessel.Once the arteries supplying the tumor are selected,angiography was performed again to confirm catheter location prior to embolization.In the chemoembolization procedure, CalliSpheres microspheres(CSM)(Jiangsu Hengrui Medicine Co,Ltd,Jiangsu Province,China) with diameters of 100 to 300 μm were used as chemoembolization reagent carriers and embolization agents.And the CSM were loaded with pirarubicin (60 or 80 mg, 20 mg/mL;Shenzhen Main Luck Pharmaceuticals Inc, Guangdong Province, China)and mixed with high concentration contrast agent as 1:1,1:1.1,or 1:1.2 ratio.Subsequently,the

CSM were infused into the target vessel through the microcatheter by pulse injection,when the flow of contrast agent stagnated,the embolization was stopped.After the embolization,the microcatheter was pulled out,and the wound was pressed for hemostasis and then bandaged.Another time of angiography was performed to detect if there was incomplete embolization.

## Evaluation of Efficacy and Safety

All of the patients underwent contrast-enhanced computed tomography(CT) (Figure 1A)or enhanced magnetic resonance imaging (MRI)prior to endovascular treatment and at follow-up.Tumor response was assessed by enhanced CT or MRI(Figure 1B) according to the modifified Response Evaluation Criteria in Solid Tumors(mRECIST)[7-8],including complete response(CR),partial response(PR),stable disease(SD),or

progressive disease(PD).The adverse events were assessed during and after the treatment.Patients were followed up by outpatient visit or phone calls with the last follow-up date on 30 June 2020.Progression free survival(PFS) is the duration from treatment time to the date of disease progression, and overall survival(OS) is the duration from treatment time to the date of death. Kaplan-Meier curves were performed to evaluate the PFS and OS.Statistical analysis was performed using SPSS 22.0 software (IBM, USA). Data was presented as count, count (%).

# Results

### Patient Characteristics

37 eligible patients were enrolled in this study.The patient characteristics are shown in Table 1.Median age was 70.2 years(range:33-92 years among 18 males and 19 females.The number of patients with an Eastern Cooperative Oncology Group(ECOG) performance status of 0,1,2 was 7(18.9%),20(54.1%) and 10(27.0%),respectively.

### Safety

The post-embolisation syndrome occurs 1-3 days after DEB-TACE operation(Table 2).12(32.4%) patients had flank pain,5(13.5%) patients had fever,5(13.5%) patients had nausea and vomiting,and 4(10.8%) patients had hypertension.All the symptoms were significantly relieved by clinical treatment.

### Tumor response

Response to treatment was evaluated at 1 month after endovascular procedure,and the results are shown in Table 3.7(18.9%) patients achieved CR and 21(56.8%) patients achieved PR after DEB-TACE treatment,with ORR of 75.7% and DCR of 91.9%.In addition,6(16.2%) patients were SD,while 3(8.1%) patient with disease progressed(PD).

Kaplan-Meier curves for OS and PFS are depicted in Figure 2 and Figure 3.The median PFS was 13.2 months (95% CI:5.9-20.5 months), and the median OS was 23.6 months (95% CI:18.5-28.7 months).

# Discussion

Renal carcinoma is a common malignant tumor in the urinary system.Due to the poor effect of radiotherapy and chemotherapy,surgical resection is the main treatment method[9].But for the patients who are not suitable for surgical resection,interventional therapy has become the major strategy for treatment. Renal arterial chemoembolization is one kind of interventional therapy,Iodide oil was first mixed with chemotherapy drugs and was injected into the tumor-feeding artery,good embolization effect was achieved,and resulting in tumor necrosis in different degrees[10].Drug-eluting beads as a novel drug delivery and embolization material,which are capable of being impregnated with anti-tumor drugs and continuously delivering the drugs, accomplishing more stable and constant drug concentration[11].

Drug-eluting beads have been widely used in the treatment of liver cancer,and it has been shown to prolong the patient's survival[12–15].However,the efficacy of pirarubicin-loaded microspheres in the treatment of renal carcinoma remains unclear.

According to previous studies,the smaller size of microsphere could not only embolize the smaller blood vessels in tumors, but also increase the concentration of drugs in the arterial network of the tumor[16–17].In our study, 100 to 300 μm drug-eluting beads were used in the chemoembolization procedure,we need more research to show the effect of using smaller size(75–150 μm) of microsphere.

In this study,imaging examination was used for diagnosis and prognosis of renal carcinoma.The sensitivity of CT in the diagnosis of small renal masses is higher than 90%,and nearly 100% for lesions larger than 2 cm[18].MRI is similar to CT in the sensitivity and specificity of diagnosing renal masses[19].The patients in this study were all patients who were unable or unwilling to undergo surgery,so they did not have biopsies.

The study has several limitations.Our sample size was small, mainly because CSM is a novel microsphere and the number of patients who received DEB-TACE treatment using CSM was very limited.The follow-up time was relatively short,some patients were still alive by the end of the follow-up.Our study was an observational and retrospective study and was conducted in a single center,which causes selection bias.Therefore, multi-center prospective studies with larger sample size and longer follow-up time are needed in the future, or multi-center randomized clinical trials with larger sample size and longer follow-up time.

# Conclusions

In short, DEB-TACE with pirarubicin-loaded beads is a feasible and well-tolerated treatment for patients with renal carcinoma.However, more studies are warranted to confirm these findings.

# Abbreviations

TACE
transarterial chemoembolization
mRECIST
modified Response Evaluation Criteria in Solid Tumors
OS
Overall survival
PFS
progression-free survival
DEB-TACE
drug-eluting Bead transarterial chemoembolization
ORR

objective response rate
DCR
disease control rate
TAE
transarterial embolization
ECOG
Eastern Cooperative Oncology Group
CSM
CalliSpheres microspheres
CT
computed tomography
MRI
magnetic resonance imaging
CR
complete response
PR
partial response
SD
stable disease
PD
progressive disease

# Declarations

### Ethics approval and consent to participate

This study was approved by the Ethical Committee of Affiliated Hospital of Jining Medical University and followed the Declaration of Helsinki principles. All patients signed the informed consents.

### Consent for publication

Not applicable.

### Availability of data and material

All data generated or analysed during this study are included in this published article.

### Competing interests

The authors have declared that no competing interests exist.

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**Authors' Contributions**

**Conception and design:** ZB, YQ

**Data** collection: HW,YY,XW,ZR,HS

TACE procedure: ZB, ZQ,MH,SL

**Analysis and interpretation of data :** ZB, HW

**Writing the manuscript:** ZB, HW

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# Tables

**Table 1.** Baseline characteristics of patients.

| Parameters | Patients |
|---|---|
| Median Age, Range (Years) | 70.2□33-92 |
| Male/Female | 18/19 |
| ECOG performance status | |
| 0, n (%) | 7(18.9%) |
| 1, n (%) | 20(54.1%) |
| 2, n (%) | 10(27.0%) |

Abbreviations:ECOG,Eastern Cooperative Oncology Group.

**Table 2.** Adverse Reactions.

| Adverse Reactions | n(%) |
|---|---|
| Flank pain | 12(32.4%) |
| Fever | 5(13.5%) |
| Nausea and Vomiting | 5(13.5%) |
| Hypertension | 4(10.8%) |

**Table 3.** Tumor response according to mRECIST criteria

| Parameters | n (%) |
|---|---|
| Total patients | 37(100%) |
| CR | 7(18.9%) |
| PR | 21(56.8%) |
| SD | 6(16.2%) |
| PD | 3(8.1%) |
| ORR | 28(75.7%) |
| DCR | 35(91.9%) |

Abbreviations:CR,complete response;PR,partial response;SD,stable disease;PD,progress disease;ORR,objective response rate;DCR,disease control rate.

# Figures

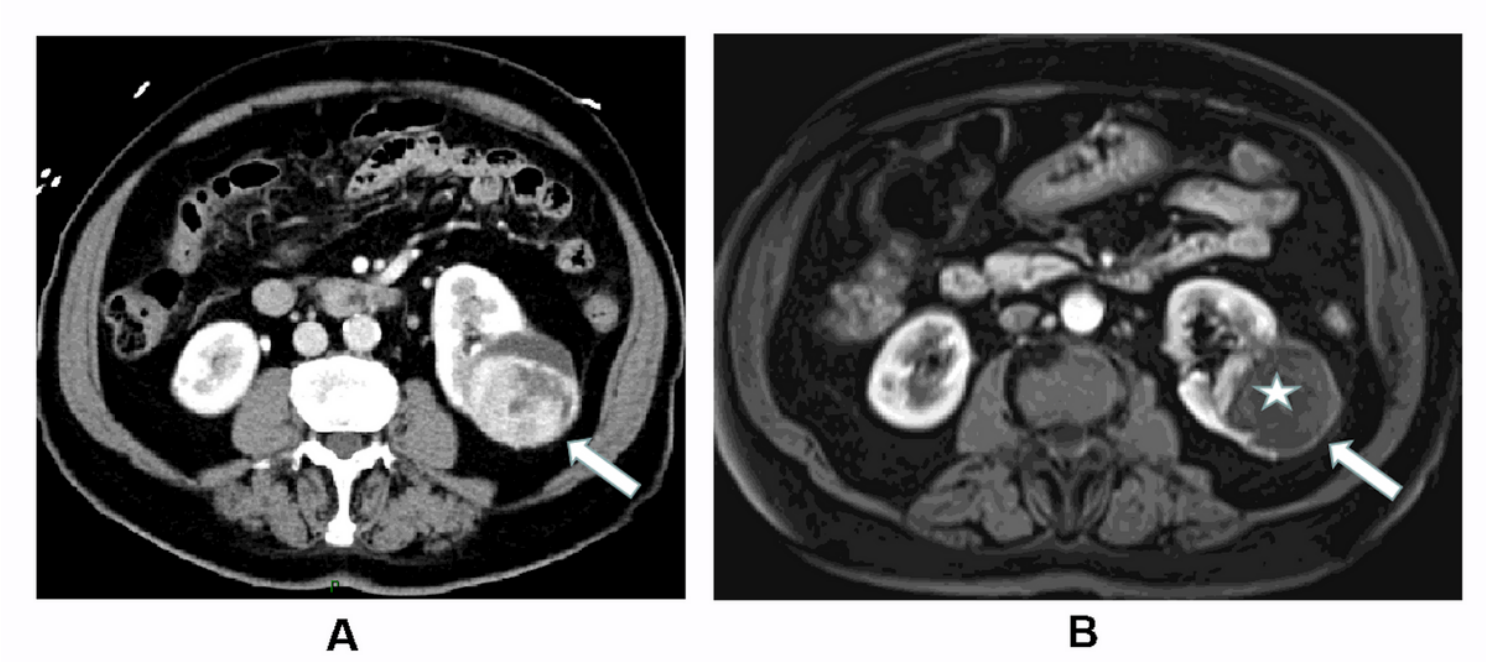
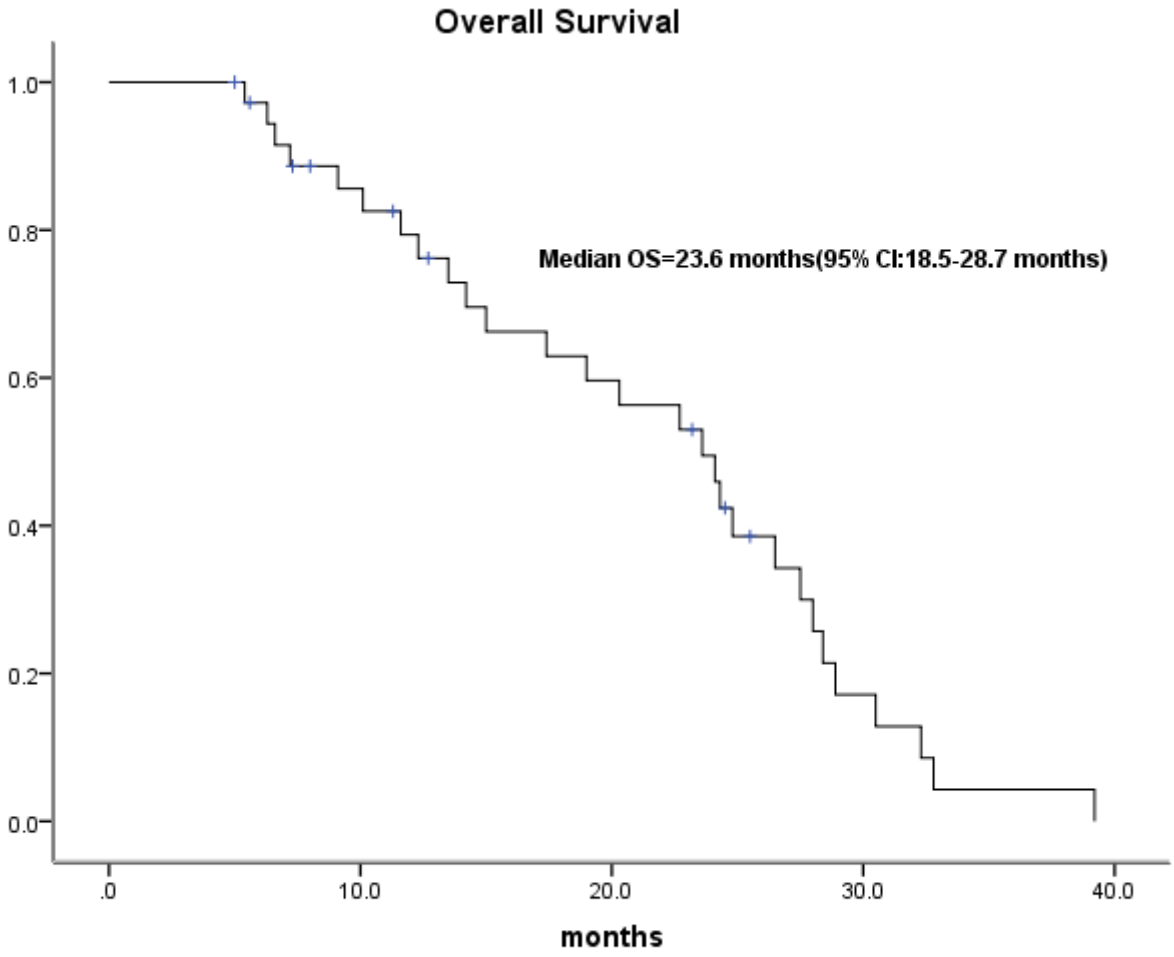


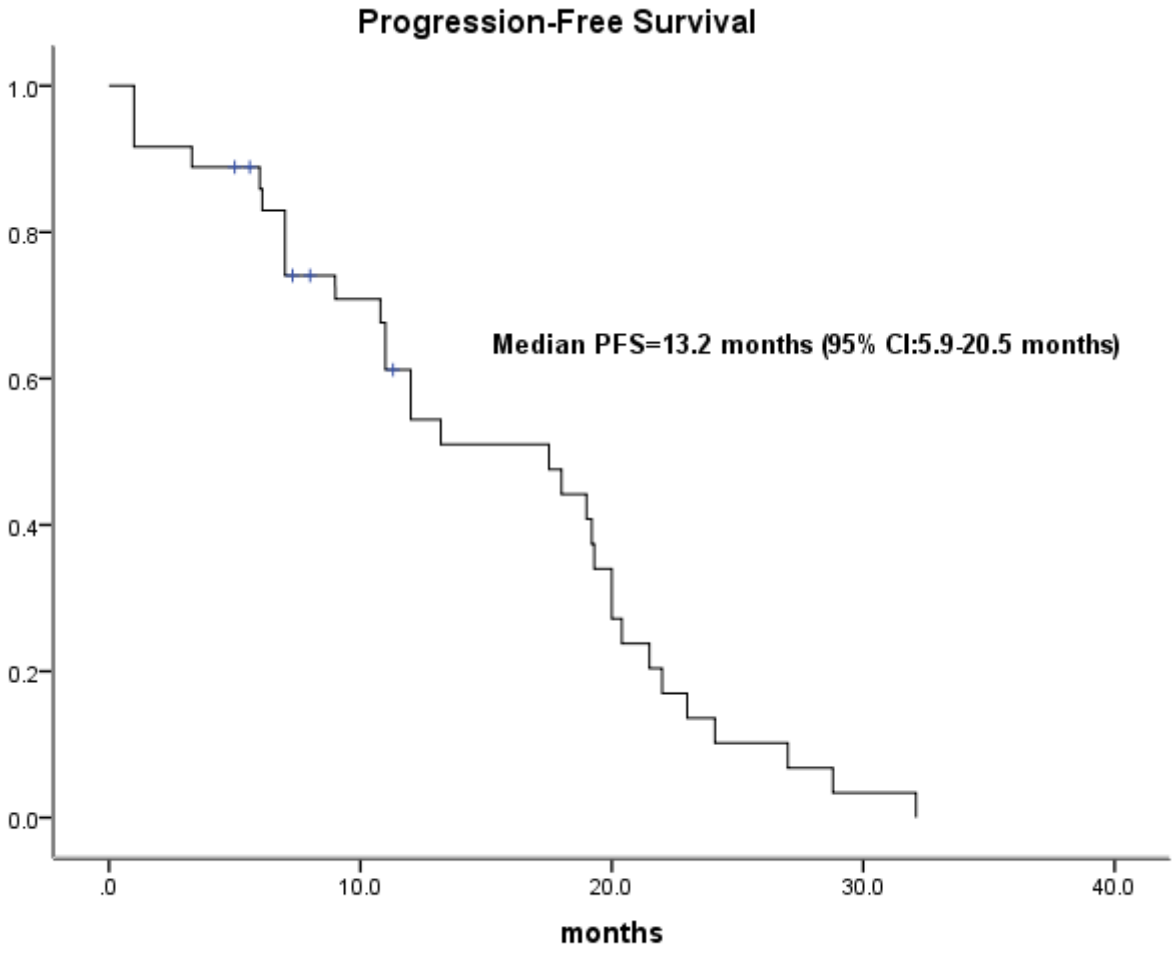

**Figure 1**

(A)Abdominal CT(arterial phase)showing a 5cm renal carcinoma(arrows) in one patient.(B)Abdominal MRI (arterial phase) performed one month after DEB-TACE showing that the tumour(arrows) reach complete response (star) upon mRECIST.




## Figure 2

Kaplan-Meier survival analysis of overall survival.




## Figure 3

Kaplan-Meier survival analysis of progression free survival.