

## **Transarterial chemoembolization in patients with hepatocellular carcinoma and renal insufficiency.**

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### **Abstract**

#### **BACKGROUND:**

Renal dysfunction is often present in patients with cirrhosis and hepatocellular carcinoma (HCC). Acute renal failure (ARF) may occur after transarterial chemoembolization (TACE) owing to radiocontrast agent. This study investigated the incidence and risk factors of ARF and prognostic predictors in HCC patients with preexisting renal insufficiency undergoing TACE.

#### **METHODS:**

A total of 566 HCC patients undergoing TACE were enrolled. Renal insufficiency was defined as an estimated glomerular filtration rate less than 60 mL/min/1.73 m.

#### **RESULTS:**

In a mean follow-up duration of 18+/-16 months, 231 (40.8%) patients undergoing TACE died. Renal insufficiency that was present in 134 (23.7%) patients at baseline, independently predicted a poor prognosis in the Cox proportional hazards model [risk ratio (RR): 1.47, P=0.012]. Of them, 13 (10%) and 6 (5%) patients had transient and prolonged ARF after TACE, respectively. Post-TACE gastrointestinal bleeding [odds ratio (OR): 16.54, P=0.001] and higher Cancer of the Liver Italian Program (CLIP) scores (> or =2; OR: 4.22, P=0.02) were independent risk factors for ARF in the multivariate logistic regression analysis. In the Cox model, prolonged ARF (RR: 3.28, P<0.001) and higher CLIP scores (> or =2; RR: 2.13, P<0.001) were independent poor prognostic predictors for HCC patients with renal insufficiency receiving TACE.

#### **CONCLUSIONS:**

Gastrointestinal bleeding and higher CLIP scores are associated with the development of ARF in patients with HCC and renal insufficiency undergoing TACE. Higher CLIP scores and renal insufficiency, either preexisting before TACE or as a complication of TACE, are poor prognostic predictors in HCC patients receiving TACE.

# Renal Failure in Patients with Hepatocellular Carcinoma and Ascites Undergoing Transarterial Chemoembolization

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## Disclosures

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## 1. Comment



## Abstract and Introduction

Patients and Methods

Results

Discussion

References

## Abstract and Introduction

### Abstract

**Background:** Ascites is often present in patients with hepatocellular carcinoma (HCC) with cirrhosis. Advanced cirrhosis may predispose to renal dysfunction. Acute renal failure (ARF) may occur after transarterial chemoembolization (TACE) for HCC because of radiocontrast agents. This study aimed to investigate the incidence and risk factors of ARF and prognostic predictors in HCC patients with ascites undergoing TACE. **Methods:** A total of 591 HCC

patients receiving TACE were enrolled. **Results:** In a mean follow-up duration of 19±17 months, 239 (40.4%) patients undergoing TACE died. Ascites, which was present in 91 (15.4%) patients at entry, independently predicted a poor prognosis in the Cox proportional hazard model [risk ratio (RR): 1.71,  $P=0.002$ ]. Of these, 11 (12.6%) of 87 patients with complete follow-up developed ARF after TACE. Serum albumin level <3.3 g/dl (odds ratio: 7.3,  $P=0.009$ ) was the only independent risk factor associated with ARF in the logistic regression analysis. ARF (RR: 2.17,  $P=0.036$ ),  $\alpha$ -fetoprotein >400 ng/ml (RR: 1.84,  $P=0.04$ ), multiple tumours (RR: 2.11,  $P=0.013$ ), tumour size  $\geq 5$  cm (RR: 2.32,  $P=0.006$ ) and serum sodium level <139 mmol/L (RR: 2.4,  $P=0.005$ ) were independent poor prognostic predictors for HCC patients with ascites receiving TACE. **Conclusions:** Pre-existing ascites is associated with increased mortality in HCC patients receiving TACE. In HCC patients with ascites, hypoalbuminaemia is associated with the occurrence of post-TACE ARF. Post-TACE ARF is a poor prognostic predictor in this subset of HCC patients.

## Introduction

Hepatocellular carcinoma (HCC) is a common malignancy in South Africa and Asia, and an increasing incidence of HCC has been observed.[1, 2] The majority of symptomatic HCC patients were diagnosed at an advanced stage and their prognosis was usually poor.[3] Among various therapeutic strategies, surgical resection remains the standard treatment modality. For patients with unresectable lesions, a better survival benefit can be achieved from liver transplantation and various forms of local treatment such as percutaneous ethanol/acetic acid injection or radiofrequency ablation. For patients who are not suitable for the aforementioned therapeutic modalities, transarterial chemoembolization (TACE) is a useful alternative anticancer treatment that may prolong survival in selected patients.[4, 5]

The oily contrast medium and chemotherapeutic agents used in TACE may result in ischaemic necrosis of HCC nodules. Nevertheless, the administration of intravascular radiocontrast agent used in the angiographic procedure such as TACE may induce renal vasoconstriction and subsequently cause acute reversible or irreversible renal injury. HCC patients frequently have coexisting cirrhosis, which is a predisposing factor for the development of renal

dysfunction because of intravascular volume depletion, inadequate renal vasoconstriction and hyperaldosteronism.[6, 7] Ascites, a common complication of cirrhosis, occurs as a result of arterial vasodilatation in advanced cirrhosis and may aggravate renal flow insufficiency.[8] Ascites and concomitant radiocontrast agent exposure could worsen renal function in patients with cirrhosis.[9] Therefore, cirrhosis with ascites formation and contrast medium used in TACE might be associated with the development of post-TACE renal injury in HCC patients. In our previous study, the cumulative incidence of acute renal failure (ARF) was up to 23.8% in HCC patients and 11% of patients suffered from prolonged renal function impairment after multiple sessions of TACE.[10] In spite of the prominent clinical importance of ascites in HCC patients receiving TACE, no study to date has specifically assessed the impact of post-TACE renal injury in patients with HCC and ascites. In this study, we have investigated the incidence and risk factors for the development of ARF in patients with ascites after TACE. Long-term survival and prognostic predictors for HCC patients with ascites undergoing TACE were determined.

## Patients

Our hospital, the Taipei Veterans General Hospital, provides primary to tertiary medical care to the residents of northern Taiwan, an area of 12 million inhabitants. During a 7-year period from 2002 to 2008, patients who underwent TACE as the primary treatment for unresectable HCC were prospectively enrolled and evaluated. Unresectable HCC nodule(s) was defined as multifocal lesions with extensive liver parenchymal involvement or insufficient hepatic reserve with an indocyanine green 15-min retention rate over 30%. All study patients fulfilled the following criteria before TACE: (i) no main portal vein trunk involvement or extrahepatic metastasis; (ii) Child–Turcotte–Pugh (CTP) functional class A or B; (iii) platelet count  $>60\,000/\text{mm}^3$ ; (iv) absence of ongoing spontaneous bacterial peritonitis. In addition, patients with recently increased abdomen girth or body weight, upward titration of diuretics, tense ascites requiring paracentesis, reduced urine output, progressive change of hepatic encephalopathy and deterioration of performance status were considered not suitable for TACE because the risk of liver failure was high. However, patients with minimal ascites, which could only be

detected by sonography or computed tomography scan but not by physical examination, patients with stable body weight and abdominal girth under consistent dosage of diuretics and patients who did not receive therapeutic paracentesis were included in this study. Because maintenance haemodialysis may hinder the analysis of the incidence of ARF after TACE, patients receiving regular haemodialysis were excluded from this study. To eliminate the cumulative effect of the contrast medium used in multiple TACE administrations, all collected data were analysed based on the first TACE session of the study patients. This study complies with the standards of the Declaration of Helsinki and current ethical guidelines.

## **Diagnosis and Definitions**

The diagnosis of HCC was histologically confirmed or based on the findings of typical radiological characteristics in at least two imaging modalities including ultrasound, contrast-enhanced dynamic computed tomography, magnetic resonance imaging and hepatic arterial angiography, or by a single positive imaging technique accompanied by serum  $\alpha$ -fetoprotein (AFP) level  $>400$  ng/ml.[4, 11] Hepatitis B virus (HBV) was regarded as the underlying aetiology of HCC if serological detection of HBsAg was positive (RIA kits; Abbott Laboratories, North Chicago, IL, USA). A diagnosis of hepatitis C virus (HCV) infection was established if patients were seropositive for an antibody against HCV (anti-HCV) by a second-generation enzyme immunoassay (Abbott Laboratories). Alcoholism was diagnosed in subjects with daily consumption of at least 40 g of alcohol for 5 years or more.[12] Ascites was recognized as free peritoneal fluid identified by ultrasound or computed tomography. The diagnosis of cirrhosis was defined as typical computed tomography or ultrasound manifestations of cirrhosis plus at least one of the following: development of ascites, hypersplenism, oesophageal or gastric varices or hepatorenal syndrome.[13] Performance status evaluation was executed at entry according to Eastern Cooperative Oncology Group criteria.

The baseline serum creatinine level was determined as the most recent creatinine measurement before TACE administration. The estimated glomerular filtration rate (eGFR) was calculated with the modification of diet in renal disease (MDRD) formula, which is

considered more accurate than other equations for eGFR from the serum creatinine level in adults and in cirrhotic patients who may have ascites.[14, 15]

The MDRD formula for males:

$$\begin{aligned} \text{GFR (ml/min/1.73 m}^2\text{)} &= 186 \times (\text{creatinine mg/dl})^{-1.154} \\ &\times (\text{age})^{-0.203} \\ &(\times 1.21 \text{ if African American}) \end{aligned}$$

The MDRD formula for females:

$$\begin{aligned} \text{GFR (ml/min/1.73 m}^2\text{)} &= 0.742 \times 186 \\ &\times (\text{creatinine mg/dl})^{-1.154} \\ &\times (\text{age})^{-0.203} \\ &(\times 1.21 \text{ if African American}) \end{aligned}$$

All patients in this study were ethnically Chinese. The equation does not require body weight because the results were reported normalized to 1.73 m<sup>2</sup> body surface area, which is an accepted average adult surface area.

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The development of ARF was defined as an abrupt elevation in the serum creatinine level of 50% or more with respect to the baseline level, or an absolute increase in the serum creatinine concentration of at least 0.5 mg/dl to a level >1.5 mg/dl within the first 7 days after TACE.[16] These criteria were chosen because cirrhotic patients with a serum creatinine concentration above this cut-off value were shown to have apparently diminished GFR,[17] and this has been the cut-off level used in the definition of hepatorenal syndrome.[18]

Concomitant nephrotoxic agents including non-steroid anti-inflammation drugs and aminoglycoside administered between 2 days

before and 3 days after TACE were recorded. Post-TACE gastrointestinal bleeding was defined as new onset of haematemesis or tarry stool occurring within 3 days after TACE, accompanied by at least a 2 g/dl decline in the haemoglobin level or upper gastrointestinal lesions confirmed by endoscopic examination. Post-embolization syndrome was defined as the collective symptoms of nausea, vomiting, abdominal pain and fever over 38 °C after TACE.

## **Treatment and Follow-up**

Seldinger's technique of arterial embolization was administered as the standard TACE procedure in our hospital.[19] The equipment for selection of proper or common hepatic artery angiography was LCN (GE Medical System; Waukesha, WI, USA) or Diagnost 3 (Philips; Amsterdam, the Netherlands). The four-French catheter (Terumo; Tokyo, Japan) was used for femoral artery puncture. Hepatic arteriography and superior mesenteric arterial portovenography were performed to localize tumour nodules. During the sequential scanning of the liver, a 100–150 ml radiocontrast agent (Telebrix; Laboratoire Guerbet; Aulnay-Sous-Bois, France or Ultravist; Schering; Berlin, Germany) was injected using a power injector (CT9000 ADV; Liebel-Flarsheim, St Louis, MO, USA) to evaluate the vascularity of the tumour (tumour stain). An infusion of a mixture of 20–30 mg adriamycin (Carlo Erba, Milan, Italy) and 5–10 ml Lipiodol (Laboratoire Guerbet) was performed after the arteries supplying the tumour were catheterized superselectively. Sufficient amount of emulsion was delivered to the tumoral area. Under fluoroscopic control, the feeding arteries were subsequently embolized with 2–3 mm strips of Gelfoam (Upjohn; Kalamazoo, MI, USA) until complete flow stagnation was achieved. After TACE, laboratory follow-up including blood cell counts and biochemical tests were assayed serially. In patients experiencing ARF (oliguria with daily urine output <500 ml and/or an increase in the serum creatinine level), albumin or fresh frozen plasma was administered as a volume expander after obstructive nephropathy was excluded by renal sonography. Post-treatment follow-up including renal sonography, dynamic imaging studies of the liver, measurement of serum biochemistries and AFP levels was performed every 2–3 months. If residual viable tumour was confirmed by dynamic imaging studies, TACE was repeatedly performed in eligible individuals.

## Statistical Methods

The  $\chi^2$ -test or Fisher's exact test (two-tailed) was performed for categorical data comparison, and continuous data were analysed by the Mann–Whitney ranked sum test. The possible risk factors associated with the development of a post-TACE renal injury were investigated using the logistic regression analysis. For risk factor and prognostic predictor analysis, continuous variables were divided by the median values and treated as dichotomous covariates, except for the factor serum AFP, because a cut-off value of 400 ng/ml for AFP has been used as a diagnostic criterion for HCC. The comparison of survival distributions and prognostic factor analysis, which were performed in all HCC patients and in patients with ascites undergoing TACE, were performed by the Kaplan–Meier method and compared by a log-rank test. Factors that were significant in the univariate analysis were introduced into the multivariate Cox proportional hazard model to determine the adjusted risk ratio. All statistical analyses were conducted using the SPSS for Windows version 14 release (SPSS Inc.; Chicago, IL, USA). For all tests, a *P* value <0.05 was considered statistically significant.]

## Characteristics of Patients Undergoing Transarterial Chemoembolization

A consecutive series of 601 patients who received TACE as their primary anti-HCC treatment were identified in our database during the study period; 10 of them were excluded because they had received regular haemodialysis before TACE. The remaining 591 patients formed the basis of the study. The mean age at entry was  $66\pm 12$  years, and 456 (77%) patients were male. The most common aetiologies of HCC were hepatitis B (47%) and hepatitis C (35%). Eighty-two percent of patients were classified as CTP class A and 307 (52%) patients had the largest tumour <5 cm in diameter. There were 295 (50%) patients who had a single HCC tumour at initial presentation.

A comparison of baseline demographics between HCC patients with and without ascites is shown in [Table 1](#). There were a total of 91

(15.4%) patients who had ascites at the time of diagnosis. The aetiology of ascites was considered to be because of cirrhosis in all patients; of these, two patients also had functional class B congestive heart failure and non-uremic renal dysfunction was recognized in 11 patients (median serum creatinine level, 1.9 mg/dl).[20] In comparison with patients without ascites, patients with ascites more often had CTP class B ( $P<0.001$ ), alcoholism ( $P=0.035$ ), a large HCC tumour ( $P=0.01$ ), vascular invasion ( $P=0.024$ ) and poor performance status ( $P<0.001$ ). In addition, ascitic patients more often had lower serum albumin ( $P<0.001$ ) and sodium ( $P=0.018$ ) levels, a higher serum bilirubin level ( $P<0.001$ ) and a prolonged prothrombin time (PT) ( $P<0.001$ ). With regard to renal function, a significantly higher serum creatinine level ( $P=0.002$ ) and lower calculated eGFR ( $P=0.004$ ) were found in HCC patients with ascites.

### **Incidence and Risk Factor Analysis of Acute Renal Failure in Hepatocellular Carcinoma Patients with Ascites**

Of the 91 HCC patients with ascites undergoing TACE, four patients who did not receive serial follow-up of serum creatinine level were excluded from the analysis. Of the remaining 87 patients, 11 (12.6%) patients developed ARF after TACE. Among these, seven patients had recovered renal function to their baseline serum creatinine levels; the other four patients suffered from persistent renal insufficiency until discharge from hospital or death. No patients received haemodialysis for post-TACE ARF. The results of the risk factor analysis are shown in [Table 2](#). Comparison of patients with and without ARF showed that a serum albumin level  $<3.3$  g/dl (82 vs. 38%) was the only risk factor for developing ARF in HCC patients with ascites [odds ratio: 7.3, 95% confidence interval (CI): 1.47–35.7,  $P=0.009$ ].

### **Survival Analysis of All Patients Undergoing TACE**

The comparison of long-term survival according to the presence of ascites in HCC patients receiving TACE is given in Figure 1. During a follow-up period of  $19\pm 17$  months, 55 (60%) patients with ascites and 184 (37%) patients without ascites died ( $P<0.001$ ). Potential prognostic predictors, including age, gender, HBV infection, HCV infection, alcoholism, CTP class, number and size of tumour nodules,

eGFR, diabetes, serum biochemistries and AFP level, performance status and vascular invasion were investigated in the survival analysis. Prognostic factors predicting a decreased survival rate included a low serum albumin level ( $P<0.001$ ), alcoholism ( $P=0.035$ ), ascites ( $P<0.001$ ), CTP class B ( $P<0.001$ ), a higher serum AFP level ( $P<0.001$ ), performance status 2–4 ( $P<0.001$ ), PT prolongation ( $P=0.011$ ), a lower serum sodium level ( $P<0.001$ ), a history of spontaneous bacterial peritonitis ( $P=0.006$ ) and vascular invasion ( $P<0.001$ ). As shown in [Table 3](#), in the adjusted Cox proportional hazard model, six factors, serum AFP level  $>400$  ng/ml [relative risk (RR): 1.84, 95% CI: 1.38–2.44,  $P<0.001$ ], serum albumin level  $<3.8$  g/dl (RR: 1.86, 95% CI: 1.4–2.47,  $P<0.001$ ), ascites (RR: 1.71, 95% CI: 1.21–2.4,  $P=0.002$ ), serum sodium level  $<140$  mmol/L (RR: 1.45, 95% CI: 1.11–1.89,  $P=0.007$ ), performance status 2–4 (RR: 1.81, 95% CI: 1.27–2.95,  $P=0.001$ ) and vascular invasion (RR: 2.19, 95% CI: 1.58–2.4,  $P<0.001$ ), were identified as independent poor prognostic predictors.

### **Survival Analysis of Patients with Ascites Undergoing Transarterial Chemoembolization**

During a follow-up period of  $17\pm 13$  months in 87 HCC patients with ascites receiving TACE, 43 (57%) of 76 patients without ARF and nine (82%) of 11 patients with ARF died respectively. Two patients who had ARF died within 1 month after TACE because of profound liver ( $n=1$ ) and renal ( $n=1$ ) failure. Survival analysis showed that patients who developed ARF had a significantly decreased survival in comparison with patients without ARF (Fig. 2). Univariate survival analysis showed that serum AFP level ( $P=0.029$ ), number of tumour ( $P=0.019$ ), size of tumour ( $P=0.005$ ), performance status ( $P=0.037$ ), ARF ( $P=0.029$ ) and serum sodium level ( $P=0.002$ ) were significant prognostic predictors. These factors were then introduced into the Cox proportional hazard model to determine the adjusted risk ratio. Serum AFP level  $>400$  ng/ml (RR: 1.84, 95% CI: 1.03–3.31,  $P=0.04$ ), multiple tumours (RR: 2.11, 95% CI: 1.17–3.82,  $P=0.013$ ), size of tumour  $\geq 5$  cm (RR: 2.32, 95% CI: 1.27–4.26,  $P=0.006$ ), serum sodium level  $<139$  mmol/L (RR: 2.40, 95% CI: 1.31–4.43,  $P=0.005$ ) and ARF (RR: 2.17, 95% CI: 1.05–4.48,  $P=0.036$ ) were independently associated with an increased mortality rate in HCC patients with ascites undergoing TACE

## Discussion

The contrast medium used in the angiographic procedure could cause acute or chronic nephropathy and was the third leading cause of ARF in hospitalized patients.[21] In addition, a variety of contributory factors including sepsis, dehydration, nephrotoxic agents and advanced cirrhosis may also be linked to a post-TACE renal injury. In cirrhotic patients, ascites was validated as an independent risk factor for development of contrast medium-related nephropathy.[9] Although TACE has been commonly used to treat unresectable HCC, very few studies have specifically investigated the outcome of HCC patients with ascites receiving TACE. In this study, we analysed 591 HCC patients and found that 15.4% of patients had ultrasound- or computed tomography-identifiable ascites before TACE. Ascites is one of the manifestations of hepatic decompensation and may affect the long-term survival in HCC patients receiving TACE.[22] However, whether ascites should be considered a contraindication of TACE or not is still open to debate. The impact of the presence of ascites on the long-term survival was determined in this study. We found that, in addition to other tumour- and cirrhosis-related prognostic predictors, HCC patients with ascites before TACE had 71% increased risk of mortality in the adjusted Cox model.

Among patients without ascites undergoing TACE for HCC, the published incidence of ARF after TACE was 6.6–8.6%.[10, 23] Importantly, our study showed a substantially increased incidence of ARF (12.6%) in patients with ascites undergoing TACE; the estimated increased risk of ARF was 47–91%. Renal dysfunction associated with chronic liver disease is commonly seen in patients with ascites. Fluid in peritoneal cavity and peripheral vasodilatation contributed to a decreased effective blood volume,[24] which further compromised renal blood flow, especially perfusion of the renal cortex.[25] As the after effect of renal hypoperfusion, activation of the renin–angiotensin system, accompanied by increased sympathetic system activity,[26, 27] upgraded antidiuretic hormone secretion and enhanced sodium and water reabsorption were observed in the kidney.[28] These mechanisms may aggravate or at least maintain ascites development and sustain the vicious cycle that compromises renal function.[8]

Contrast medium-associated nephrotoxicity is not rare in clinical practice. Several possible mechanisms have been proposed. The osmolarity and viscosity of the contrast medium could influence renal haemodynamics and result in direct toxicity against renal tubular cells.[29] The increment of adenosine and endothelin, accompanied by the decrement of prostaglandin synthesis, has been observed in radiocontrast-related renal injury.[30] Altogether, diminished renal perfusion because of insufficient effective blood volume, the activation of vasoconstrictor systems triggered by advanced cirrhosis or radiocontrast agents and inflammatory cytokines released from necrotic tumour nodules could all or in part induce the development of ARF in our patients.[31]

In patients with HCC and ascites receiving TACE, risk factor analysis showed that a low serum albumin level (<3.3 g/dl) was the only factor predicting the occurrence of ARF. Hypoalbuminaemia is highly associated with advanced cirrhosis and was associated with post-TACE hepatic failure in HCC patients.[19] Therefore, decreased liver functional reserve may play a role in post-TACE ARF via further haemodynamic impairment resulting from peripheral vasodilatation and renal vessel constriction in HCC patients with ascites. Alternatively, this result also indicates that the possible negative impact on renal function is because of a reduced effective blood volume in HCC patients with ascites.[32] A previous study reported a favourable effect on renal blood flow and GFR after the administration of albumin in cirrhosis patients.[33] In addition, patients receiving albumin infusion after therapeutic paracentesis showed significantly less changes in electrolyte and serum creatinine levels.[34] Furthermore, using albumin as a plasma expander after abdominal paracentesis may prevent subsequent activation of vasoconstrictor systems and renal function impairment.[34, 35] Consistent with these studies, our results indicate that a low serum albumin level is closely associated with the occurrence of ARF in HCC patients with ascites undergoing TACE.

Renal failure has accounted for a major cause of mortality in patients with HCC.[36] In agreement, we found that patients with post-TACE ARF had a 2.17-fold increased risk of mortality in the Cox model in comparison with patients without ARF among patients with pre-existing ascites undergoing TACE. This finding underlines the crucial

role of ARF as an important prognostic predictor in HCC patients with ascites. In this regard, previous studies suggested incorporating renal function into the prognostic models for HCC to further enhance the predictive ability.[37, 38] In addition to the renal factor, consistent with published series,[3, 5, 39] survival analysis showed that tumour- and cirrhosis-related parameters such as serum AFP level, number and size of HCC nodules, and a low serum sodium level were also important prognostic factors in predicting the long-term survival (Table 3).

In this study, patients with ascites at study entry had significantly lower serum albumin and sodium levels, and higher bilirubin and creatinine levels. The eGFR calculated by the MDRD formula showed a decreased renal function in HCC patients with ascites. In addition, ascitic patients also more often had large HCC and vascular invasion, suggesting that the cause of ascites formation could be both cirrhosis and tumour factor. Consistent with this finding is that tumour recurrence may predispose to hepatic decompensation in HCC patients undergoing surgical resection.[40] Given this, ascites was identified as an independent prognostic predictor in the survival analysis, suggesting its pivotal role in predicting the outcome of patients with HCC.

There are a few potential limitations of this study. Firstly, in this single-centre study, about half of our patients had HBV infection. This feature is distinctly different from western countries and Japan, where HCV infection is the predominant aetiology of chronic liver disease. Secondly, because many HCC patients with ascites may have been treated with on-demand diuretics that may influence renal function, the individual impact of diuretics on the outcome and survival was difficult to determine. Thirdly, the initial and subsequent anticancer treatment might be different in some patients depending on the status of tumour progression and the severity of cirrhosis during the follow-up period. This may influence the assessment of overall survival.

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In conclusion, our results indicate that ascites is often present in patients with HCC undergoing TACE and independently predicts a poor prognosis. The development of ARF after TACE is not uncommon in HCC patients with pre-existing ascites.

Hypoalbuminaemia is closely associated with development of ARF in these patients. In the subset of HCC patients with ascites, post-TACE ARF is an independent poor prognostic predictor. Future studies are warranted to evaluate the effective measures to reduce the risk of TACE-associated renal injury especially in high-risk patients.