

## Chemoembolization of Hepatocellular Carcinoma, Experience of the Radiology Department at Mohamed VI University Hospital in Marrakech

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### Abstract

### Original Research Article

**Purpose:** Review the efficiency of chemoembolization and discuss the place of this technique in the strategy of management of hepatocellular carcinoma. **Materials and Methods:** This is a retrospective and prospective study including 25 patients who received 40 sessions of lipiodolated chemoembolization for hepatocellular carcinoma between 13/07/2018 and 26/11/2021, performed at the Radiology Department of Mohamed VI Hospital in Marrakech in collaboration with our expert Pr El Hajjam from Ambroise-Paré Hospital in Paris. **Results:** The average age of the patients was 61 years, with a sex ratio of 1.4. Among the 22 patients, 21 were cirrhotic. The etiologies of cirrhosis were dominated by HVC in 10 patients (50%), followed by HVB in 7 patients (35%). The circumstances of discovery of hepatocellular carcinoma were dominated by right hypochondrial pain in 12 patients (48%). Biologically, 14 patients (56%) had secreting hepatocellular carcinoma with high AFP level. In the radiological assessment, nodules were located in the right lobe only in 15 patients (68,2%), in both right and left lobe in 5 patients (22,8%), in left lobe only in one patient (4,5%) and in the caudate lobe in one patient (4,5%). Arterial mapping on abdominal CT angiography was modal in 13 patients (59 %), whereas anatomical variations were observed in 9 patients (41%). Patients were classified according to the Barcelona clinic liver cancer classification as follows: 9 patients (41%) were classified as BCLC B, 10 patients (45,5%) were classified as BCLC C, and 3 patients (13,5%) as BCLC A. During the chemoembolization sessions, several types of catheters were used in all our patients for selective catheterization of the celiac trunk and common hepatic artery, whereas a 2.7F microcatheter was used in 14 sessions (35%) for more selective catheterization of segmental hepatic arterial branches. Embolization agents were administered to patients in 32 sessions, resorbable (gelatin) was used in 8 sessions (25%) and microparticles were used in 14 sessions (43,8%). Post-chimioembolization complications were dominated by post-embolization syndrome (chills, abdominal pain and nausea) which was reported after 25 sessions (62.5%). Response to treatment was assessed by the modified RECIST criteria: 17 patients (77,3%) had a partial response, 1 (4,5%) had progression, 1 (4,5%) had stable lesions and one patient (4,5%) had a complete response. Patient survival at 1 year was 91%, at 2 years was 86,4% and reached 81,82% at 3 years. **Conclusion:** Current advances in the field of interventional radiology aim to broaden the indications for this type of treatment and to make chemoembolization not only a first-line palliative alternative, but a true curative treatment for hepatocellular carcinoma.

**Keywords:** Chemoembolization, cirrhosis, hepatocellular carcinoma, CT, MRI, Arteriography.

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## 1. INTRODUCTION

Hepatocellular carcinoma (HCC) is a malignant epithelial tumor developed in liver parenchymal cells and is the most common primary liver cancer (85%) [1].

It is also the fifth most common cancer in the world and the second most common cause of death by cancer [2]. Its incidence is increasing and represents a major health problem worldwide.

The management of HCC must be multidisciplinary, requiring consultation between radiologists, gastroenterologists, oncologists and surgeons. Several treatments are available, some of which are curative (surgery, liver transplantation and percutaneous destruction), but for more than 60% of patients, the diagnosis is made at an advanced stage. Palliative treatment (chemoembolization and systemic chemotherapy) will then be required.

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Currently, the choice of treatment takes into account the severity of the underlying liver disease and the extent of the tumor, following the recommendations of the Barcelona Consensus Conference [3].

Chemoembolization is an interventional radiology technique that is among the main palliative treatments for HCC in patients with intermediate stage disease.

The aim of our study is to share our experience at the Mohamed VI University Hospital of Marrakech, to review the efficiency of chemoembolization and to discuss the place of this technique in the therapeutic management of HCC.

## 2. MATERIALS AND METHODS

This is a retrospective and prospective study including 22 patients who underwent 32 sessions of lipiodolated chemoembolization for HCC between 13/07/2018 and 26/11/2021, performed at the radiology department of ARRAZI hospital at Mohamed VI university in Marrakech in collaboration with our expert Pr El Hajjam from Ambroise-Paré hospital in Paris.

- Inclusion criteria:
  - HCC diagnosed by the association of a typical radiological image on a cirrhotic liver according to the Barcelona criteria adopted by the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) [4, 5].
  - Histologically proven HCC for atypical cases on imaging.
  - Patients with a normal:
    - Liver function: Child A or B.

- Renal function.
- Hemostasis assessment.
- Preanesthetic consultation.

- Exclusion criteria:
  - Advanced liver disease (Child C).
  - Very altered general state (WHO index >2).
- Equipment used:
  - Artis Zee arteriography (Siemens)
  - 64 bars CT (Siemens)
  - MRI 1.5 Tesla (Siemens)
- The informations were collected using an anonymous data collection form, the data were entered using Microsoft office Excel software and then validated for analysis by SPSS software.

## 3. RESULTS

The average age of the patients was 61 years, with a M/F sex ratio of 1.4. Among the 22 patients, 20 were cirrhotic. The etiologies of cirrhosis were dominated by HVC in 10 patients (50%), followed by HVB in 7 patients (35%).

The circumstances of discovery of HCC were dominated by right hypochondrial pain in 12 patients (48%), 8 patients (32%) had presented an oedemato-ascitic decompensation and a suspicious nodule on screening ultrasound was discovered in 4 patients (16%).

The main clinical signs were asthenia (80%), splenomegaly (40%) and moderate ascites (28%) (Table I).

**Table I: Summary table of patients' clinical information**

	Number	Percentage
<b>Sex :</b>		
Male	13	60%
Female	09	40%
Sex ratio	--	1.4
<b>Age :</b>		
Minimum	27	--
Maximum	75	--
Average age	61	--
<b>Etiologies of cirrhosis :</b>		
HVC	10	50 %
HVB	7	35 %
Co-infection B et C	2	9.6%
Etiology undetermined	1	4.8%
<b>Circumstances of discovery of HCC :</b>		
Right hypochondrial pain	12	48%
Oedematous cirrhotic decompensation	8	32%
Suspicious nodule on screening ultrasound	4	16%
Hemorrhagic cirrhotic decompensation	3	12%
Abnormalities in the biological screening test	2	8%

	Number	Percentage
Icteric cirrhotic decompensation	1	4%
<b>Clinical signs :</b>		
Asthenia	20	80%
splenomegaly	10	40%
moderate ascites	7	28%
collateral venous circulation	6	24%
hepatomegaly	6	24%
jaundice	3	12%

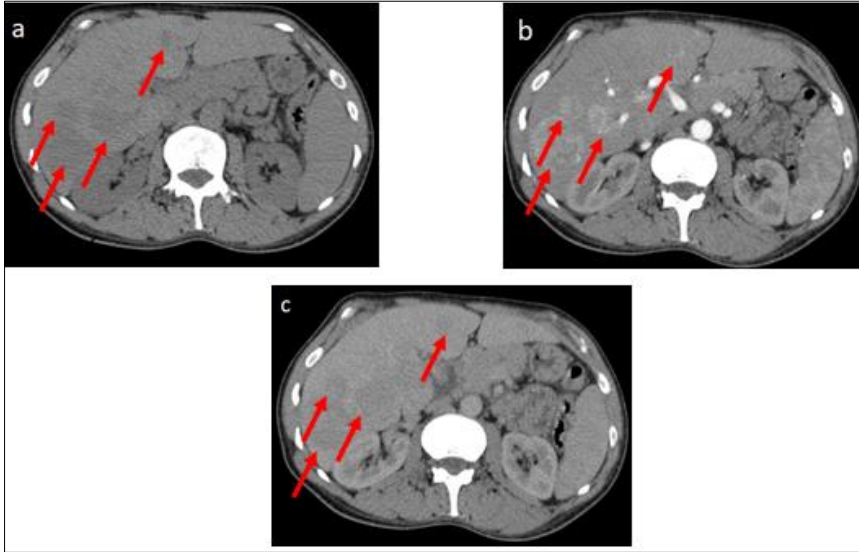
Biologically, the alpha-fetoprotein level was less than 10 ng/ml (non-secreting HCC) in 8 patients (36,7%) while 14 patients (63,3%) had secreting HCC with high AFP level.

In the radiological assessment, all our patients underwent ultrasound and abdominal CT angiography. Only 14 patients (56%) had completed their radiological assessment with a hepatic MRI before the chemoembolization session. Mono-nodular HCCs were noted in 12 patients (54,5%), bi-nodular in 4 patients

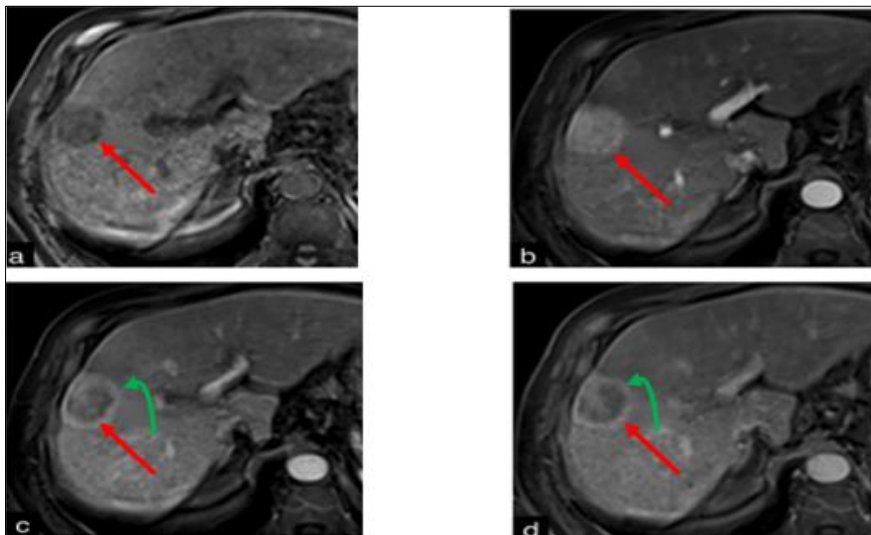
(18,2%) and multinodular in 6 patients (27,3%), located in the right lobe in 15 patients (68,2%), right and left lobe in 5 patients (22,8%), left lobe only in one patient (4,5%) and in the caudate lobe in one patient (4,5%) . A portal thrombosis was noted in 4 patients (18,2%). These patients received selective arterial chemotherapy without embolization. Arterial mapping on abdominal CT angiography was modal in 13 patients (59%), whereas anatomical variations were observed in 9 patients (41%) (Table II).

**Table II: Summary table of patients radiological information**

Parameter	Number	Percentage
<b>Number of nodules:</b>		
Mono-nodular	12	54,5%
bi-nodular	4	18,2%
Multi-nodular	6	27,3%
<b>Nodule location:</b>		
Right lobe only	15	68,2%
Right and left lobe	5	22,8%
Left lobe only	1	4,5%
Caudate lobe	1	4,5%
<b>Nodule size:</b>		
Maximum	200 mm	--
Minimum	4 mm	--
Average size	61 mm	--
<b>Scannographic appearance of the nodules:</b>		
Typical	18	81,8%
Atypical	4	18,2%
<b>Portal thrombosis :</b>		
Present	4	18,2%
Absent	18	81,8%
<b>Arterial vascular mapping :</b>		
Modal	13	59%
Anatomical variations	9	41%



**Figure 1:** Axial sections of an abdominal CT angiography without and with contrast injection illustrating spontaneously hypodense multi-nodular HCC (a), showing arterial wash-in (b) with portal wash-out (c)



**Figure 2:** Axial sections of a hepatic MRI in T1-weighted sequence with saturation of the fat signal obtained before and after injection of gadolinium at the following phases: arterial (a), portal (b), and delayed (c), showing a mononodular HCC in hyposignal T1 with hypervascularization at the arterial phase, a washout at the portal and delayed phases, surrounded by an enhanced capsule at the portal and delayed phases (ART: lirads)



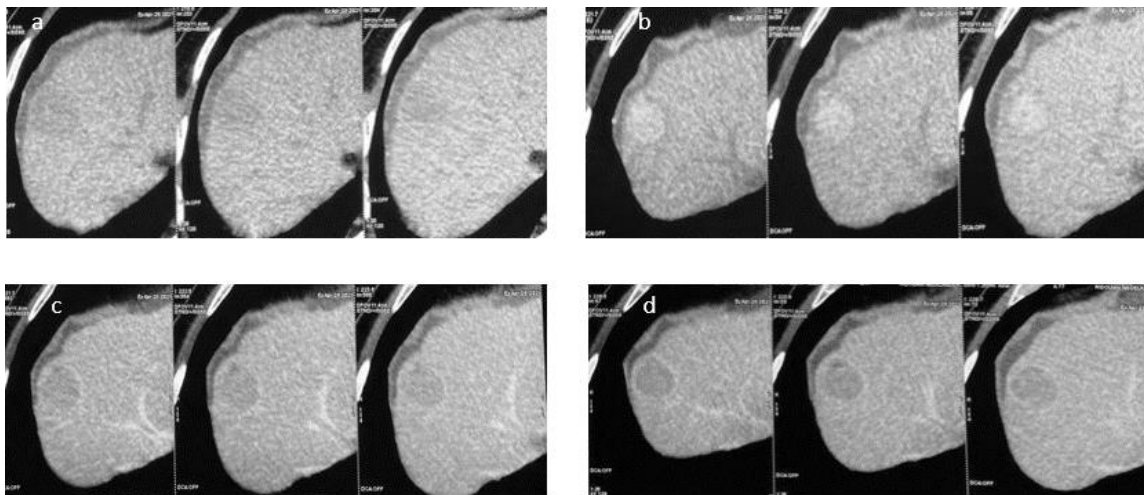
**Figure 3:** Sagittal section of an abdominal CT angiography (arterial phase) showing a common origin for the celiac trunk and the superior mesenteric artery from the aorta.

The data used in the diagnostic confirmation of HCC were the following: hepatic MRI showing a typical appearance of HCC in 11 patients (50%), abdominal CT angiography alone in the presence of characteristic vascular kinetics in favor of HCC in 18 patients (81,8 %). The diagnosis of HCC was confirmed by histological data (hepatic biopsy) in 4 patients in our series (18,2%).

Patients were classified according to the Barcelona clinic liver cancer classification as follows: 9 patients (41%) were classified as BCLC B, 10 patients

(45,5%) were classified as BCLC C, and 3 patients (13,5%) as BCLC A.

Regarding the therapeutic aspect 16 patients in our series received lipiodolated chemoembolization alone, 5 with absolute contraindications to embolization had received selective arterial chemotherapy without embolization, 2 had received oral chemotherapy before the chemoembolization session and 2 other patients with HCCs ranging in size from 3 to 5 cm had received a combined treatment: lipiodolated chemoembolization associated with radiofrequency during the same session (Figure 4-6).

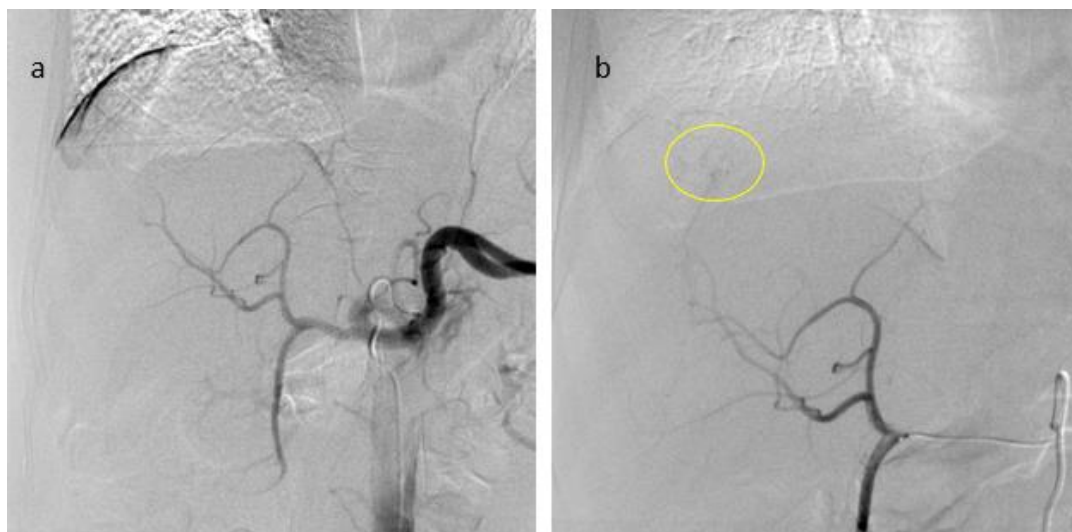


**Figure 4: Abdominal CT angiography of 75-year-old patient, followed for liver cirrhosis of undetermined etiology complicated by a subcapsular HCC transplant of the hepatic dome**

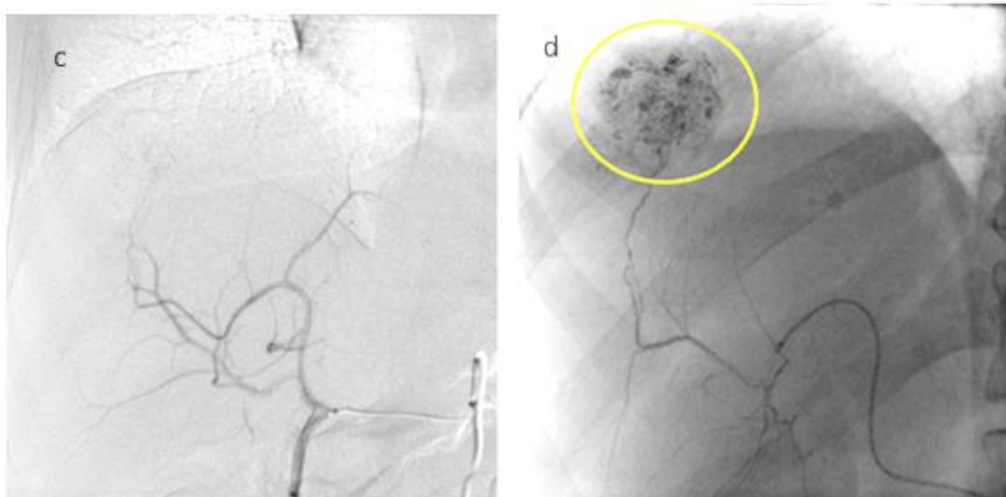
It's showing a well-limited nodular lesion, spontaneously hypodense (a), intensely and homogeneously enhanced at the arterial phase (b) with washout at the portal (c) and the late phase (d) and a

peripheral capsule enhancement at the portal phase (c) persisting at delayed phase (d) (LIRADS 5)

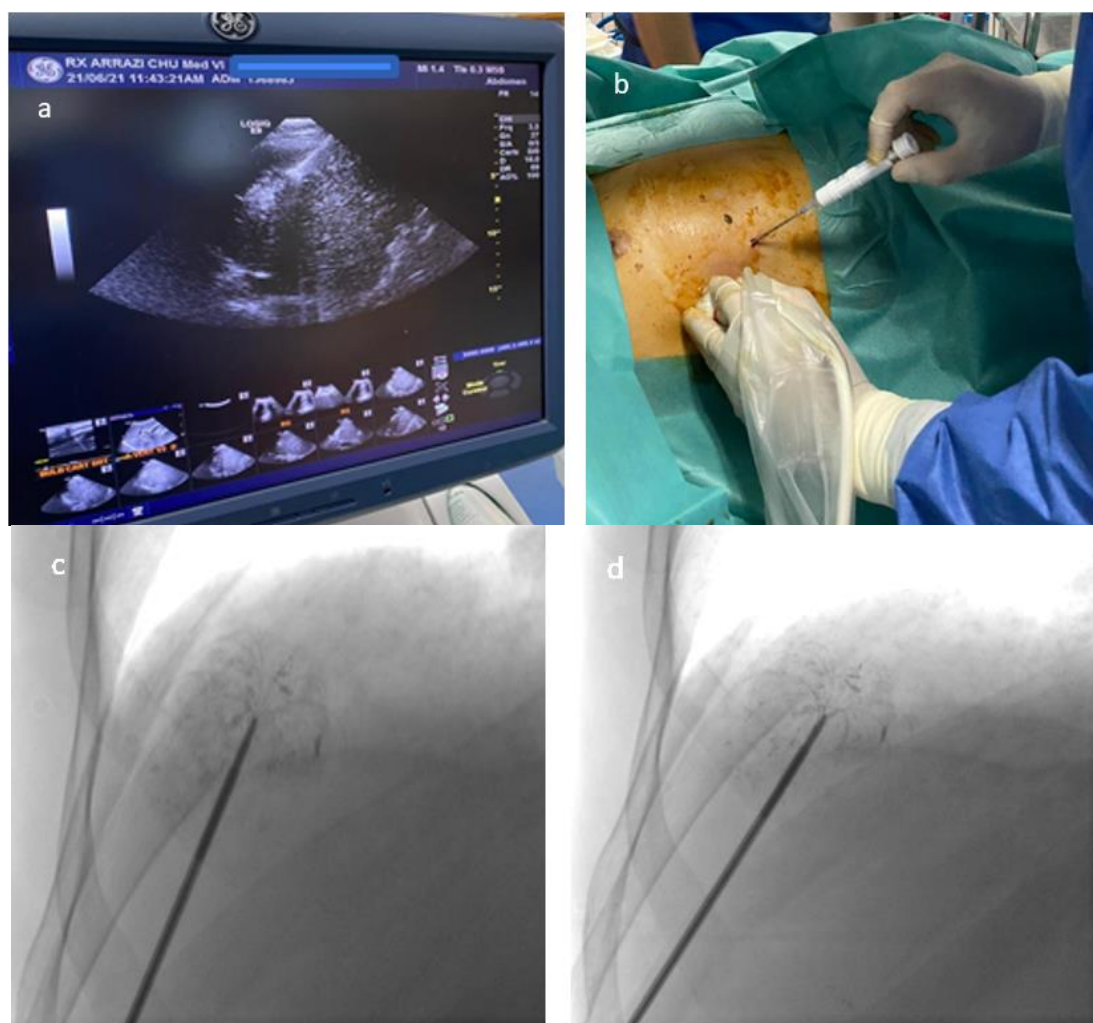
A session combining lipiodolated chemoembolization and radiofrequency at the same operative time was indicated for this patient.







**Figure 5: 1st stage of treatment: chemoembolization: a: Opacification of the celiac trunk shows a modal hepatic arterial pattern. b: Catheterization of the right hepatic artery with opacification of a blush at the level of the hepatic dome. c: Administration of chemolipiodolate emulsion at this level completed by embolization with microparticles until stagnation of the emulsion within the lesion and stagnation of the flow at the arterial level. d: Satisfying angiographic control**



**Figure 6: 2nd stage of treatment: Biopsy + Radiofrequency: a: Under ultrasound and scopic control, placement of the coaxial at the level of the lesion of the hepatic dome; b: Intratumoral biopsy; c, d: Treatment by radiofrequency with a deployable whalebone device in two steps 180w in 15 minutes and 40w in 1 minute on the lower lesion edge**

The steps for performing the lipiodolated chemoembolization were as follows:  
After locating the femoral pulse, local anesthesia at the puncture site was performed

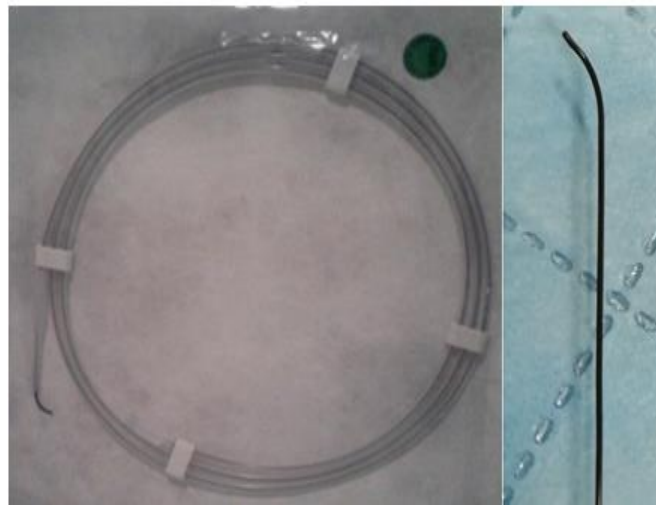
The right common femoral artery was punctured with a teflon-coated 18-gauge needle below the crural arch at an angle of approximately 60° (Figure 7).



**Figure 7: 18G Teflon coated puncture needle**

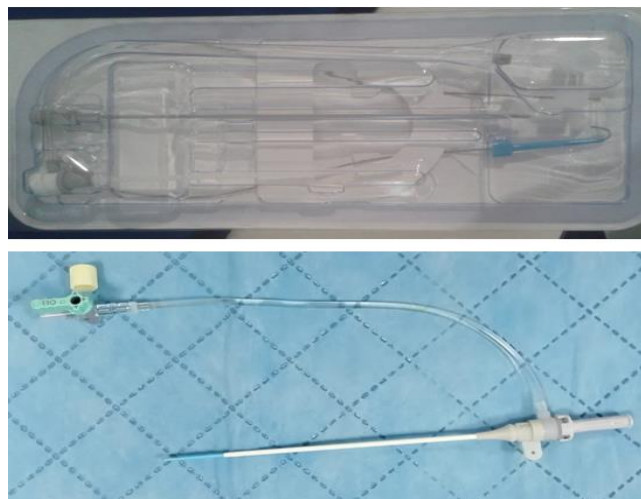
The guidewire was inserted into the cannula and then pushed into the aorta by its soft tip. The

cannula was removed with compression of the puncture site (Figure 8).



**Figure 8: Hydrophilic guide 0.035. 180cm**

A Desilet was inserted to dilate the puncture site and to reduce trauma caused by the catheter's back and forth motion (Figure 9).



**Figure 9: Desilet 5F**

During the chemoembolization sessions, several types of catheters were used in all our patients for selective catheterization of the celiac trunk and common hepatic artery (figure10-11), whereas a 2.7F

microcatheter (Figure 12) was used in 11 sessions (34,4%) for more selective catheterization of segmental hepatic arterial branches.



Figure 10: COBRA C2 glide 5F catheter



Figure 11: Simmons 1 5F catheter



Figure 12: Microcatheter Progreat® 2.7

The chemotherapy molecule used was doxorubicin in 32 sessions (70%) and farmorubicin in 12 sessions (37,5%) with a dose of 50 milligram.

The volume of lipiodol administered to all patients was 10 milliliter.

The emulsion of Lipiodol with anticancer agent was prepared just before injection, obtained after ten rapid successive passages of the contents of one 50mL luer lock syringe to the other using a three-way valve, and then the injection was performed in ten minutes (Figure 13).





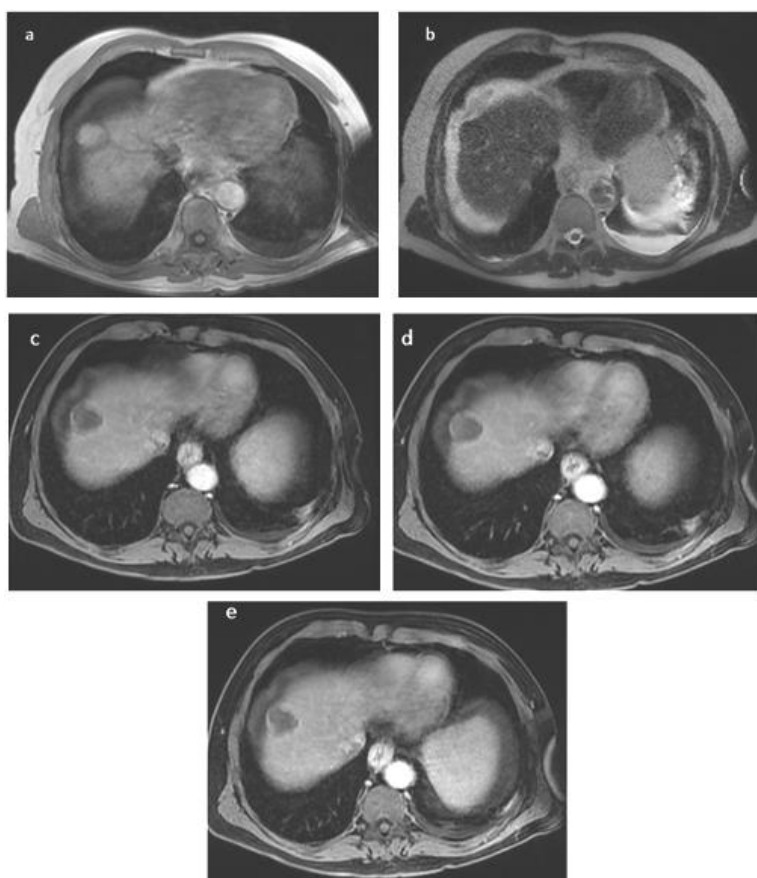
**Figure 13: Emulsion of 10 mL of lipiodol with an anticancer agent (Farmorubicin) and obtaining a homogeneous emulsion**

Embolization agents were administered to patients in 22 sessions (68,8%), resorbable (gelatin) was used in 8 sessions (25%) and microparticles were used in 14 sessions (43,8 %).

In our study, the main complication observed was the post chemoembolization syndrome (chills, abdominal pain and nausea), which was reported after 20 sessions (62.5%), followed by edemato-asciatic decompensation (18,7%), hemorrhagic decompensation

(3,1%) and a pseudoaneurysm (3,1%) which required the reinjection of embolization agents to achieve an almost complete obturation of this pseudoaneurysm.

Response to treatment was assessed by the modified RECIST criteria: 17 patients (77,3%) had a partial response, 1 (4,5%) had progression, 1 (4,5%) had stable lesions and one patient (4,5%) had a complete response.



**Figure 14: 2-month follow-up hepatic MRI images of the patient who received the combined lipiodolated chemoembolization and radiofrequency treatment showing the totally devascularized liver dome lesion, in T1 hypersignal (a), T2 hyposignal (b), without vascular enhancement at the arterial phase (c) nor wash out at the portal and delayed phase(d,e), This is a complete response according to the m-RECIST criteria**

Patient survival at 1 year was 91%, at 2 years was 86,4% and at 3 years reached 81,82%.

#### 4. DISCUSSION

Hepatocellular carcinoma is the most common primary liver cancer (85%) (1). It is also considered the fifth most common cancer in the world and the second most common cause of cancer death [2]. Morocco is one of the areas with low incidence of HCC, since the average annual incidence is 3.1% of all cancers [4].

The average age of the patients in our series was 61 years. This is in line with the results of the Moroccan retrospective studies of HCC chemoembolization performed at the Mohamed 5 Military Hospital in Rabat, at the FES University Hospital and at the ibn sina University Hospital in Rabat.

A male predominance was noted in our study with a sex ratio of 1.4, which is consistent with data from Moroccan retrospective studies dealing with HCC chemoembolization and this predominance was observed in the Tunisian and Algerian studies as well as

in the BRIDGE study dealing with the epidemiological characteristics of HCC.

In our series, the most frequent etiology of liver cirrhosis was viral hepatitis C, which is consistent with national data and those of our North African neighbors. On the other hand, in the BRIDGE study, viral hepatitis B predominated in China and South Korea, whereas viral hepatitis C and alcoholism were the most common in Europe, especially in France.

More than half of the HCCs in our study were secretory with an AFP level >10 nanogram/milliliter. This result is consistent with data from retrospective Moroccan studies of HCC chemoembolization.

The radiological characteristics of our series showed that more than half of our patients were carriers of mono-nodular HCC. The location in the right lobe was the most frequent. An atypical aspect was found in 18,2% of cases. These results are similar to the Moroccan retrospective studies, in particular the one carried out by Pr Mahi at the Mohamed 5 military hospital in Rabat. Similarly, our results are comparable to those reported in a Senegalese retrospective study conducted by Diop *et al.*, (Table III).

**Table III: Comparative table of the appearance of HCC on imaging according to studies**

	<b>A Diop <i>et al.</i>, [6]</b>	<b>Shashi Bala Paul <i>et al.</i>, [7]</b>	<b>M Mahi, J El Houssni <i>et al.</i>, [8] (HMIMV- Rabat)</b>	<b>M Maaroufi, O Addou <i>et al.</i>, [9] (CHU Hassan II de Fes)</b>	<b>S Bouklata, R Chibli <i>et al.</i>, [10] (CHU Ibn Sina de Rabat)</b>	<b>Notre série</b>
<b>Number of nodules:</b>						
Mono-nodular	42.8%	46.5%	44.44%	60%	24 %	<b>54,5%</b>
bi-nodular	28.6%		16.67%		43%	<b>18,2%</b>
Multi-nodular	28.6%	53% ( $\geq 2$ )	38.89%	40% ( $\geq 2$ )	33%	<b>27,3%</b>
<b>Nodule location:</b>						
Right lobe only						
Right and left lobe	46.6%	--	72.22%	--	75%	<b>68,2%</b>
Left lobe only	13.3%		8.33%		13%	<b>22,8%</b>
Caudate lobe	33.4%		19.44%		12%	<b>4,5%</b>
	--		--		--	<b>4,5%</b>
<b>Nodule size:</b>						
Maximum	140mm	160 mm	--	--	130mm	<b>200mm</b>
Minimum	30 mm	10mm			12mm	<b>4 mm</b>
Average size	61 mm	66 mm			66mm	<b>61 mm</b>
<b>appearance of the nodules:</b>						
Typical	--	--	75%	--	--	<b>81,8%</b>
Atypical			25%			<b>18,2%</b>

In our study, the main complication observed was the post chemoembolization syndrome, followed by edemato-ascitic decompensation. Results also found in the Moroccan study conducted by Pr Maaroufi *et al.*, at the University Hospital of FES, as well as in the

study conducted at the Ibn Sina University Hospital in Rabat where the major complication observed in the two cohorts compared was the post chemoembolization syndrome.

In regards to m-RECIST criteria, the partial response rate was the highest at 77,3 %. This is consistent with the results of the literature. We note that the Moroccan study conducted at the Mohamed 5 military hospital in Rabat found a complete response rate in 44% of cases

In our series, the overall survival at 1, 2 and 3 years was 91, 86,4 and 81,82% respectively . These

results are comparable to those of the Ibn Sina University Hospital in Rabat. In addition, the overall survival rate at 1, 2 and 3 years was 55, 45 and 30% in the study conducted at the Mohamed 5 Military Hospital in Rabat. The Senegalese study conducted by Diop *et al* found an overall survival rate at 1 and 2 years of 78 sixty 18 and 50% (Table IV).

**Table IV: Comparison of our survival rate results with other studies**

Study	Survival rate at one year	Survival rate at 2 years	Survival rate at 3 years
A Diop <i>et al.</i> , [6]	78.56%	50%	-
Shashi Bala Paul <i>et al.</i> , [7]	66%	47%	36.4%
M Mahi, J El Houssni <i>et al.</i> , (HMIMV-Rabat) [8]	55%	45%	30%
S Bouklata, R Chibli <i>et al.</i> , (CHU Ibn Sina de Rabat) [10]	87.1%	77.42%	70.97%
<b>Notre série</b>	<b>91%</b>	<b>86,4%</b>	<b>81,82%</b>

## 5. CONCLUSION

Hepatocellular carcinoma is constantly progressing in the world. It often occurs on cirrhotic liver, it is a tumor with a poor prognosis since the diagnosis is often made at an advanced stage of the disease.

Chemoembolization is part of the therapeutic arsenal that is currently under development, proposed mainly in the intermediate stage of the disease (BCLC stage B). Careful selection of patients during multidisciplinary consultation meetings and a rigorous procedure are essential to ensure a better tumor response.

The inclusion of patients in randomized trials should be encouraged to improve this techniques.

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