What is hepatocellular carcinoma?

Hepatocellular carcinoma (abbreviated "HCC"), also known as liver cancer, is the most common malignant tumor of the liver. HCC arises directly from malignantly altered liver cells and should not be confused with metastases from other types of cancer (e.g. liver metastases of colorectal cancer). HCC is the 5th most common type of tumor worldwide. In Austria, HCC is one of the rarer types of cancer, with around 500 new cases per year.

Are there risk factors for hepatocellular carcinoma?

In 80-90% of cases, hepatocellular carcinoma (HCC) develops in a so-called cirrhosis of the liver. Liver cirrhosis is advanced scarring of the liver, usually caused by years of inflammation in the liver. This inflammatory and scarring process is called "fibrosis" and is divided into four stages of fibrosis (F1-4), with F4 already corresponding to cirrhosis of the liver.

The causes of this inflammatory process can be chronic viral hepatitis (B or C), but also alcohol consumption, an inflamed fatty liver ("non-alcoholic steatohepatitis", NASH), autoimmune diseases (primary biliary cirrhosis "PBC" autoimmune hepatitis "AIH") or metabolic diseases (iron storage disease "hemochromatosis"). In some patients, the cause remains in the dark despite all diagnostic efforts (“cryptogenic cirrhosis”). Essentially, the following rule applies: any chronic liver disease, regardless of the cause, can lead to liver cirrhosis and ultimately HCC due to a chronic inflammatory process.

Does every patient with chronic liver disease eventually develop liver cirrhosis and then hepatocellular carcinoma?

Most chronic liver diseases have a rather slow course. In the case of untreated chronic hepatitis C, the rule of thumb is that around 30% of patients develop cirrhosis of the liver after the disease has lasted around 20-30 years. The same applies to chronic hepatitis B. In the case of untreated autoimmune hepatitis, the course is much faster, with most patients developing liver cirrhosis within 10 years.

In the case of alcohol, the course is also lengthy and very dependent on the amount of alcohol consumed and gender. However, the individual risk of the individual patient is not always easy to assess. On the one hand, this risk depends very much on how advanced the liver disease is at the time of diagnosis, i.e. how long the disease has been hidden and undiagnosed. The progression to liver cirrhosis also depends on the genetic disposition and on the type and number of co-existing risk factors (e.g. alcohol consumption, obesity, diabetes, co-infection with HIV and/or hepatitis B, C): for example, an overweight Hepatitis C patients with diabetes who drink alcohol regularly have a higher risk of developing cirrhosis of the liver much more quickly.

Once cirrhosis of the liver occurs, the risk of developing liver cancer is on average about 1-6% per year. In this situation, too, the following applies: the more advanced the liver cirrhosis, the more additional risk factors and the less favorable the genetic one Disposition, the higher the individual risk of developing hepatocellular carcinoma. In the case of an unfavorable constellation, this risk can be up to 16%/year and more.

Can you get hepatocellular carcinoma without liver cirrhosis?

Yes, that is possible in principle, albeit rather rarely. About 20% of all hepatocellular carcinomas are diagnosed in patients with a non-cirrhotic liver. However, most of these patients have a chronic liver disease, primarily fatty liver hepatitis (NASH), hepatitis B or C. Studies have shown that many of these patients already have an advanced degree of scarring (degree of fibrosis 2-3), but no cirrhosis consists.

Very few patients develop hepatocellular carcinoma in a completely healthy liver (grade 0 fibrosis) or without risk factors.

What can be done to reduce the risk of liver cancer?

The most important thing is the successful treatment of the underlying liver disease from the time of diagnosis, but no later than the diagnosis of liver cirrhosis. Depending on the cause found, this means, for example, abstaining from alcohol, starting antiviral therapy (for viral hepatitis), immunosuppression (for autoimmune hepatitis, AIH), bloodletting (for hemochromatosis) or ursodeoxycholic acid (for primary biliary cirrhosis, PBC). In addition, some general measures can be recommended, which were associated with a lower HCC risk in various epidemiological studies. These include regular moderate coffee consumption (3-4 cups/day), optimal diabetes control (especially with metformin), lowering the cholesterol level with statins and a Mediterranean diet.

Is there a screening test for hepatocellular carcinoma?

All patients with advanced liver disease (from fibrosis grade 3 or cirrhosis) and patients with active hepatitis B, regardless of the degree of liver disease, should have a high-quality liver ultrasound performed twice a year. The aim of this examination is to detect HCC in its early stages in order to be able to cure it. It should be noted at this point that even after successful treatment of the underlying liver disease (e.g. elimination of the hepatitis C virus in cirrhotic patients), there is still a relevant residual risk of developing HCC. Therefore, cirrhotic patients should continue to undergo HCC screening even after successful therapy. If the patient's constitution is poorly "soundable", cross-sectional imaging (ideally MRI) can be used at least once a year.

Is there also a tumor marker for hepatocellular carcinoma?

The determination of the tumor marker alpha fetoprotein (AFP) was withdrawn from the HCC screening guidelines of all Professional societies banned for lack of cost-effectiveness. Hepatitis C patients in particular often show increased and fluctuating AFP values as a phenomenon of virus multiplication, which can possibly cause costly "overdiagnosis".

On the other hand, a doubling of the AFP triggered 21% of all HCC early diagnoses in a prospective study, so that an AFP determination for prevention appears justifiable in the absence of cost pressure. How is hepatocellular carcinoma diagnosed? If an ultrasound examination of the liver finds a lump ("mass"), a CT scan or an MRI scan must be performed. This examination often provides the diagnosis. In some cases, a sample of tissue must also be taken from the lump (“biopsy”).

How to treat hepatocellular carcinoma?

What is special about hepatocellular carcinoma (HCC) is that, as already mentioned, the tumor usually develops in a diseased (cirrhotic) liver and the patient therefore suffers from 2 diseases at the same time (HCC and cirrhosis of the liver). Any therapy should therefore ensure that liver function is maintained. The choice of therapy is therefore complex and depends on 3 factors: the tumor burden (number, size and extent of the tumor nodules), the liver function (“Child Pugh stage”, “MELD points”) and the general condition of the patient.

The so-called BCLC staging takes all of these factors into account and links them to concrete therapy recommendations. According to this classification, a distinction is made between the stages BCLC-0 or BCLC-A, which are treated with the intention of healing, and the stages BCLC-B, BCLC-C or BCLC-D, which are usually only treated palliatively be able. The decision as to which therapy to choose should always be made in an interdisciplinary tumor discussion (tumor board) at a large, specialized center.

Potentially curative treatment methods are surgical removal of the HCC (“resection”), liver transplantation and radiofrequency ablation. Soothing (palliative) therapy methods are transarterial chemoembolization (TACE) or drug therapy with sorafenib (Nexavar®).

Under what circumstances can hepatocellular carcinoma be surgically removed?

Surgical removal is an option in BCLC stage 0. The ideal patient for surgery has an excellent general condition, normal liver function, no evidence of hypertension (=no clinically significant portal hypertension) and a single tumor nodule with no visible growth into the blood vessels of the liver or metastases. If all of these conditions are met, larger tumors (>5cm) can also be operated on, provided at least 30% of the liver remains in the body to ensure liver function.

If there is a relevant liver hypertension, which by means hepatic venous catheter, surgery is associated with an increased risk of death and should therefore not be the first choice. With regard to the success of the operation, the following rule applies: the larger the tumor, the higher the risk that it will come back after surgical removal ("recurrence") and the shorter the long-term survival after an operation.

Under what circumstances can a liver transplant be performed?

Liver transplantation is an option in BCLC stage A. The optimal patient for liver transplantation has no comorbidities that would prevent such major surgery and a low tumor burden. Both are carefully examined as part of an inpatient admission (“transplant evaluation”). The tumor burden should correspond to the so-called "Milan criteria". The Milan criteria are met (and therefore a transplantation is possible) if there is a numerical tumor that is no more than 5 cm in size, or a maximum of 3 tumor nodules, each of which is less than 3 cm in size.

Patients with tumors outside the Milan criteria are not transplanted because the risk of tumor recurrence after transplantation is too high. If a patient does not have any relevant comorbidities and the tumor meets the Milan criteria, they will be placed on the transplant waiting list. The average waiting time for a new liver is about 1 year. During the waiting period, the tumor is often treated with radiofrequency ablation or transarterial chemoembolization to prevent the tumor from growing beyond the limits of the Milan criteria, which would also make transplantation impossible.

Under what circumstances is radiofrequency ablation performed?

Radiofrequency ablation (RFA) is performed by the interventional radiologist and is an option in BCLC stage 0 or A if there are up to 3 tumors with a maximum size of 3 cm, but unfortunately a reason for exclusion (contraindication) for surgical removal or for a liver transplant is available. In addition, RFA is used to treat eligible tumors on the transplant waiting list. In RFA, a probe is inserted into the tumor node from the outside under anesthesia, which is used to destroy (“cook”) the tumor using alternating current.

Depending on the location of the tumor, other physical methods (ethanol, microwaves, cryotherapy) can also be used according to the same principle, with the best data available overall for RFA. Here, too, the success of therapy decreases with the number and size of the tumors.

Under what circumstances is transarterial chemoembolization performed? Transarterial chemoembolization (TACE) is also performed by the interventional radiologist. TACE is sometimes used to treat patients on the transplant waiting list and is the standard of care for patients with intermediate stage BCLC-B.

A patient with an intermediate HCC (BCLC-B) is in a very good general condition, has good to moderate liver function (Child-Pugh A or B) and an inoperable or transplantable tumor (1 tumor node >5cm or 3 tumor nodes> 3cm) with no evidence of vascular involvement or distant spread (metastases).

Furthermore, the patency of the so-called portal vein, which carries blood from the intestine to the liver transported, an absolute condition for carrying out the TACE. As part of TACE, the large inguinal artery (A. femoralis) is punctured under local anesthesia and a catheter is advanced through the main artery (aorta) into the hepatic artery (A. hepatica).

From there, the blood vessels that supply the tumor with blood are probed. The catheter is positioned in these tumor-supplying blood vessels. In "conventional TACE", a mixture of chemotherapy (doxorubicin) and lipiodol (an oily contrast medium to improve absorption of the chemotherapy) is injected into the tumor via the tumor blood vessel and the blood vessel is finally sealed from the inside with embolization material (e.g. Gelfoam, etc.). With DEB-TACE, the chemotherapy (doxorubicin) is coupled to the tiniest spheres, which accumulate in the tumor, close the smallest tumor vessels and slowly Deliver chemotherapy locally.

DEB-TACE has the advantage of fewer chemotherapy side effects. Depending on the number and size of the tumor, 2-3 (or sometimes more) sessions are usually necessary to treat the tumor properly. Since the rest of the liver can also be damaged with every treatment, the liver function must always be analyzed in detail at the beginning and before any further treatment in addition to the response to the therapy decide whether another TACE is possible.

Under what circumstances is drug therapy initiated?

In Austria, drug therapy for HCC is usually prescribed by a gastroenterologist/hepatologist (sometimes also by an oncologist) and is used in the advanced BCLC-C tumor stage.

Patients with Advanced HCC have good to moderate general health (ECOG 1-2), good to fair liver function (Child-Pugh A or B, respectively), or a tumor of any size with evidence of extrahepatic spread or ingrowth into the blood vessels of the liver. Therapy with the drug sorafenib (Nexavar®) is currently an option for these patients. For the sickest of all patients in stage BCLC-D, i.e. those with severe liver dysfunction (Child C) or those who are confined to bed most of the day due to weakness (ECOG 3-4), there is currently nothing other than optimal palliative care reasonable therapy options.

On the one hand, sorafenib can directly inhibit the growth of tumor cells, on the other hand, it can block the formation of new blood vessels supplying the tumor. The goal of therapy is to slow down or stop growth and thus tumor control. A disappearance of the tumor is not to be expected. The therapy is therefore used indefinitely. The side effects affect the skin (hand-foot syndrome, rash), the gastrointestinal tract (especially diarrhea) and general well-being (tiredness/appetite/weight loss etc.) and vary greatly between individuals.

Should I take part in a scientific study?

Scientific studies are a legal prerequisite for new therapy methods or drugs to be approved for use by the authorities and thus made accessible to affected patients. Patients who take part in therapy studies are thus given the opportunity to try out new, potentially effective therapies at an early stage. Every scientific study is strictly checked by an ethics committee before it starts. Furthermore, close controls during the Study contributes significantly to patient safety. The central focus of research is currently studies for patients with advanced HCC, even after the failure of the standard therapy with sorafenib (Nexavar®). Please contact the liver tumor outpatient clinic for personal information.