INTRODUCTION

A significant number of patients with cancer on comitantly suffer from liver cirrhosis for several reasons. First, the fact that both diseases are relatively common among the general population increases the probability of suffering from both diseases simultaneously. Cancer is a leading cause of death and its incidence is expected to rise globally due to the growth and aging of the population. It has been estimated that there than three million new cancer cases Europe and 14.1 million new cases globally in 2012.[1]

Liver Cirrhosis

General Liver cirrhosis represents the final stage of liver fibrosis, the wound healing response to chronic liver injury. Cirrhosis is characterized by distortion of the liver parenchyma associated with fibrous septae and nodule formation as well as alterations in blood flow.[2] The most common primary liver cancer, can develop at any stage of cirrhosis. Liver transplantation often represents the only possibility of cure for liver cirrhosis and can improve survival and quality of life in selected patients with end-stage liver.[3]

Staging of Liver Cirrhosis

Prognostic models and staging systems are inevitable for adequate management of patients with liver cirrhosis, especially when it comes to selecting patients for liver transplantation.[4] The Child-Pugh score was initially developed about 50 years ago to predict the prognosis after surgery for portal hypertension (portocaval shunting, transection of oesophagus) in patients with liver cirrhosis.[5]
Primary Liver Cancer and Liver Cirrhosis

Hepatocellular carcinoma staging and liver function. HCC is the most common primary liver cancer and the second most common cause of cancer-related mortality globally. Importantly, HCC usually develops in patients with underlying liver cirrhosis. Importantly, HCC usually develops in patients with underlying liver cirrhosis. Hence, unlike in most other solid malignancies, the prognosis of patients is not only determined by the cancer itself but also by the degree of underlying liver cirrhosis and its complications including portal hypertension, ascites, and life-threatening bleeding events from gastroesophageal varices.

Liver Transplantation

Liver transplantation is recommended for patients with small tumours and advanced liver function impairment. Transplantation is the only treatment modality that can simultaneously cure both, the tumour as well as the underlying liver cirrhosis, and the success of treatment is not affected by the severity of liver dysfunction. According to the landmark paper published by Mazzaferro et al., patients with single tumours ≤5 cm or extra hepatic metastases are the best candidates and can achieve survival rates comparable to those of patients transplanted for non-malignant indications.

Transarterial Chemoembolisation

TACE is the first treatment choice for patients with compensated liver disease and large or multifocal HCC without vascular invasion or extrahepatic spread. Contraindications for TACE have been reviewed elsewhere. Absolute contraindications related to liver cirrhosis include decompensated status (Child-Pugh score >8), and impaired portal-venous blood flow (thrombosis, hepatofugal blood flow), while untreated oesophageal varices with high bleeding risk represent a relative contraindication for TACE.

Treatment of the Underlying Liver Disease and Portal

A large proportion of patients with HCC dies from complications of liver cirrhosis and portal hypertension (ie, gastrointestinal bleeding, infections, renal failure) rather than from clearly tumour-related causes. Hence, not only effective anti tumour treatment but also adequate evaluation and treatment of portal hypertension can reduce liver disease-related mortality.
**Transplantation**
Liver transplantation is not recommended as a standard treatment for iCCA since survival rates, derived from heterogeneous and often small patient populations, were markedly below those reported for cirrhotic patients undergoing transplantation.[12]

**Chemotherapy**
Based on data derived from studies conducted in patients with advanced biliary tract cancer the combination of cisplatin plus gemcitabine became the chemotherapy practice standard for iCCA, even though, given the limited data available on iCCA, current guidelines do not recommend this regimen as a standard of care for iCCA. Gemcitabine commonly causes transient elevation of transaminases, but liver failure is rare.[13] Dose reduction is recommended in patients with significant underlying liver disease. Cisplatin can induce a transient increase of transaminases, especially at higher doses, as well as steatosis and cholestasis, which are rare and usually reversible though.[14]

**Management of the Underlying Liver Diseases**
Similar to HCC, patients with underlying liver cirrhosis should be screened for portal hypertension and its complications and undergo adequate management if present. Additionally, modifiable causal factors (ie, alcohol, hepatotoxic drugs) should be managed adequately and decisions regarding treatment of the underlying liver disease (ie, viral hepatitis) should be based on the liver disease-related and cancer-related prognosis.[15]

**Non-Hepatic Cancer and Liver**
General Cancer and liver cirrhosis represent major health burdens and account for about 1.75 million and 170 000 deaths per year in Europe, respectively. Given the high prevalence of each disease and the fact that common habits among the general population like tobacco, alcohol, abuse and the metabolic syndrome represent risk factors for both, cancer and cirrhosis, one can assume that a remarkable number of patients with solid tumours concomitantly suffer from liver cirrhosis.[16]

**Surgery**
Surgical treatment is frequently indicated in patients with cancer especially at early tumour stages and often the only curative treatment option. In general, the severity of liver dysfunction is a main prognostic factor in patients with liver cirrhosis undergoing surgery.[17]
Chemotherapy
Cytotoxic chemotherapy is another mainstay in cancer treatment. Several chemotherapeutical agents can cause liver toxicity of varying degree ranging from mild transient elevation enzymes to severe or even fatal hepatic failure. The liver itself is fundamentally important in drug metabolism (ie, activation, inactivation, excretion) and patients with abnormal drug metabolism have an increased risk of experiencing severe hematological as well as non hematological adverse events.\[18\]

Management of Liver Disease
Careful evaluation of the etiology and severity of liver cirrhosis is necessary prior to initiation of anticancer treatment. Modifiable causal factors (e.g, alcohol, liver toxins including drugs with known hepatotoxicity, diabetes) should be corrected in order to prevent worsening of the liver disease.\[19\]

Reactivation of Viral Hepatitis
In general, reactivation of viral hepatitis during chemotherapy can be divided into three different stages. First, chemotherapy-induced immune suppression facilitates viral replication by reducing immune response that controls viral infection. The second stage is characterized by an ‘immunological rebound’ after cessation of chemotherapy, characterised by restored immune function and rapid destruction of viral-infected hepatocytes leading to increased liver inflammation and hepato cellular injury.\[20\]

CONCLUSIONS
The degree of underlying liver cirrhosis significantly influences treatment decisions and prognosis of primary liver cancer and non-hepatic liver cancer. Adequate assessment of liver function and stage of cirrhosis prior to treatment initiation and close monitoring during anticancer treatment are inevitable. Patients with compensated liver cirrhosis, whose prognosis is mostly determined by the cancer, should be considered for anti tumour treatment. In contrary, management of patients with decompensated stages should rather focus on liver cirrhosis and its complications since life expectancy is mainly influenced by the liver disease and anti tumour treatment itself can further worsen liver function. In patients with underlying HBV infection antiviral treatment should be initiated prior to chemotherapy and close monitoring of liver function is recommended in patients with HCV infection.
REFERENCES


