Ablations and Embolisms in the Treatment
of Advanced Stage Hepatocellular Carcinoma

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Abstract

Hepatocellular carcinoma is one of the most common cancers in the world. It is linked to cirrhosis, hepatitis B and hepatitis C. There are several treatments used to destroy tumors and prolong a patient's life when they have advanced stage tumors. Some of the treatment types used are thermal ablation, transcatheter arterial chemoembolism, chemical ablation, and high-intensity focused ultrasound. Factors such as size of the tumor, number of tumors, and liver function affect which treatment to use and how successful it will be.
Ablations and Embolisms in the Treatment of Advanced Stage Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is one of the most common types of cancer affecting 2.5 people out of 100,000 in the United State and upwards of 40-60 people per 100,000 in African and Far East countries (John Hopkins Medicine, Introduction Section). HCC is a cancer that develops from the hepatocytes in a liver afflicted by cirrhosis, hepatitis B or C. Due to the mitotic rate, liver cells are highly predisposed to abnormal changes. Tumors are highly vascularized so they are vulnerable to ablation and embolism treatments that cut off blood-flow.

One of the primary treatments for the past several decades was surgical resection or liver transplant. Staging the tumor, (See Fig. 1) ultimately defined whether a patient would qualify for surgery or transplant. (John Hopkins Medicine, Diagnosis Section)

Unfortunately by the time most tumors have been diagnosed they are too large, widespread in the liver, or the patient has poor liver function for the surgery to be successful. Transplants are also
limited in success due to the lack of optimal donors, but HBV and HCV are known to remain in the body and infect new livers (Davis, 2010). “The recurrence rate of HCC after surgical removal can reach as high as 60%, and even with small HCCs that have been radically resected, the recurrence rate can still reach 40%-50%” (Zhang, 2009).

In recent years numerous new techniques have been studied to find treatment options that are safe, noninvasive, and improved survivability for patients with tumors that cannot be resected safely. Currently thermal ablation, transcatheter arterial chemoembolism (TACE), chemical ablation, and high intensity focused ultrasound (HIFU), have all been used with varying success.

These techniques are often used in patients with no more than a few small tumors but for whom surgery is not a good option (often because of poor health or reduced liver function). These treatments are not usually considered curative but may produce survival rates equal to surgery in people with small tumors. They are also sometimes used to treat cancers in patients waiting for a liver transplant.

Ablation is best used for tumors no larger than about 3 cm across. For slightly larger tumors (3 to 5 cm across), it may be used along with embolization (American Cancer Society, Liver Cancer-Tumor Ablation Section, paragraph 1).

Ultrasound is the most favored modality due to low cost, lack of radiation, no iodinated contrast, and real time images. Computed tomography provides clearer images when inserting needles and catheters. Choosing the right treatment plan is dependent on liver function tests, vascularity of the tumor, and condition of the patient at time of treatment (Davis, 2010).

**Thermal Ablation**

Radiofrequency Ablation (RFA) is the most common treatment since it is the most effective against HCC. The process involves placing a probe that uses electromagnetic radiation
to heat the area (See Fig. 2). With the assistance of CT or US for guidance, the probe can be inserted percutaneously, laparoscopically, or after laparotomy. The electromagnetic radiation produces ionic vibrations that cause coagulative necrosis of the tumor (Ghanaati, et al. 2010). The size of the ablation zone is dependent on temperature and length of time. Successful removal of tumors occurred with diameters < 5 cm, while tumors with a diameter > 5 cm were not successful in removing all affected areas. Risks of RFA are possible tumor seeding when pulling the probe out of the ablation area. Injury to normal liver tissue, pneumothorax, hemorrhage, and abscesses were also potential risks (Davis, 2010).

Cryoablation is the freezing of tumor tissue as treatment. One of the benefits of performing this treatment is the formation of an “ice ball” that shows up on CT and US (See Fig. 3). This allows for better visualization of the ablation zone when compared to tumor margins in order to shift location or add additional probes. Freezing also maintains cellular integrity of
vessels, connective tissue, and visceral linings so probes can be placed in tumors that are close to those types of anatomy (Ghanaati, et al. 2010). In terms of patient comfort this procedure can be used under conscious sedation for patients that do not want to undergo full sedation or are unable to. The primary risks are hemorrhage and cryoshock. Hemorrhage is common in all procedures since freezing does not cauterize the tissue in ablations of any size. Cryoshock causes multiorgan failure, coagulopathy, and disseminated intravascular coagulation (DIC) which leads to death of the patient within 24 hours after treatment (Davis, 2010).

Microwave (MWA) is a newer treatment that is more reliable on tumors < 2cm or smaller with complete ablation, but is ineffective on larger tumors. This procedure tends to require at least two full sessions to be effective. When compared to other thermal treatments, MWA requires additional sessions, produces a smaller necrotic area, has a higher recurrence rate, and more complications develop after each session (Ohmoto, et al. 2009).

Transcatheter Arterial Chemoembolism (TACE)

Since HCC has a high vascular requirement, TACE has been effective due to staunching blood-flow enough to cause tumor necrosis. The main cytotoxin used is lipiodol which is iodinated poppy seed oil. The chemical is drawn into the tumor cells more readily than normal liver cells and occludes the capillaries which prevent blood-flow to the tumor (See Fig. 4). Unlike normal cells, tumors are unable to process the oil because they do not contain Kupffer
cells. Any tumors that contain lipiodol can be visualized on CT so performing the procedure with image guiding is beneficial (Davis, 2010). Occasionally, lipiodol is preferably combined with a chemotherapeutic drug such as doxorubicin or cisplatin. The combination creates a higher concentration of drugs around the tumor.

Success with TACE is dependent on the number of arteries to the tumor. HCC is highly vascularized and multiple nutrient pathways are common. The process of breaking down lipiodol is stressful and can exacerbate an already poor liver function (Zhang, 2009). Possible dilation and blockage of the intrahepatic ducts and common hepatic ducts can occur if lipiodol is injected near the bile ducts. Rarely lipiodol enters the gastrointestinal, pulmonary, or cerebral circulation systems causing occlusion of those vessels. Other complications are septicemia and necrotic tissue forming an abscess (Ghanaati, et al. 2010). A radioactive agent on the market for several years that is gaining popularity is yttrium-90. This comes in the form of microbeads (See Fig. 5) that flow into the tumor vessels partially blocking them while emitting radiation to the abnormal cells (Davis, 2010).
Chemical ablation can be used on tumors near critical anatomy where other forms of treatment would damage those areas also. There are two types of chemicals commonly used for this type of treatment. Percutaneous Ethanol Injection (PEI) uses 95% ethanol and Percutaneous Acid Injection (PAI) uses acetic acid are the more known chemicals used. Ethanol is the most common chemical used since it causes cellular dehydration, coagulation necrosis, cell fibrosis, thrombus of small vessels and ischemia of neoplastic tissues (See Fig. 6). Acetic acid diffuses into tumor tissue more readily than ethanol which provides better outcomes, but post procedure infections are higher with acid, especially with larger tumors. Most treatment plans using this procedure requires 4-6 procedures over the course of 2 to 3 weeks (Ghanaati, et al. 2010). Complete necrosis occurs in 80% of tumors smaller than 3 cm, but the larger the tumor the less effective the procedure, usually 50% success with tumors 3.0-5.0 cm. Although, using a multi-pronged injection needle has been 90% successful with tumors ranging 3.0 to 5.0 cm (Kuang, et al. 2009).

**High Intensity Focused Ultrasound (HIFU) Ablation**

HIFU is a very precise procedure that uses heat to destroy tumor cells. The heat output is much lower in general compared to true thermal ablation procedures. This is accomplished by
using a transducer to focus the acoustic waves to affect the deep tissues (See Fig. 7). Focused waves generate heat which forms microbubbles that react to the US field called cavitation. When the microbubbles begin to expand and vibrate, the temperature in the center increases. Eventually the microbubbles implode sending the extreme heat to the surrounding tissues damaging them. This event is unpredictable so makes applying the procedure to therapeutic setting is not as well received as other procedures. (ENotes Web Site, How HIFU Works Section)

The procedure is minimally invasive to non-invasive and is able to reach deep tissue accurately. Since there is no radiation, this procedure can be used in as many sessions necessary to completely destroy the tumor. Large and/or irregular sized tumors can be successfully ablated when under imaging guidance. Pain is minimal and surface skin burns were non-existent which grants a high level of patient comfort as an additional benefit (Wang, 2010).

Conclusion

There are several procedures that can be used to treat HCC. Unfortunately, they are not a cure. The lifespan is increased for the patient when successful and as new techniques are developed additional years are granted. For a person facing death, a few extra years can be a big difference in their life.
References


