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Review Article

Role of Therapeutic Interventional Radiology in Tumor Management

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Abstract

Background: The number of cancer cases and death rates due to cancer are increasing everyday worldwide. Interventional radiology procedures are used in cases where patients have cancer but they can be used also in non- malignant patients, the fields of using Interventional radiology in cancer patients are many such as detection and diagnosis of the patients, treating them and management of any complications associated with cancer.

Aim: In this review, we will look into the role of interventional radiology in diagnosis and management of tumor.

Conclusion: As having less invasive techniques in treatment of many diseases especially the wide spread ones is important and also is the main focus of the research fields nowadays. Interventional radiologists prove that the new technique of IR (interventional radiology) is a promising candidate to achieve this goal. More efforts should be made for complete understanding of IR technology and how it could be used in more efficient way to decrease the side effects of traditional treatment, improve the efficacy and improve the quality of the patient's life.

Keywords: *Therapeutic Interventional Radiology; Management of Cancer; Tumor Diagnosis; Tumor Management with Interventional Radiology*

Introduction

The number of cancer cases and death rates due to cancer are increasing everyday worldwide [1]. The new advances in different sciences made us able to understand how cancer happens in more details also it enabled us to find out new strategies for diagnosis and

treatment of cancer [1,2]. All the previously mentioned achievements did not enable us to find successful therapies that are satisfactory to us. Understanding how treatment of cancer started takes us to the traditional ways of treatment that act on the cell division steps and aim to prevent the completion of the cell division cycle, but the huge side effects of this traditional therapy made it necessary to find more targeted therapies for cancer to increase the treatment efficiency and decrease the side effects [3].

Interventional radiology procedures are used in cases where patients have cancer but they can be used also in non- malignant patients, the fields of using Interventional radiology in cancer patients are many such as detection and diagnosis of the patients, treating them and management of any complications associated with cancer. Regarding diagnosis of patients with cancer imaging-guided biopsies is one of the most important procedures to get samples from the affected tissue without hurting the other tissues next to it, also this technique enables us to collect the different fluid samples, moving to the treatment where Transcatheter chemoembolization enables us to deliver the chemotherapeutic agent directly to the tumor mass, also the complications that come together with cancer could be managed using Interventional radiology, examples of these complications such as pain and drainage of obstructed organs [4].

Many advantages of Interventional radiology made it a promising candidate for cancer treatment, although the traditional treatments such as radiation, surgery and chemotherapy are still the main treatments [4], Interventional radiology is making a place itself between these alternatives due to many causes as it could be done for outpatients or those who stay in hospitals for short times so it is less expensive than other alternatives and also the mortality rate of it is less than the traditional treatments [5,6]. The economic impact of Interventional radiology was shown by this study where radiologic placement of hemodialysis catheter saved 50% of the cost comparing to the surgical placement [5].

The role of Interventional Radiology (IR) is promising now in the management of cancer [7] taking hepatocellular carcinoma (HCC) as a n example where surgery is considered the most efficient treatment but it is not suitable for all patients so Interventional Radiology (IR) can replace it based on the patient's condition. The Barcelona Clinic Liver Cancer system (BCLC) [8] is the system used to classify (HCC) into five grades (0, A, B, C, D) where Interventional Radiology is suitable for stage 0 and stage B patients.

In this review, we will look into the role of interventional radiology in diagnosis and management of tumor.

Participants and Methods

Study design: Review article.

Study duration: Data were collected between 1 June and 30 October 2020.

Data collection: Medline and PubMed public database searches have been carried out for papers written all over the world on the most notable advances in therapeutic interventional radiology. The keyword search headings included "therapeutic interventional radiology, management of cancer, tumor diagnosis, tumor management with interventional radiology", and a combination of these will be used. For additional supporting data, the sources list of each research was searched. Criteria of inclusion: the papers have been chosen on the basis of the project importance, including one of the following topics: therapeutic interventional radiology, management of cancer, tumor diagnosis, tumor management with interventional radiology. Criteria for exclusion: all other publications that did not have their main purpose in any of these areas or multiple studies and reviews were excluded.

Statistical analysis

No predictive analytics technology has been used. In order to evaluate the initial results and the methods of conducting the surgical procedure, the group members reviewed the data. The validity and minimization of error were double revised for each member's results.

Interventional radiology in the diagnosis of cancer

Diagnosis of cancer is the first step toward its treatment; the accurate and definitive diagnosis allows us to know the stage and severity of the condition which assists the physicians in determining the regimen of treatment for each patient [9]. The techniques of imaging the cancer without invasion of the tissue are promising now and enable us to assess and determine the stage of the cancer, but the histological diagnosis is still the main and the basic determinant of many tumours. Interventional radiologists now are developing the main non-invasive techniques for diagnosis of cancer; the usage of such techniques is increasing day by day [10].

Visualization using image guidance while doing biopsy allows us to have safe diagnosis as it shows us the passageway of the needle into the organ which improves the efficacy and decrease the damage to the surrounding tissues, we can use these non-invasive techniques over wide range of sites with high accuracy and low complications rate [10]. New cross-sectional imaging techniques are used to ensure the suitability of biopsy, knowing the site and location of the tumor and also make sure that sampling is made for the right lesion in case of presence of many lesions [11]. With the great advancement in histological and cytological diagnosis techniques we became able to determine the primary site of the tumor with more certainty and also guess whether or not it will be sensitive to the chemotherapy [12]. In some cases where physicians prefer surgery based diagnosis for getting biopsy, image guidance can also be used to localize the tumor site before the operation; wire-localization before getting a breast biopsy is an example for this usage of image guidance [13]. Another example is the removal of the lung nodules using thorascopic surgery assisted with video, this technique compensate for having open thoracotomy. Patients with febrile neutropenia, percutaneous biopsy is mostly used to determine the presence of any opportunistic infections, this is the main field of interest for microbiologists [14]. Deciding to use guided imaging will give you multiple choices where you can choose what suits your work and get you to the most efficient results. Ultrasound have 2 main advantages as it enables real-time imaging that improves the efficacy and accuracy of needle visualizing while moving within the tissue and also both the patient and the staff are protected from the ionizing radiation during the biopsy [15].

Computed tomography (CT) is another technique that provide better details of the tissue anatomy and more accurate positioning of the needle compared to ultrasound, another advantage of CT over ultrasound that any complications could be easily detected, all the previously mentioned advantages made CT a promising target for the difficult biopsies such as pelvic, retroperitoneal, and thoracic biopsies [14]. The main advantage of CT is the exposure of both the patient and the staff to the radiation during the biopsy time, this exposure varies depending on the scan time, the size of the patient and the part of the part that is imaged. The time of exposure could be shorten using CT fluoroscopy. Fluoroscopic images allows using less dose of radiation to the patient but increases the staff and assistant's exposure to radiation [16]. During ultrasound-guided procedures, where a needle is projected in real time, the use of modality fused image guidance systems improves the accuracy of needle positioning while minimizing radiation exposure to patients, doctors and staff on a pre-existing CT or MRI image [17].

Interventional radiology in the treatment of cancer

Central venous access: As the sampling is a frequent procedure in cancer patients, vascular access is an important aspect of the health care of the cancer patient, this is used to administrate chemotherapy, nutrients and medication also allow taking blood samples without having to use venipuncture, in UK, it is estimated that about 200,000 access devices are used, most of them for cancer patients, the role of IR technique in this is that it enable us to site these devices with high accuracy [18]. Ultrasonography and fluoroscopy as examples of real-time imaging allows percutaneous venous access where a catheter is positioned mostly in the right atrium [19]. Complications that could happen during insertion of the catheter are injury to the structures surrounding it and also positioning the catheter in wrong position, but image guidance decreases the incidence of these complications comparing to the blind techniques that uses external markers [20].

Foe venous access the right jugular vein is the most used site for access, but the image guidance allows the usage of alternative ways in different conditions [21]. Using these central access devices has some complications over long time usage as it causes infection and

thrombosis. The incidence of thrombosis in cancer patients is 4 - 6 times more than the normal population. Using Central Venous Catheter (CVC) increases this risk more [22]. The incidence of deep venous thrombosis (DVC) in cancer patients due to using CVC is about 28%, while the incidence of pulmonary embolism is between 15 - 25% [23] the rate of thromboembolism can also increase in patients with prothrombotic tendencies and when the catheter is inserted in the left vein. Using anticoagulants such as warfarin and heparin did not show improvement of the cases, but treatment for 6 weeks to year with anticoagulant still exists and the response varies the presence of any thrombophilic factors and the extent of the thrombus [24,25].

Arterial embolisation techniques: The less invasive techniques for cancer treatment based on using imaging is increasing and it is used as an alternative to surgery in many cases due to efficient management of malignancy [26] Transcatheter embolisation after knowing the exact supply of the solid tumor using CT or MRI allows devascularisation of the tumor [27]. Mechanical closure can be done by polyvinyl alcohol, Amplatzer occlusion devices and blood clots, using IR these clots are inserted in the vessels that feeds the solid tumor tissue [28]. Usage of this technique could be done alone where the reduction of the blood supply to the tumor tissue results in hypoxia that stops the growth of the tumor or combined with surgery or treatment [27]. Arterial Embolisation can also be used to before the surgery to decrease the blood loss during operation; it could also be used to relieve systematic pain. Massive hemoptysis which is one of the major complications of cancer is also managed using IR embolisation [29].

A modification of the previously mentioned technique that is used mostly in hepatic tumor is the Transarterial chemoembolization (TACE), in this technique one or more chemotherapeutic agents are added together and injected into the catheretic artery. The hepatic artery is the main feeding source for the hepatic tumors; trials showed that radio-labelled albumen is taken by the hepatic artery infusion ten times more than the portal vein infusion [30]. The main advantages of TACE over the systemic chemotherapy is that it enables targeted delivery of the chemotherapy to the cancer lesions this increases the concentration of the medication and decrease systemic doses. Chemoembolisation also have a n important advantage, that it can be repeated, and the patient can have many sessions till the whole tumor is devascularized [15] as the liver have 2 blood supplies, it is not affected by this procedures, but it should be done with caution in absence of blood supplying the liver to, prevent liver necrosis [31].

Another modification is the Radioembolisation, which is used mainly for hepatic tumors [32], using microspheres made of glass or resin, radioisotopes that emits beta radiation could be introduced directly into the tumor mass [33], the choice of the radioisotope is based on the nature of the tumor. The choice of beta radiation is mainly because of its low penetration so the necrosis will be localized. During this process, some of the gamma radiations are emitted, they have high penetration rate so using gamma camera we can detect and localize the radioisotope [34]. Reports about Radioembolisation showed that it has good response and promising treatment for metastatic liver and colorectal cancer [35].

Gene therapy: Treatment of cancer using gene therapy is available due to the advances in tumor immunology and the understanding of the molecular oncology [36], the treatment using gene therapy based on different strategies such as activating the immune response to fight the tumor, activating the tumor necrosis genes, change the susceptibility of the tumor tissue to the chemotherapeutic agents and modifying angiogenesis [37]. Similar to chemoembolisation, the genetic agents could be injected directly to the tumor tissue using the arterial injection [38]. As the DNA cannot cross the cell membrane, a vector should be used such as virus or plasmid to affect the cell.

Ablative techniques: This technique is used in patients of early stage malignancy when resection is not recommended, ablation using IR causes necrosis of the tumor tissue by utilizing of different energy sources such as laser, radiofrequency (RF), ultrasound, cryotherapy, and microwave [39]. Radiofrequency ablation (RFA) is based on using energy in the range of the radiofrequency by administrating electrode connected to closed circuit, this cause heating of the tissue surrounding the electrode to a heat up to 60 degree Celsius which cause thermal damage of the tissue and cell death [40].

RFA is considered a safe method for management of both hepatic and lung tumor, also could be used in management of other tumors such as renal, skeletal and adrenal lesions [41], this technique has a mortality rate about 0.3% and complications rate 2.2%. In the

contrary to RFA, cryotherapy uses subfreezing temperature to make cells die by applying argon gas under high pressure. The alternating cycles of freezing and thawing is the cause of the stress applied to the cell membrane and finally cell death. The microwave is the last discussed energy source where energy is applied in the microwave range, this energy cause water agitation and cell death. Comparing microwave to RFA, results showed that microwave could ablate larger volumes of the tumor, it also provides perfect heating of the tumor with less pain [42].

Interventional radiology in the management of the complications of cancer

Cancer most commonly causes the loss of the function of the affected organs and systems, these complications could be managed using IR method that improves the quality of the patient's life. The following are some examples that comes together with management of the cancer patients.

Biliary obstruction: Patients who are diagnosed with malignant biliary obstruction have mostly a pancreatic neoplasm which cause the pressure on the distal bile duct, this problem could be solved easily using endoscope, but in some cases this obstruction could be due to metastatic hepatic or peripancreatic cancer where symptoms of malignancy are revealed due to affection of the bile tree, if simple endoscopy failed in management off this condition, percutaneous intervention could be used as alternative. Also a contrast will be injected to the hepatic biliary duct to localize the site of the obstruction and help managing it [43]. Appropriate prophylactic antibiotics to minimise septic complications, including coverage for *Escherichia coli, Klebsiella, Enterococcus, Streptococcus, Enterobacter* and *Pseudomonas aeruginosa* should be provided to all patients before starting percutaneous biliary procedures [15].

Renal obstruction: This is one of the bad signs in the cancer patients and happens mostly due to high compression or excessive cancer invasion. This obstruction could happen in different types of cancer such as those of urologic gastrointestinal or gynaecologic origin. Management is done mostly by percutaneous nephrostomy (PCN), that is considered the first line for management of this condition, in this case a renal intervention is made through IR, allowing an access to the urinary tract to drain all its content and also could be used in other uroradiologic interventions as the pathway is already established [44].

Usage of PCN in emergency cases is very common, these cases such as urinary tract sepsis, deterioration of renal function and disturbance of electrolytes [15]. The catheter used for the drainage should be chosen carefully as it differs depending on the nature of the fluid to be drained [44].

Upper gastrointestinal obstruction: Esophageal, neck and head malignancy in the patients are accompanied with difficulty in feeding due to swallow impairment, this require using gastrojejunostomy or gastrostomy to feed the patient. The role of interventional radiologist in this case is important and significant as they could provide feeding tube, which is guided by using imaging to make it safer and increase the rate of success; this is proved to be better than using surgery or endoscope to place the tube. Some complications might occur after gastrostomy insertion such as discomfort on feeding in 33% of cases and infection in 23% of cases [45].

Pain: Pain due to cancer in late stages is the cause of the high morbidity, the incidence ranges from 40% to 90% in severe conditions. According to World Health Organization (WHO) analgesic ladder; opiates are considered the first line of treatment of the pain accompanying cancer disease, although it has many side effects, it controls 80-90% of the pain, that's why it is still the first line of treatment due to its high efficacy. Interventional pain management measures could be used in patients who cannot tolerate the side effects of the analgesics or who don't respond to them [46]. Percutaneous vertebroplasty is a new technique that arouse in the last decades and prove to be effective in management of pain due to vertebral fracture with the least invasion to the tissues. This technique is also proved to decrease the need for using analgesics so it is used in management of fractures that result from malignant osseous infiltration [47].

Neuropathic pain that originates from tumor in upper abdomen mostly don't respond to analgesic therapy. In cases of resistance to analgesics, nerve block and neurolysis of celiac ganglion could be done to alleviate the pain especially in gastric, pancreatic and biliary

cancer [48]. Many substance could be used such as triamcinolone that causes reversible blockage of nociceptor and alcohol which cause permanent damage of the nerve roots it is used locally and phenol could be used for the same purpose as an alternative to alcohol. Imaging is used to guide the blockage of celiac axis; CT is the most used one with the least complications which are diarrhea in 73% and orthostatic hypotension in 12% [49].

Conclusion

As having less invasive techniques in treatment of many diseases especially the widespread ones is important and also is the main focus of the research fields nowadays. Interventional radiologists prove that the new technique of IR (interventional radiology) is a promising candidate to achieve this goal. It could be used in any step of the medical care starting from diagnosis the disease especially cancer with different strategies, moving to treatment of malignancies either alone or in combination with surgery or chemotherapy and finally managing any complications that could happen due to the disease itself or the treatment. More efforts should be made for complete understanding of IR technology and how it could be used in more efficient way to decrease the side effects of traditional treatment, improve the efficacy and improve the quality of the patient's life.

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