

NewsLetter

Issue: December 2021 | Vol. XXV

No. 12 | Price: 50 Paise

EDITORIAL

MALE INFERTILITY AND CANCER

The number of men surviving cancer at a young age has increased dramatically in the past 20 years as a result of early detection and improved cancer treatment. Quality of life has become an important issue in childhood and adult cancer patients. Fertility is often impaired after chemotherapy and radiation therapy.

Malignant diseases might influence gonadal function through hormonal alterations and metabolic conditions. Reproductive hormones might be low in cancer patients as a result of stress, downregulation by endocrine substances produced by some tumors, such as β -human chorionic gonadotrophins by some TGCT, and as a consequence of a metabolic condition. In leukemia, lymphoma and in central nervous system tumors, the hypothalamus and the pituitary gland function might be directly impaired by tumor cell invasion or damaged by radiation therapy. Malignancy might also result in malnutrition, with deficiencies in the vitamins, minerals and trace elements needed for optimal gonadal function. Some malignancies are accompanied by periods of fever that negatively influence spermatogenesis. Finally, tumor released cytokines might affect spermatozoa function, resulting in low sperm motility.

Surgery might be needed for a tumor that's in or near an organ, such as a testicle, or the penis, bladder, or rectum. It might also be needed for a tumor that's in or near nervous system, such as the brain or spinal cord. These surgeries may affect a man's fertility. A few types of cancer surgeries can damage nerves that are needed to ejaculate semen. They include removing lymph nodes in the abdomen which may be part of the surgery for testicular cancer and some colorectal cancers. Nerves can be damaged when lymph nodes are being removed, and this can cause problems with ejaculation. Sometimes surgery can permanently damage the nerves to the prostate and seminal vesicles causing retrograde ejaculation.

The negative effect of cytotoxic drugs on spermatogenesis has been extensively investigated. Most harmful drugs are nitrogen mustard derivatives, such as busulphan and melphalan, and alkylating drugs, such as cyclophosphamide and procarbazine. Combination chemotherapy, such as (MOPP)-regimen given for Hodgkin's disease, has a high chance of sterilizing the patient. Other multi-drug regimens applied (ABVD) for Hodgkin's disease and BEP regime for TGCT, have a lower risk of permanent infertility. Recovery of spermatogenesis depends on the drugs used and on the cumulative dose given. Cyclophosphamide is one of the most commonly used alkylating agents in paediatric cancer treatment. Patients receiving a total cumulative dose of more than 10 grams/m² are at a high risk of developing permanent gonadal damage. The testes are very sensitive to irradiation, especially the germ cells. A dose of more than 4 Gys can cause permanent damage to the germ cells. The Leydig cells are more resistant to irradiation and a dose of more than 20 Gy is needed to produce hypogonadism.

Patients pre-treatment fertility appears to be of prognostic value for future sperm recovery. In men with Hodgkin's disease receiving >3 courses of MOPP, azoospermia is found in 85–90% of patients after a follow-up of >1 year. The only established method to secure fertility in male cancer patients before gonadotoxic therapy

is semen cryopreservation, which in time can be used for assisted reproduction techniques (ART). The patients who are unsuccessful in sperm banking are of younger age, and show higher levels of anxiety and more reluctance to talk about future fertility. Cryopreservation induces the deterioration of semen quality. On an average, sperm freezing decreases motility by 31%, morphology by 37% and mitochondrial activity by 36%. The utilization rate of cryopreserved semen is often less than 10–15%.

Difficult psychosocial and ethical decisions should sometimes be made regarding the possibilities of future parenthood in case of limited life expectancy. The issue of post-mortem use should be discussed if semen is cryopreserved. Informed consent of the patient is usually required for the post-mortem use of banked sperm. So far, the reproductive outcome of children born from fathers that had previous cancer treatment has shown no differences to the outcome of newborn children of a non-cancer population. Importantly, no reported increased risk for congenital malformations is found. In contrast to the situation in children from female cancer survivors, the offspring of male cancer survivors showed no increased risk for obstetric and perinatal problems or decreased birth weight. In boys in whom spermatogenesis has not yet started, no good options for securing their future fertility are available yet. Potential new fertility preservation techniques might use spermatogonial stem cells, which can be harvested from testicular tissue before cancer treatment. Other options, such as *in vitro* maturation of stem cells into spermatogonia and subsequent xenografting, need further investigation. Harvested germinal cells could be matured *in vitro* and cryopreserved to be used for future ICSI. Harvesting testicular tissue from prepubertal boys should, therefore, be considered experimental.

Continued on Page 4

*RGIRC wishes you
Healthy, Prosperous &
Happy New Year*



INTERVENTIONAL ONCOLOGY – THE FOURTH PILLAR OF CANCER CARE

“There is no time like the present”. This phrase cannot be more apt than writing an article to create awareness about Interventional Oncology (IO) – the newest/ minimally invasive and one of the most advanced and exciting branches of medicine, which is changing the lives of cancer patients across the globe. October 25-31 is celebrated as the IO Awareness Week to increase awareness about this field and its benefits for cancer patients.

IO is an emerging subspecialty of interventional radiology that “uses image-guided procedures to enhance cancer care,” according to a recent paper published in *The Oncologist*.¹ The combination of skill sets of Interventional procedures and Radiological knowledge helps the Interventional Radiologists to reach the most difficult parts of the body in a minimally invasive manner, thus improving the accuracy of the procedure and at the same time reducing the risks and complications associated with such procedures. The application of such advanced procedures into the field of oncology have led to the development and tremendous growth of this field called as the- Interventional Oncology (IO).

IO has advanced over the past few years as improved hardware, imaging technologies and new procedures are being developed. IO aims at using minimally invasive techniques to diagnose (providing a tissue for diagnosis of the smallest lesions in the body) or treat tumours (like radiofrequency ablation (RFA) / microwave ablation (MWA)/ cryoablation of tumours, thorough which the tumours are killed by heating/ cooling with only a thin needle without the need of a surgery). Liver cancer can be treated effectively through minimally invasive angiographic procedures such as Trans-arterial chemoembolization (TACE) or (Trans-arterial Radioembolization) in which drugs or radioactive particles are injected directly into the tumour cells without any major systemic side effects.

Cancer is associated with a lot of problems for the patients, bleeding from cancer is one of the major one which could be even life threatening. A major role of IO is stoppage of these cancer related bleedings by stopping the abnormal blood vessels which supply these tumours, all through fine needles, catheters and wires combination. The importance of palliative care cannot be over-emphasized and IO plays a critical role in providing palliative care to cancer patients in the form of pain relief, mitigation of cancer related symptoms and end of life care.

The role of IO in the management of cancer has been growing and has now established itself as the fourth pillar of Modern Oncology care” (the other three being medical, surgical, and radiation), as is evident by its increasing role in cancer treatment guidelines. Most of the IO procedures require only local anesthesia or mild sedation and the patient can be discharged the next day.

A lot of patients with Gall bladder and Bile ducts cancer develop jaundice due to obstruction by the tumour. A major role of IO is opening up these bile ducts and placing stents in them so that the patient is relieved of jaundice and can go for further treatment of the cancer. This has drastically changed the lives of patients suffering from these cancers who otherwise used to suffer a lot without cancer related treatment in the presence of jaundice.

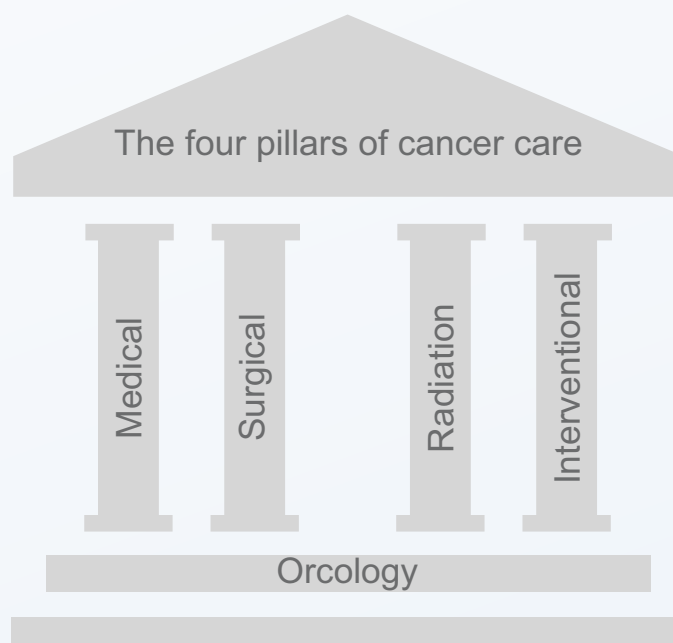


Fig. 1: Interventional oncology plays a key role in integrated cancer care is part of the four pillars of cancer care: medical oncology, surgical oncology, radiation oncology, and interventional oncology.

A more patient centered and personalized treatment approaches has also led to further development of IO. IO is focused on three main areas in cancer management: diagnosis, therapy, and symptom palliation.¹ A major advantage of IO is localized effect on the tumor or a single organ in the body with minimal systemic side effects. Numerous studies have shown that cancer patients treated in multidisciplinary environments benefit greatly from the combined expertise. Interventional Radiologists are seen as playing a major role in multidisciplinary cancer teams where they provide innovative solutions to improve combined therapies and to treat complications. IO has evolved in the treatment of liver malignancies, both primary and secondary in the form of liver directed therapies including chemoembolization/ radioembolization and ablative therapies as described above. The ablative therapies have further advanced with increasing role in lung, kidney and bone neoplasms as well.

Over the past few years, as the scope of IO has expanded, many big hospitals across the world are establishing subdivisions of IO. My institute, Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC) has also established the sub-division of IO in January 2021 and we are providing services to the hospital round the clock with an exclusive IO Cath Lab. The Society of Interventional Oncology (SIO) is a global non-profit association that supports and promotes the field of IO and we were associated with this global society for the launch of IO at our institute.

As we move into the era of Artificial intelligence and robotic technologies, the scope and utility of IO is only going to increase further.

Cath Lab Team
Department of Interventional Radiology,
RGCIRC, Rohini

ROLE OF MICROBIOTA IN CARCINOGENESIS AND CANCER TREATMENT

Human body has around 30 trillion human cells, but microbiome in human body is constituted by estimated 39 trillion microbial cells including bacteria, viruses and fungi that live on and in us. They make up about 1-3 per cent of our total body mass but have huge potential implications on physiology and diseases. We now have plenty of literature that demonstrates an association between disruptions in the homeostasis of microbial communities (termed as dysbiosis) and varied pathologic conditions. In addition, there is a link between the disruption of commensal microbiota and carcinogenesis, including compelling evidence regarding the role of the gastrointestinal (gut) microbiota in modulating responses to cancer immunotherapy and data demonstrating that the microbial communities within the tumor microenvironment can contribute to therapeutic efficacy.

Gut dysbiosis and cancer development

There is evidence supporting that generalized dysbiosis of the gut microbiota may contribute to carcinogenesis. An association between repeated courses of antibiotics and the development of a variety of both gastrointestinal (GI)-tract and non-GI-tract tumors has been demonstrated in large case-control studies. The mechanisms through which dysbiosis is proposed to affect tumorigenesis and/or tumor growth across cancer types are varied (Fig. 1). The role of microbiota in genesis of colon, breast, liver/biliary tract and stomach is being investigated and is linked to various mechanisms. Comprehensive insights are lacking at the moment but studies are underway to better understand pathways; how gut microbes may influence carcinogenesis?

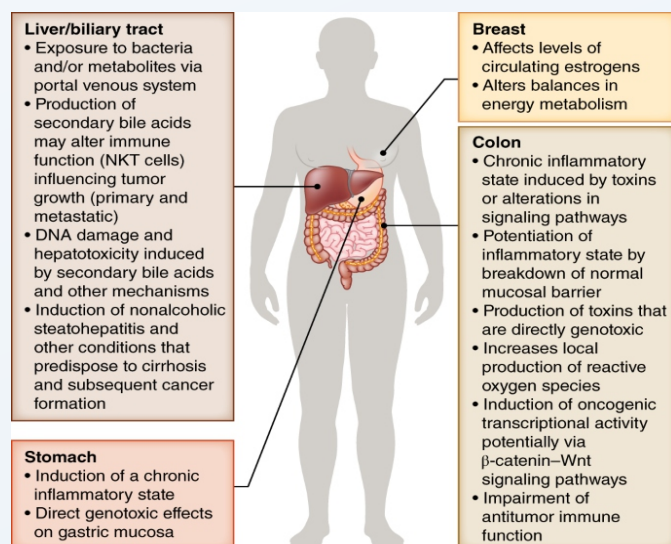


Fig 1. The influence of gut microbiota on cancer development.

The gut microbiota and cancer therapy

Different types of gut microbiota 'signatures' exist in patients who respond to cancer treatment. These favorable signatures are associated with enhanced systemic immunity and intratumoral immune infiltrates. Additionally, many studies have demonstrated that the 'responder' and 'nonresponder' phenotypes could be recapitulated in germ-free or antibiotic-treated mouse models via fecal microbiota transplant (FMT)—and that manipulation of the gut microbiota with specific bacterial taxa could enhance therapeutic responses. In addition, there is now evidence that the gut microbiota may shape responses to other forms of cancer therapy including chemotherapy and targeted therapy.

On the other hand Chemotherapy can cause profound dysbiosis and affect multiple metabolic pathways. Antibiotics are frequently prescribed during the course of chemotherapy that also impact the microbiota; this is important, as concurrent antibiotic administration has now in several studies been shown to negatively impact the outcomes of cancer immunotherapy. In addition to modulating treatment responses the differential microbome signatures are also associated with differential cancer therapeutic toxicities in different individuals such as development of graft versus host disease (GVHD) in allotransplant candidates.

The microbiome as a therapeutic target in cancer therapy

The famous Hippocrates quote "Let food be thy medicine and medicine be thy food," recorded around 431 bc supports the notion of food and the gut microbiota to mediate many benefits within the human body. Efforts are currently underway to enhance therapeutic responses and/or decrease treatment-associated toxicity via modulation of the gut microbiota. FMT was originally used roughly 2,000 years ago when Chinese researchers orally administered 'yellow soup,' a slurry of stool from a healthy individual, to patients to cure them of severe dysentery. Within last decade, FMT has been more widely used in managing refractory GVHD, checkpoint inhibitors related colitis and clostridium difficile diarrhea.

Next generation biotherapeutics involving single or multistrain bacterial consortia, with strong scientific rationale and evidence regarding their efficacy are being investigated and developed. These are different from over-the-counter probiotic formulations, which are often considered to be supplements or 'functional foods'. This field is young, and we are left with many unanswered questions. Multifaceted strategies are needed to monitor and modulate these factors to optimize health and to effectively treat diseases like cancer.

Keytake away-microbiome is the undiscovered organ of human body. It's pertinent to maintain homeostasis of our microbiome by practicing healthy habits so as to keep at bay the various pathological conditions.

Dr. Manish Sharma
Consultant - Medical Oncology
RGCIRC, Niti Bagh

CME WITH INDIAN MEDICAL ASSOCIATION (IMA) KAITHAL, HARYANA



RGCIRC organized a CME in association with IMA Kaithal on Friday, 03rd December 2021 at Mannat Hotel and Restaurant, Kaithal, Haryana. Dr. Pankaj Goyal, Consultant – Medical Oncology delivered a lecture on **Recent Updates in Breast Cancer Management** and Dr. Himanshu Rohela, Consultant – Orthopedic Oncology spoke on **Recent Updates in Orthopedic Oncology**. The CME was very well appreciated by the gathering.

Date of Printing: 25th December 2021

Date of Publishing: 30th December 2021

Posted at: Ashok Vihar, Head Post Office, Delhi - 110052
Register with Registrar of Newspaper Under No.68797/1998
Postal Department Registration No. DL(N)/004/2021-23
Licensed to Post without Prepayment Under No.: "U"(DN)-162/2021

EDITORIAL

Associations between male infertility and cancer are gaining clinical attention. Infertile men are at an elevated risk to develop various malignancies later in life, primarily genitourinary malignancies such as testicular and prostate cancer. Rates of testicular and high-grade prostate cancer in infertile men appear to be at least double the risk than in the general population. The link between infertility and malignancy highlights the importance of thorough evaluation and long-term follow up—beyond a simple semen analysis. A detailed urologic evaluation, possibly including scrotal ultrasound, may be beneficial to screen infertile men for testicular cancer. Publications have also demonstrated that male infertility can be a biomarker for cancer risk in first- and second-degree relatives. Testicular cancer risk in first-degree relatives of infertile men is 52% higher than the risk in relatives of fertile control men. Male infertility has been associated with a two- to threefold elevation in risk of childhood cancer in the siblings of infertile men. Links between infertility and malignancy are multifactorial, and exact mechanistic explanations are still not fully understood.

An infertility diagnosis in a man appears to carry health consequences for that individual, but data increasingly demonstrates that infertility may also be a biomarker of health for the infertile man's family members. Shared genetics or environmental exposures provide plausible mechanisms.



Dr. A. K. Dewan
Director - Surgical Oncology

ONCOLOGY FORUM'S 4TH DMSOG MEET



RGCIRC organized **Oncology Forum's 4th DMSOG Meet** in association with Delhi Musculoskeletal Oncology Group (DMSOG) on Wednesday, 08th December 2021 at India Habitat Centre, Lodhi Road, New Delhi. The theme of the meeting was **Ewings Sarcoma - Metastatic at Presentation**.

Dr. Himanshu Rohela, Consultant - Orthopedic Oncology gave opening remarks. The topics of scientific lectures were “**Metastatic Ewing Sarcoma-Has Anything Changed?**”, “**Systemic Treatment in Metastatic Ewings Sarcoma - Curative Intent**”, “**Local Control in Metastatic Ewing Sarcoma - is There a Role?**”, “**Palliative Treatment in Metastatic Ewing Sarcoma**” followed by panel discussion where two cases were discussed.

Eminent faculty from Delhi NCR shared their views on various aspects of management of this rare disease. The objective of this conference was to discuss case studies of stage 4 bone cancer patients and to explore alternative options which are adopted by eminent faculties in the Capital state.

Mr. D. S. Negi (CEO)
Dr. S. K. Rawal
(Medical Director)
Dr. A. K. Chaturvedi
Dr. D. C. Doval
Dr. Gauri Kapoor
Dr. Anurag Mehta
Dr. Rajiv Chawla
Dr. Sunil Kumar Puri
Dr. P. S. Chaudhury
Dr. Vineet Talwar
Dr. Munish Gairola
Dr. Dinesh Bhurani
Dr. I. C. Premsagar
Dr. Rupinder Sekhon
Dr. Shivendra Singh
Dr. Rajeev Kumar
Dr. Ullas Batra
Dr. Sumit Goyal
Dr. Rajan Arora
Dr. R. S. Jaggi
Dr. L. M. Darlong
Dr. Kundan Singh Chufal
Dr. Swarupa Mitra
Dr. Mudit Agarwal
Dr. Narendra Agrawal
Dr. Rayaz Ahmed
Dr. Jaskaran Singh Sethi
Dr. Vaishali Zamre
Dr. Himanshu Rohela
Dr. Pinky Yadav



To:

If undelivered please return to:
Rajiv Gandhi Cancer Institute and
Research Centre, D-18, Sector - 5,
Rohini, Delhi - 110085

Printed and Published by Mr. Pramod Maheshwari on behalf of Indraprastha Cancer Society and Research Centre and printed at R. R. Enterprises, 18 - A, Old Gobind Pura Ext., Street No. 2, Parwana Road, Delhi - 110051, Tel: +91- 8447494107, Published from Rajiv Gandhi Cancer Institute and Research Centre, D - 18, Sector - 5, Rohini, Delhi - 110085

Editor: Dr. A. K. Dewan