



NewsLetter

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EDITORIAL

ACT BEFORE THE RBCS IN YOUR PATIENT'S VEIN REACH A DEAD END

Venous thromboembolism (VTE) is an umbrella term for various degrees of deep vein thrombosis (DVT) and pulmonary embolism (PE). The risk statistics are alarming: One in every five cases of VTE is related to either cancer and/or its treatment. Cancer Surgery has a 7-fold higher risk of perioperative PE compared to similar surgery for benign disease. In the absence of routine thromboprophylaxis in surgical cancer patients, a majority (40-80%) develop postoperative isolated or asymptomatic calf vein thrombosis, 10-20% develop proximal DVT, 4-10% acquire symptomatic PE, and unfortunately, 1-5% exhibit fatal PE. It's no wonder that VTE-prophylaxis is a vital element of the ERAS - Protocol. There exist all three elements of the Virchow's triad namely, hypercoagulability (cancer, major surgery), vascular damage (multiple venepunctures, arterial line, central venous pressure lines, ports, PICC lines, chemotherapy) and venous stasis (frail, bedridden patients; venous compression by large tumours or bulky lymph nodes) in surgical cancer patients.

Before your patient's RBCs reach a dead end, let's check out the cafeteria choice of mechanical and pharmacological thromboprophylactic measures available to us.

Mechanical thromboprophylaxis

This includes elastic graduated compression stockings, intermittent pneumatic calf compression or sequential compression devices and foot pumps. It is extremely important to achieve the right amount of pressure for compression stockings ie 18 - 23 mmHg for primary VTE prophylaxis at ankle and 30 - 40 mmHg to prevent or treat post-thrombotic syndrome after an established DVT. Mechanical monotherapy offers a 67% risk reduction for perioperative DVT, but is much less efficacious in preventing perioperative PE. Hence, in high-risk patients a combination therapy with pharmacological thromboprophylaxis is required. Intraoperative intermittent pneumatic compression is achieved by alternate inflation-deflation of plastic/fabric sleeves, wrapped around the leg, secured with Velcro and wired to an electric pump.

Inferior vena cava (IVC) filters (temporary or permanent) have very specific and limited indications and should not be indiscriminately used because of significant complications.

Pharmacological thromboprophylaxis

Low - dose Unfractionated Heparin (UFH) effectively reduces the incidence of asymptomatic DVT by 67% and fatal PE by 68% reducing total perioperative mortality by 21%. Low-Molecular-Weight Heparin (LMWH) is obtained by fractionation of UFH and has a longer elimination half-life of 4-6 h (Kidneys). with a similar efficacy and safety profile, LMWHs have an additional advantage of a ten times reduced risk of heparin induced thrombocytopenia (HIT) and osteopenia, coupled with the

convenience of fixed once daily injections. Enoxaparin is the most commonly used LMWH in our institution.

Heparinoids like danaparoid, being heparin-free, are useful in surgical patients where heparin is contraindicated (allergy; HIT). Fondaparinux is a synthetic pentasaccharide that produces a 50% greater reduction in the incidence of VTE in major orthopaedic/abdominal surgery, compared to enoxaparin.

Vitamin-K antagonists (VKAs) like warfarin, although efficacious for perioperative VTE prophylaxis, have limited clinical utility owing to a slow onset of action (2-3 days) and a narrow therapeutic window that necessitates regular INR monitoring and frequent dose adjustments.

Directly acting intravenous thrombin inhibitors like lepirudin (recombinant hirudin) in a dose of 2 × 15 mg s/c per day provide primary VTE prevention after hip/knee arthroplasty. Argatroban is the drug of choice in HIT since it does not resemble heparin, averting any cross-reaction with HIT antibodies. Unlike lepirudin, argatroban does not induce formation of alloantibodies that can alter its clearance.

Aspirin is a notable exception in most guidelines for VTE prophylaxis which is probably industry driven. For general surgery, aspirin is NOT recommended as VTE prophylaxis but its use could be interesting in low-income countries.

Contraindications to pharmacological thromboprophylaxis include an INR > 2, thrombocytopenia (< 50000 / mm³), known bleeding disorders, any active bleeding, uncontrolled hypertension (BP > 230/120 mmHg), neuraxial block (lumbar puncture, subarachnoid block, epidural), performed within the last 4h (last 24h if traumatic) or expected to be instituted within next 12h and new onset stroke (ischemic / haemorrhagic).

Which hospitalized patients with cancer should receive anticoagulation for VTE prophylaxis?

The three prerequisites for pharmacologic thromboprophylaxis include active malignancy, acute medical illness or reduced mobility and absence of bleeding or other contraindications. Anticoagulation is contraindicated in patients admitted solely for minor procedures, chemotherapy or those undergoing stem-cell or bone marrow transplant.

Should ambulatory cancer patients receive anticoagulation for VTE prophylaxis during systemic chemotherapy?

Routine pharmacologic thromboprophylaxis should not be offered to all outpatients with cancer. The three prerequisites include high VTE risk (Khorana score ≥ 2 before a new systemic chemotherapy regimen), absence of significant risk factors for bleeding and no drug-drug interactions (CYP-3A4; P-gp). Apixaban, rivaroxaban or LMWH may be utilized for VTE prophylaxis after educating these patients about relative benefits and harms, drug cost and duration of prophylaxis.

to be continued on 4th Page

These are times of evidence based and risk adapted treatment approach in every segment of medicine. There has been gradual evolution in diagnostics and therapeutic strategies over past decades to come to this era of risk adapted approach to treatment. With advances in diagnostics, we are now able to have a better classification and risk stratification of various hematological malignancies. Similarly, treatment strategies have evolved in such a way that now we treat some good risk patients with less intensified approach to minimize toxicities while maintaining efficacy of the treatment regimes and intensifying the treatment in only those with high risk disease.

Treatment of aggressive lymphomas: Commonest example of aggressive lymphoma is diffuse large B cell lymphoma (DLBCL) and high grade B cell lymphoma (HGBCL). Currently DLBCL is further classified into several subcategories based on its gene expression profile or immune-histochemical patterns which are surrogate to molecular features. These subclasses are germinal centre type (DLBCL-GC) which is considered a good prognostic class compared to other one, the activated B cell (DLBCL-ABC) type which has got a poorer prognosis. Another advance in the management of DLBCL and High grade B cell lymphomas is identification of re-arrangement of cMyc and BCL2/BCL6 genes detectable by Fluorescent in-situ hybridization (FISH) technique. Based on cMyc and BCL2/BCL6 gene rearrangements, DLBCL and high grade B cell lymphoma can be classified into double hit/ triple hit lymphoma (DHL/THL) and non double hit lymphoma. Double hit/ triple hit lymphomas are highly aggressive and are associated with poorer prognosis. Therapy is usually intensified in such patients to achieve better results.

High grade T cell lymphomas (except lymphoblastic lymphoma which is treated with ALL like therapy) are also treated with intensive chemotherapy and Autologous bone marrow/ hematopoietic stem cell transplantation in selected patients with high risk features.

This way, it is very much needed these days to identify high risk features by molecular testing. Intensification of therapy is warranted in selected patients with high risk features to achieve outcomes comparable to good risk patients while less intensified treatment approach is maintained for those with good risk disease to minimize toxicities while maintaining good outcomes.

Treatment of Multiple Myeloma: Multiple myeloma is also called Myeloma. Myeloma was once considered a deadly and incurable disease and was usually treated with cytotoxic chemotherapies. Over past two decades, there has been development of many anti-myeloma drugs with specificity for myeloma cells (malignant plasma cells) and lesser cytotoxicity to normal tissues. These drugs are Proteasome inhibitors like Bortezomib, Carfilzomib and Ixazomib and Immuno-modulators with anti-angiogenic properties like Thalidomide, Lenalidomide and Pomalidomide most of which are available for Indian patients very easily and at affordable cost. Apart from these two major classes of drugs, now we have certain targeted therapies- immunotherapies like anti CD 38 monoclonal antibody (Daratumumab, Isatuximab), Anti SLAM F7 antibody (Elotuzumab) and anti BCMA antibody (Balantamab). Moreover, CAR-T cell therapy is promising and is in developmental phase in India. With cytotoxic therapies of past, complete remissions were uncommon and would be to the range of 30% even after an Autologous Bone Marrow Transplantation and an early relapse in majority of patients. But nowadays, with wide availability of novel agents, we are able to achieve complete remission and even deeper remissions in a significant majority of patients and that can be further improved with an Autologous Bone Marrow Transplantation and further maintenance therapy. Apart from expansion of this therapeutic armamentarium, there has been progress in understanding of cytogenetic and molecular patterns of myeloma and its prognostic and therapeutic implications. Now a day, FISH technique is widely available to identify

cytogenetics aberrations specific to myeloma and we can identify high risk myeloma (for example, those with 17p [p53] deletion, 1q gain and others like t4:14, t14:16) with help of FISH. Taking together the clinical features and cytogenetic abnormalities, we can design treatment in such a way to achieve better results in even those with very high risk myeloma.

Acute leukemias: acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) are most aggressive and deadly of hematological malignancies. Both AML and ALL are heterogenous diseases and varied widely in prognosis depending on cytogenetic and molecular profile. So, there are AML which are classified as good risk or standard risk (examples- AML with t8:21, inv16, normal karyotype with NPM1 mutated without FLT3 mutation or AML with normal karyotype with CEBPA double mutated) while others as high risk AML (examples- AML with complex karyotype or monosomal karyotype, t v:11q, monosomy 7/-7q, monosomy 5/5q-, AML with FLT3-ITD etc). Similarly, prognosis of ALL too depends upon several clinical and cytological factors. There are patients with good risk ALL (example- young age, lower WBC counts at presentation, hyperdiploid karyotype) while others with high risk ALL (example- advancing age, higher WBC counts at initial presentation, cytogenetic/ molecular features like t9:22/ BCR-ABL or t4:11/AF4:MLL). Patients with high risk leukemias not only show resistance to chemotherapy but also have a higher probability of relapse early in the course. Patients with good/ standard risk leukemias are usually treated with chemotherapy alone while patients with higher risk leukemias are usually offered chemotherapy to achieve initial disease control and then Allogeneic bone marrow transplantation as a consolidative therapy to minimize risk of relapse. We can use targeted drugs along with chemotherapies in patients having specific molecular aberration. For example, patient of ALL with BCR-ABL fusion are high risk and are treated with chemotherapy along with targeted drug (Imatinib/ Dasatinib which targets BCR-ABL gene) and this way achieve deeper remissions and better outcome. Similarly, FLT3 mutation (FLT3 ITD) confer chemo resistance in AML and nowadays is treated with targeted drug (Midostaurin/ Sorafenib) along with chemotherapy to achieve better outcome.

Bone marrow/ hematopoietic stem cell transplantation (BMT): A BMT is recommended for patients having bone marrow failure syndrome or with high risk hematological malignancies at high risk of relapse. There have been immense progresses in field of BMT over past decades. Several notable advances are matched unrelated donor transplants, haplo-identical transplants, non-myeloablative and reduced intensity transplants. This way, most of patients in need of a BMT can be taken including those with advancing age or those not having a suitable HLA matched stem cell donor in family

So in nutshell, we have come a long way to this era where we have sophisticated methods to dissect cytogenetic and molecular details of hematological malignancies, plan therapy as per risk stratification and use targeted therapies and bone marrow transplantation to get optimal outcome.

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COMPREHENSIVE ONCO ANESTHESIA TRAINING (COAT) PROGRAM: A REPORT

The first Comprehensive Onco Anesthesia Training (COAT) Program was organized by the Department of Anesthesiology and Critical Care, Rajiv Gandhi Cancer Institute and Research Centre (RGCIRC) on the 30th April 2023, at Indraprastha Hall. It was nicknamed as "RGCIRC COAT" program. The theme was 'Onco - Anaesthesia - An overview', and the tagline was 'Onco Anesthesiologist - A Silent Companion in Cancer care.'

Dr. Rajiv Chawla, Director (Anesthesiology) was the Chairman, Dr Amit Mittal and Dr Shagun Shah, Senior Consultants were the Organising Secretaries.

During the 'Welcome Address' Dr Chawla informed about the symbiotic anesthesiologist-surgeon relationship, and increasing awareness of the patients and community on the vital role of an anesthesiologist especially in cancer care. Prof Sushma Bhatnagar, Chief of DR BRAIRCH-AIIMS delivered an enlightening keynote address on **Infinity & Beyond- Past, Present & Future of Onco-Anesthesia**. Dr Sudhir Rawal, Medical Director, RGCIRC and a leading onco-surgeon informed about the progress in field of anaesthesiology that he has witnessed over the past three decades ensuring peri-operative safety. Dr AK Bhargava, the former Director (Anesthesiology- RGCIRC) was felicitated. Dr Amit Mittal in his 'Department Report' informed the growth and progress of anesthesiology department at RGCIRC over past 25 years. Dr Shagun Shah conveyed the 'Vote of Thanks.'

Over 110 anesthetists from across the country, including government organizations like Indian Railways and ESIC and hospitals of Government of NCT of Delhi participated in the program. The program consisted of 12 didactic lectures, two well-argued panel discussions covering various aspects of oncoanaesthesia, 27 posters and 8 stalls. All the sessions were well attended, and delegates were highly satisfied. *"Each attendee had something new to learn"* was a flattering comment from one of the senior guest faculty. It was agreed by the experts that with increasing incidence of cancer and cancer surgery, it is necessary that every anesthesiologist must

be made aware of the basic concepts of onco-anesthesiology. There is a need to establish a well laid referral system for cancer patients to enable right treatment at the right place. To meet these goals, it was opined that in-job training programs in onco-anesthesia should be conducted more often. It was also suggested that during post graduate training in anesthesiology (DNB/MD etc) the students must have rotation to a cancer centre to learn onco-anesthesia similar to neuro-anaesthesia and cardiac anesthesia rotation.

RGCIRC-COAT program 2023 was an academic feast with interesting and intriguing sessions by distinguished experts from leading hospitals such as AIIMS, Medanta, Indraprastha Apollo, Sir Gangaram Hospital. Faculty from various medical colleges MAMC, LHMC, UCMS, RML, PGIMS Rohtak also participated in the sessions.

The faculty and delegates opined that seeing the overwhelming response, the program should be conducted annually.



NURSES WEEK CELEBRATION 2023

The theme chosen by International Council of Nurses for the year 2023 is "Our Nurses, Our Future". Department of Nursing organized various activities during the Nurse's week from 8th to 13th May 2023. Scientific sessions, panel discussion, poem writing competition, poster competition, card making competition, quiz and other fun activities were part of Nurses Week celebration.

On 12th May, Nurses Day celebration started with lamp lighting followed by Florence Nightingale Pledge.

"I acknowledge your patient concerns with attentive listening to providing top- notch medical care, you all are the back bone of healthcare system. I want to thank you all from the bottom of my heart for all the hard work you do. Your selflessness is admirable and I am grateful for your unwavering support" Col. Madhumita Dhall (Director of Nursing, RGCIRC) said to the Nurses on her message.

Mr. D. S. Negi (CEO, RGCIRC) mentioned in his message that, "Nurses Day 2023 will mark the 201st anniversary of the birth of Florence Nightingale, the founder of modern nursing. Today, her legacy continues to inspire nurses in providing high- quality care and promote the health of patients with empathy. In celebrating Nurses Day 2023, it is our endeavor to invest in the nursing profession. This includes improving the working conditions, providing access to ongoing professional development, and enhancing compensation for the invaluable work of nurses"

Dr. Sudhir Kumar Rawal (Medical Director, RGCIRC) and Dr Gauri Kapoor (Medical Director, RGCIRC, Niti Bagh) also shared their best wishes to Nurses.

Awards were presented to Nurses of various categories to recognize and appreciate their hard work and dedication towards patient care. There was also a cultural program performed by the nurses and was cherished by the audience present there.

A Continuous Nursing Education program on the ICN theme for 2023 Nurses' day was organized on 13th May at Indraprastha hall. The event brought together more than 150 Nurses from different Health care organizations in Delhi NCR. The CNE included of interactive sessions by experienced Faculties regarding current scenario, various aspects and challenges for the future of nurses.



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EDITORIAL

Should surgical cancer patients receive perioperative VTE prophylaxis?

All cancer patients undergoing major surgery should receive pharmacologic thromboprophylaxis with UFH/LMWH unless contraindicated. A combined regimen (pharmacologic + mechanical) has enhanced efficacy in high-risk patients. Mechanical methods monotherapy is resorted to if pharmacologic methods are contraindicated. Ideally commenced preoperatively, the duration is 7 to 10 days postoperatively. Extended prophylaxis with LMWH (4 weeks) is recommended for major open/ laparoscopic/ robotic abdominal or pelvic surgery patients with high-risk features (restricted mobility, obesity, history of VTE). For lower-risk surgical settings, decision on a case-by-case basis is required.

Future directions

Future research should be directed at improving VTE-risk scores, developing and incorporating new biomarkers, oncogenes and machine learning, introducing risk scores for concurrent bleeding risk and improving prophylactic therapy by conducting clinical trials on new compounds like Factor-XI inhibitors (Abelacimab).

To conclude, the risk of VTE should be balanced against the risk of bleeding.



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