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Palliative Care

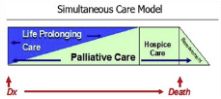
- *Integration of Palliative Care into Emergency Medicine: The Improving Palliative Care in Emergency Medicine (IPAL-EM) Collaboration.*
- Lamba S, DeSandre PL, Todd KH, et al.
- By using a case this group sought to offer guidelines to integrate palliative principals daily practice of the ED including four initiatives to jumpstart the process.

The Need

- Given the broad spectrum of patients that present to the ED those with serious illness from chronic disease are not uncommon.
- The authors delineate two themes that guide treatment that from the emergency department have long-term implications as they often guide in-patient care:
  - Best practice based clinical decision making.
  - Development of care plans that consider the patient's values and goals.
- While palliative care is recognized as important the usual barriers in the ED are extent in making it challenging to incorporate a palliative care program let alone to discuss its intricacies to a patient or their family.

Definitions

- Palliative care ***"is defined as patient care that is focused on relief of suffering (physical, spiritual, or psychological), is based on patient-determined goals, and is appropriate for all phases of a life limiting condition."***
  - Maximal benefit is derived from early integration of a plan.
  - Often palliative care is consulted when there is nothing more that can be done for the patient.
  - Hospice and palliative share many of the same principals but hospice care is prognosis based and comes into play when the expected survival is ≤ 6 months.
  - Benefits include optimal comfort, symptom control, even prolonging life.



Clinical Integration in the ED

- There a 4 clinical integration categories defined by the authors:
  - ***Traditional consultation*** – requested by the EM physician.
  - ***Basic integration*** – ED and palliative care programs work collectively on certain goals and objectives.
  - ***Advanced integration*** – ED and palliative care work on processes and protocol with the ED taking the lead.
  - ***ED-focused advanced integration*** – where the ED is highly engaged, may direct the palliative care program, often led by a dual boarded ED-palliative care trained physician.

Key Steps

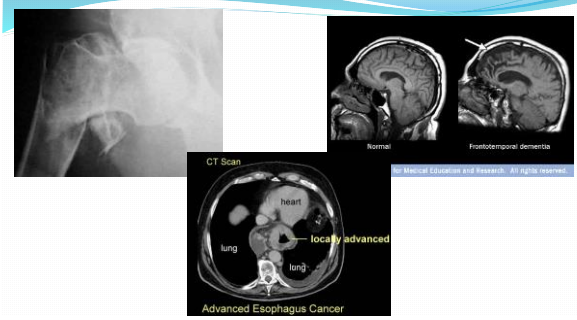
- The IPAL-EM project is a resource to help facilitate the integration of palliative care services in the ED and the authors using this platform identify 4 key steps:
  - 1 – identify ED champions.
  - 2 – explore existing literature and educational resources.
  - 3 – identify local hospice/palliative care resources.
  - 4 – complete a needs assessment.

Primary Screening Criteria

- Screening appropriately starts with a "potentially life-limiting or life-threatening condition" AND the following primary criteria that would indicate unmet palliative care needs:
  - **Surprise question** – "***Would you be surprised if the patient died within 12 months?***"
  - **Frequent admissions** for the same conditions with several months.
  - Admission for **difficult to control physical or psychological symptoms.**
  - **Complex care** requirements (functional dependency, home support, feeding, ventilator).
  - **Decline** in function

Secondary Screening Criteria

- Secondary screening criteria of unmet needs would include:
  - Admitted from ECF.
  - Elderly, demented, patient who fell and now has a hip fracture.
  - Metastatic or locally advanced incurable cancer.
  - Chronic home oxygen use.
  - Out-of-hospital cardiac arrest.
  - Current or past hospice program patient.
  - Limited social support, lack of family, chronic mental illness.
  - No known advanced care planning.



Clinical Case

- The authors use a case scenario to guide the discussion of palliative care integration to the ED.
- The case is an 85 y/o patient who is septic from a gangrenous foot with a history of CVA's, HTN, DM, PVD, nonverbal, bed bound, PEG tube feedings, and defendant for all ADL's on outside help.
- She is febrile, glucose = 400, tachycardic, was in the ED for 16 hours with consultations from podiatry, vascular surgery, orthopedics.
- The ED physician contacts the daughter to discuss the situation, the poor prognosis, and a shift to comfort care and maybe hospice.
- The primary care physician is then contacted, the care plan agreed upon by the daughter is discussed, and she is finally admitted **hours later**.

Discussion

- Starting a palliative care initiative in the ED starts with a champion(s) to push the effort to address hospital and community resources, availability of palliative care consultation, and key deficiencies that is focused on a needs assessment.
- Sensitivity to the ED and hospital metrics that are becoming more draconian including readmissions, door to physician time, ICU utilization, and ED/hospital LOS.
- Support from nursing and ED medical direct goes without saying.
- The IPAL-EM web site offers position statements, clinical guidelines, and research citations that are frequently updated.
- Identifying local hospice and palliative care resources including chaplaincy, social work, bereavement counseling, and availability of those including times.

Discussion

- Unanswered questions include:
  - Limited data on patient outcomes regarding ED palliative care.
  - Limited data on the burden imparted on ED personnel and resources.
  - Which patients are in greatest need for services in the ED.
  - The optimal role of the ED physician in caring for patients with "chronic trajectory illnesses".
  - Limited data on health care utilization of palliative care programs in the ED.
  - Data on educational priorities for ED physicians is undefined.

Summary

- Palliative care is becoming an increasing need across healthcare systems as our population ages and survives long with chronic illnesses.
- This need includes the ED and there are guidelines to integrate palliative care through the EPAL-EM initiative that is a very complete resource of guidelines, program structure, and literature.
- Each ED has its own access to the necessary resources for such a program that can be defined by a needs assessment.
- Consultation on a timely basis with palliative care specialists, social work, care coordinators, and private physicians will also be necessary.

Summary

- The role of the ED and EM physicians in this area is not well defined and the impact on ED nursing/physician resources is not well studied.
- *The paradigm of adding "just one more thing" to the role of the ED physician is a common theme in health care systems and in the opinion of some EM leaders the "plate is not just full but overflowing" [opinion of the presenter].*
- However, the role of the emergency medicine in coordinating patient care, both out-patient and in-patient, is only going to grow and according such luminaries as the ACEP immediate-past president is a role we need to embrace and start developing programs to address.

Toxic Industrial Chemicals and Weapons

- *Toxic Industrial Chemicals and Chemical Weapons – Exposure, Identification, and Management by Syndrome.*
- Tomassoni AJ, French RNE, Walter FG.
- This is another of the ongoing, frequent articles on chemical exposures from the Yale New Haven Center for Emergency Preparedness and Disaster Response that offers little if any new approaches for the emergency clinician are particularly helpful accompanied by a long laundry list of toxins, symptoms, and treatments that one would have to look up anyway should one have patients who are exposed.

Introduction

- There are over 100,000 chemicals used daily in U.S. industries many of which are potentially injurious.
- Increasing population density, proximity of plants to population centers, dependency on industrial chemicals, human error, and terrorism are factors that drive the concerns in this area.
- Exposure can be unnoticed or even covert, even brief exposures can have lasting health consequences.

[presenter note: while not explicitly stated in the article there was no mention that possibly the the most salient aspect of addressing these types of toxic exposures is that the emergency medicine system on the average day is at or over capacity.]

Basic Principals

- Timely recognition is the "sine qua non" of care goes without saying along with a thorough understanding of the properties of the toxin and routes of exposure.
- Treatment and diagnosis is straightforward when the agent is known.
- Multiple casualties, concomitant trauma, or victim co-morbidities can complicate treatment.
- **Treatment starts with:**
  - **Preventing secondary exposure to staff and patients.**
  - **Significant versus trial exposures differentiated.**
  - **Decontamination initiated.**
  - **Surge capacity and capability assessed and plans executed.**
  - **Public health and public safety agencies notified.**

Patient Assessment

- Exposures can mimic nonspecific illnesses or common medical problems making an identifying history challenging.
- Lack of exposure data, exposure to a mix of chemicals, limitation of toxicology studies, and limited knowledge of the effects of the chemicals potentially involved complicates patient assessment.
- Routes of exposure include inhalation, dermal, ocular, mucosal, and ingestion are salient pieces of the history.
- The dose response principal states that as the dose of a toxicant increases more individuals are affected and the magnitude of patient response increases – as the LD50 is approached this can be a crucial part of the assessment.

Clinical Manifestations and Management

- Syndromic recognition given the huge number of potential chemicals and the vast array of effects make this a daunting challenge.
- So with each chemical can have its own toxidrome there are some common ones and some more dramatic than others.
- For the most dangerous toxins treatment is often limited to decontamination and supportive care.
- For a limited number of agents specific antidotes do exist and there are comprehensive lists both within the article and rapid available on-line to emergency physicians.

[it is not the intention here to go through the long list of 11 toxidromes, 23 specific agents with antidotes, and 13 specific industries and potential exposures from them.]

Clinical Manifestations and Management

- Examples of medical problems seen with toxic exposures include:
  - Dermatoses from metal such as Cr, Ni, fibrous glass, soaps, and solvents.
  - Headache from CO and solvents.
  - Acute psychosis from lead mercury, and carbon disulfide.
  - Asthma or dry cough from formaldehyde, toluene, animal dander.
  - Pulmonary edema or pneumonitis from nitrogen oxide, phosgene, halogen gases, or cadmium.
  - Cardiac arrhythmias from solvents or fluorocarbons.
  - Angina from CO or methylene chloride.
  - Abdominal pain from Pb.
  - Hepatitis from halogenated hydrocarbons can be a long-term effect.

Long Term Effects of Toxic Exposures

- Long term effects can include:
  - Lung cancer from arsenic, asbestos, nickel, and uranium.
  - Bladder cancer from dyes and naphthylamine.
  - Aplastic anemia or leukemia from benzine and ionizing radiation.
  - COPD, pulmonary fibrosis, and mesothelioma from asbestos.
  - COPD, chronic bronchitis, Tb from silica and cotton fibers.
  - Black lung disease from coal dust.
  - Pulmonary fibrosis from beryllium.

Target Organs

- The injured organ can also give a clue to the possible agent:
  - Lung – smoke, asbestos, paraquat, silica.
  - Liver – carbon tetrachloride, ethanol, arsenic, vinyl chloride, yellow PO_4.
  - Kidney – heavy metals, solvents, toluene.
  - Blood – benzene, nitrates, CO.
  - Cardiovascular – CO, tobacco smoke.
  - CNS – hydrogen sulfide, organic solvents.
  - Skin – halogenated aromatic hydrocarbons.
  - Reproductive – lead, carbon disulfide.
  - Ocular – acid, alkali agents.

Summary

- The ED is the front line for the recognition, treatment, mitigation, and prevention of toxic exposures both from industry and weapons.
- Causes can be difficult to ascertain unless a specific exposure history is available and mixtures of chemicals a patient could be potentially exposed to just complicates matters all the more.
- Using a systematic approach to address exposure history can improve diagnostic accuracy of the history.
- Recognition of common toxidromes may help diagnosis and treatment when the agent is unknown.
- Use of specific antidotes can rescue the patient and knowing the availability of those antidotes by the ED physician is important.
- Being familiar with available outside resources is also important.

Trauma Airway

- *Trauma Airway Management.*
- Horton CL, Brown CA, Raja AS.
- This review of the managing the trauma airway was timely, relevant, and geared towards the emergency physician with the authors from the ED from *THE BRIGHAM* (or for us more lowly physicians Brigham and Women's Hospital affiliated with the Harvard School of Medicine).
- Like many of the articles presented it starts off with a case presentation to illustrates the points.

[presenters note: for those of you needing trauma CME this article counts.]

Case

- A 34 y/o man comes in from an MVA, unrestrained, ran off the road and hit a tree, confused, perseverating, stable vital signs, with obvious head/face/chest injuries.
- Exam – decreased breath sounds on the right, symmetrical pulses, chest wall echymoses, BP = 95/70, pulse = 115, Pox = 96% on RA, GCS = 11.
- FAST = fluid in Morrison's pouch, normal lung slide bilaterally.
- Secondary survey – 15 cm laceration from forehead to occiput, PERRL, ecchymosis and edema to the anterior neck, no stridor, decreased breath sounds on the right, tender right chest and RUQ.
- CXR = opacity RML, no pneumothorax.

Initial Evaluation and Intervention

- Trauma airway management can be complex due to:
  - Unstable hemodynamics that rapidly change.
  - Cervical immobility.
  - Direct airway trauma.
  - Direct chest trauma.
  - Oral, upper airway, and facial trauma.
  - Complex decision making.
- **Deciding to intubate is the first step with 3 main indications:**
  - **Failure to maintain or protect the airway.**
  - **Failure to oxygenate or ventilate.**
  - **Anticipated clinical course that might mandate airway control.**

Initial Evaluation and Intervention

- Failure to maintain the airway is not always obvious.
- Using the GCS to assess that aspect of trauma airway management is generally well accepted:
  - GCS ≤ 8 is considered clinical coma and it is generally accepted that intubation is necessary if not mandatory.
  - GCS ≤ 12 indicates a significant brain injury and if not due to a readily reversible cause most patients with need to be intubated.
- Assessment of the airway should include the ability to phonate and handle secretions and should NEVER be done by testing the gag reflex.*

[presenter's suggestion: ask the patient to "swallow", if they are able to without difficulty they can protect their airway, this is untested and unverified by research.]

Initial Evaluation and Intervention

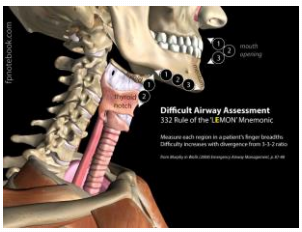
- Failure to oxygenate and/or ventilate can be assessed by respiratory effort, oxygen saturation, and overall sense of the injuries sustained.
- The anticipated clinical course is also helpful in deciding whether to intubate the patient and the authors advice erring on the side of early airway intervention.
- Supplement oxygen should be started immediately in any hypoxic trauma patient.
- **A nasal cannula can suffice or a non-rebreather mask at 15 & 30 L/min.**
- Pre-oxygenation in anticipation of intubation can begin with 3-5 minutes of supplemental oxygen, getting the patient to take full tidal volume breaths for 2-3 minutes with the **NC being left in place** during the entire intubation sequence to facilitate apneic oxygenation.

Intubating the Trauma Patient

- An essential key to intubating the trauma patient is assessing for the potential for a difficult airway that is not uncommonly encountered.
- The acronyms:
  - Assess for difficult laryngoscopy – **LEMON**
  - Difficulty using a BVM – **MOANS**
- For patients with an obvious difficult airway RSI is generally felt to be the safest and most effective way to secure a definitive airway.
- The authors suggest with anticipated difficulty with the airway calling for anesthesia and/or surgery colleagues and consideration of performing it in the OR should be entertained.

LEMON – **L**ook Externally

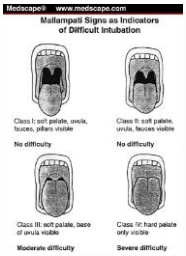
LEMON – **E**valuate 3-3-2 Rule



LEMON – **M**allampati Score*

Mallampati Score

- Class I
  - visualization of the soft palate, fauces, uvula, and both anterior and posterior pillars
- Class II
  - visualization of the soft palate, fauces, and uvula
- Class III
  - visualization of the soft palate and the base of the uvula
- Class IV
  - soft palate is not visible at all



**This is the poorest of the screening items*

LEMON – **O**bstruction, **O**besity

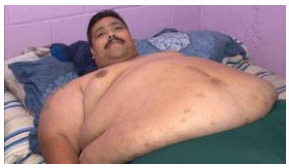
LEMON – Neck Mobility

Missing Assessments [presenter's note]

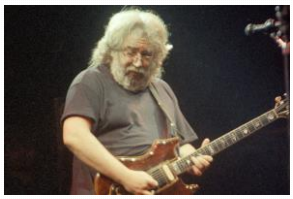
- *To LEMON I add an "S" for oxygen saturation that is a key determinant of how much time one might have to intubate the patient.*
- *The authors also did not mention the "HOP" patient:*
  - *H – hypotensive.*
  - *O – oxygenation, hypoxia, saturation reserve.*
  - *P – pH abnormalities, acidosis or alkalosis can influence both the ability to withstand intubation and setting the ventilator.*
- *There was also no mention of the newer concepts such as delayed or resuscitation sequence intubation.*

MOANS – **M**ask Seal

O - Obesity




MOANS – Age (> 55 years old)




MOANS – No Teeth


Stiff Lungs


Awake Intubation

- If the need for intubation is immediate a full assessment, extra staff, and management planning might not be feasible.
- But if there is time for an defined difficult airway an awake intubation or awake evaluation should be performed using a topical anesthetic and judicious use of sedation* to permit laryngoscopy (direct, video, fiberoptic) and one of three things can be then done:
  - Intubation.
  - Visualization of the glottis to assess if full RSI is feasible.
  - Oral intubation is impossible and an alternative approach is needed.

[*presenter's note: recommended sedation cocktail for awake intubation – ketamine + propofol.]

C-Spine Precautions

- The authors state **all** patients who have had significant blunt trauma are assumed to have a have a cervical spine injury.
- Intubation can be challenging if positioning the patient is sub-optimal as movement of the neck should be minimal.
- A second provider **stabilizes** the neck.
- Video laryngoscopy is recommended and may reduce neck movement.

*This is an example of how **not** to do it – using a video laryngoscope, CMAC, but has left the C-collar on that restricts visualization of the glottis and is not as good to restrict c-spine movement.*

Pre-Medications

- No study has demonstrated that any premedication prior to intubation have improved outcomes common sense would suggest their benefit including:
  - **Lidocaine** 1.5 mg/kg is felt to attenuate neural mediated reflex that is assumed to increase ICP.
  - **Fentanyl** 2-3 mg/kg given 3-5 minutes prior to intubation is felt to blunt the reflex sympathetic response that with the rise in BP and pulse is felt to also increase ICP.

RSI Sedative Medications

- The sedatives most commonly used for trauma patients are:
  - **Etomidate** –
    - It is the most **hemodynamically stable** sedative and causes almost no change in MAP in normal and hypovolemic patients
    - There appears to have some **cerebral protective** effect
    - The dose is **0.3 mg/kg** in patients in frank shock the dose should be reduced to 0.15 mg/kg; based on lean body weight.
    - The significance of the transient adrenal suppression is unknown but to date no increase in mortality has been seen.
  - **Ketamine** –
    - Is an attractive induction agent due to its **cardiovascular stability**.
    - Can be used to facilitate awake intubation or airway inspection.
    - Bronchorrhea can be reduced with glycopyrrolate or atropine.
    - Dose **is 1.5 mg/kg** reduced to 1 mg/kg in patients in shock.
    - In patients in refractory shock ketamine can depress myocardial contractility and "must be used with caution".

RSI Medications - Paralytics

- The recommended paralytics by the authors are:
  - **Succinylcholine** –
    - Is the **paralytic of choice** for RSI in the polytrauma patient.
    - Is a direct depolarizing agent.
    - Its rapid onset of action and relatively short duration of action recommend it.
    - Dose **is 1.5mg/kg**.
  - **Rocuronium** –
    - Is also a **recommended** paralytic.
    - Its onset of action is similar to that of succinylcholine at **1.0 mg/kg** dose.
    - Its duration of action though is much **longer lasting** ~ 45 minutes.
- Concurrent volume resuscitation should occur along with the preparation for intubation though if the need for intubation can be delayed it is advise to hold off to allow infusion of fluids.

Tracheobronchial Injuries

- Tracheobronchial injuries are rare but should be suspected in blunt or penetrating trauma to the neck or chest representing 0.5-2% of blunt trauma victims .
- Complete transactions most often die before arrival in the ED, in one study 78% died in the field, 21% within 2 hours of ED arrival.
- Patients present with dyspnea or respiratory distress (76-100%), hoarseness or dysphonia (46%).
- Signs include pneumothorax (20-50%), subQ emphysema (35-85%), and hemoptysis (14-25%).
- The paramount goal is not to convert a partial transection to a complete one with intubation best done in the OR typically by fiberoptic laryngoscope and very small endotracheal tube as cricothyrotomy is unlikely to be successful.

Case Resolution

- Initial management focused on fluid resuscitation and stopping ongoing blood loss so the laceration was stapled, NS given along with a unit of PRBC's.
- With a GCS of 11 and the expected clinical course he was intubated prior to moving to CT with a double set up of prep' ing the neck in case orotracheal intubation failed.
- A chest tube was deferred given the CXR showing the lung contusion and negative E-FAST ultrasound.
- Topical anesthesia with nebulized lidocaine and IV glycopyrrolate was given along with 0.5 mg/kg of etomidate to sedate.
- Under fiberoptic visualization a partial tracheal tear was seen, the scope was passed beyond the tear and a 6.0 ETT was passed with further sedation obtained with fentanyl and midazolam.

Summary

- Trauma patients who need a secure airway require rapid evaluation for the potential of a difficult airway (LEMON, MOANS), a rescue plan in the event of intubation failure, and a willingness to act with very incomplete information or rapidly deteriorating clinical status.
- Often the need to intubate is clear and one needs to wary of mistaking that the airway is stable and missing the opportunity to intubate the patient safely.
- Distortion of the airway can occur with soft-tissue swelling, hematoma, or subQ air can indicate lethal airway distortion.
- This is a time for early assessment and decisive action.

Summary

- The trauma airway is a challenging aspect of airway management due to a number of issues:
  - Unstable patient with limited history and time to obtain information.
  - The clinical status of the patient can change rapidly.
  - Often the time to prepare the patient for intubation is limited.
  - Positioning the patient is limited as cervical spine injury is assumed.
  - Intubation is advised in patients who cannot protect their airway, cannot oxygenate or ventilate, or the anticipated clinical course necessitates it.
  - GCS score < 8 needs automatic intubation, < 12 most likely.
  - Involving ones anesthesia and surgery colleagues is often necessary.
  - Assume the patient is a difficult intubation and rapidly assess for such.

Summary

- If possible fluid resuscitation to address hypotension and impaired perfusion before intubation is desirable.
- Preoxygenation with NC plus NRB mask oxygen supplementation is important to extend apneic oxygenation and give one sufficient time to intubate the patient.
- Awake intubation is recommended if there is the potential for a difficult airway.
- Sedation with etomidate with ketamine as an alternative and paralysis with succinylcholine or rocuronium are the recommended agents.

Summary

- The potential for the rare case of tracheobronchial disruption should be suspected with neck or chest trauma particularly if the patient is hoarse, has subQ air, or pneumothorax as intubation can convert a partial to complete disruption that is almost always fatal.
- What was not addressed by the authors is what does one due once the airway is secured in terms of ventilating the patient which in the case example could be difficult given the lung contusion and partial tracheal tear.
- RSI in the "HOP" patient was also not addressed.

VTE

- *Treatment of Venous Thromboembolism.*
- Wells PS, Forgie MA, Rodger MA.
- JAMA 2014;311:717-728.
- This was a literature review of the etiology of VTE and the 3 phases of treatment – acute (first 5-10 days), long-term (3-6 months), and extended (beyond 3-6 months).
- Obviously both long term and extended have little relevance for ED patients in most cases.

Introduction

- VTE includes both DVT and PE with an annual incidence of 0.1-0.27% affecting ~5% of the U.S. population in their lifetime.
- **PE mortality is 20%** either before the diagnosis is made or within the first 24 hours with another 11% dying in the next 3 months even with adequate therapy (much of that is due to co-morbidities).
- Long-term complications include postphlebitic syndrome in up to 40% from DVT and chronic pulmonary hypertension in 1-4% of PE patients.
- Prior to anticoagulation untreated VTE was fatal in 30% of cases, now lower with the use of anticoagulants but hemorrhage is more common that can be fatal in up to 25% of cases.
- **Risk/benefit balance for treatment is best looked at in 3 phases**; acute (5-10 days), long-term (3-6 months), and extended (>3 months) along with being provoked, unprovoked, or associate with cancer.

Study Methodology

- This literature review was performed in 2013 starting with PubMed yielding 1,535 articles in addition to another 8,753 is other databases.
- 222 meta-analysis articles coming down to 80 related to treatment, 68 being actual meta-analyses, and finally 57 being relevant to the present article.

Treatment of Acute VTE – Initial Treatment

- The goals of initial therapy once a VTE is diagnosed are:
  - Prevention of **DVT extension**.
  - Prevention of **PE occurrence or recurrence**.
  - Relief of a **acute symptoms**.
  - Averting hemodynamics **collapse or death**.
- The authors clearly state that ***"when diagnostic testing . . . is delayed, empirical administration of low-molecular weight heparin (LMWH) is indicated.***

Treatment of Acute VTE – Initial Treatment

- Initial treatment of VTE requires therapeutic doses of:
  - **Unfractionated heparin – IV/subQ monitored, fixed-dose subQ.**
  - **LMWH.**
  - **Rivaroxaban (Xarelto).**
  - **Fondaparinux (Arixtra).**
- Comparing LMWH with unfractionated the LMWH was associated with fewer deaths, less major hemorrhage, lower rates of recurrent VTE, and is the preferred anticoagulant irrespective of VTE treatment in either the in-patient or out-patient settings.
- The only exception to that would be in patients with ***renal insufficiency*** as LMWH is primarily excreted by the kidneys, then unfractionated heparin would be the treatment of choice.

Treatment of Acute VTE – Initial Treatment

- Initial therapy with vitamin K antagonists (VKA) alone is not recommended because of the several day period of time to reach therapeutic levels of anticoagulation.
- Trials demonstrated more recurrent VTE when a VKA is used as the sole initial treatment.
- If a VKA is going to be used **bridging** with one of the heparins for a minimum of 5 days until a therapeutic INR is achieved with 10mg of coumadin for days 1 and 2 then 5-10mg daily adjusted to the INR.
- VKA pharmacogenetic testing while available is expensive ($172,000/quality adjusted life-year) and not recommended.

Treatment of Acute VTE – Initial Treatment

- Rivaroxaban is one of the NOAC's indicated for acute and long-term treatment of both DVT and PE.
- It is a a direct F-Xa inhibitor and compared with LMWH/VKA treatment was noninferior for recurrent VTE and similar or fewer major hemorrhages.
- To date the direct F-Xa inhibitors have no reversal agent but one should note that while coumadin is reversible that has not improved outcomes in VKA associated intracranial hemorrhage.
- Dosage recommendations for the other NOAC's; apixaban, edoxaban, and dabigatran are cited in a table by the authors.

Treatment of Acute VTE – Thrombolysis

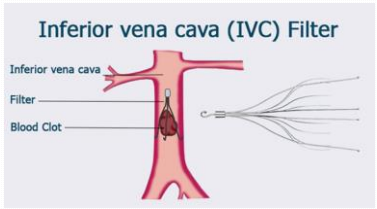
- The prospect of going in a dissolving the offending clot is attractive as it can restore blood flow to the occluded vein and potentially reducing the incidence to postthrombotic syndrome.
- While earlier patency is achieved thrombolysis **does not reduce the incidence of PE, recurrent VTE, recurrent PE, or death.**
- Some data suggests that catheter-directed thrombolysis might be better than systemic but clear evidence is lacking.
- The best evidence for catheter-directed therapy is in iliofemoral DVT (unstable clot), symptoms for < 2 weeks, good functional status, life expectancy > 1 year, and a low risk of bleeding.

Treatment of Acute VTE – Thrombolysis

- Thrombolytic therapy for upper extremity DVT has been used and some success has been seen.
- The authors note there are no randomized trials comparing anticoagulation with thrombolysis or any treatment for arm DVT.
- **Thrombolytics for submassive PE** has been studied in 2 good trials and **did not reduce mortality**, did have a higher rate of hemorrhage, and is only recommended for PE associated with hemodynamic compromise or deteriorate while on standard anticoagulation.

Treatment of Acute VTE – Filters

- The main indication of vena cava filters is where there is a contraindication to anticoagulation in patients with newly diagnosed DVT/PE (e.g. recent surgery or hemorrhage).
- One risk of both permanent and retrievable filters is developing thrombosis on the filter itself and has be be considered.
- As such should the contraindications to anticoagulation resolve anticoagulant therapy should be initiated and the filter removed once therapy is accomplished.
- The placement of IVC filters plus anticoagulation has not been found to improve survival in VTE except in patients with hemodynamically unstable PE or after thrombolytic therapy.



Postthrombotic Syndrome

- Postthrombotic syndrome (PTS) is both a frequent and important complication of VTE.
- Prediction of patients at risk or how to prevent PTS in unknown.
- Graduated compression stockings while a good idea have not been shown to reduce the incidence but can improve the edema and pain seen with acute DTV's.
- They can also improve the symptoms of PTS but just not prevent its occurrence.

Out-Patient vs. In-Patient Treatment

- The paradigm of admitting all VTE patients was primarily due to having to use unfractionated heparin.
- With the advent of LMWH out-patient management is becoming more attractive.
- The literature supports the **safety and efficacy of LMWH out-patient treatment** in patients without severe symptoms, renal insufficiency, poor social circumstances, or are a high risk for bleeding.
- Ambulation in patients with DVT's has less optimal support in the literature by meta-analyses suggest it has benefits.

Out-Patient vs. In-Patient Treatment

- In Canada it is standard for VTE treatment to be initiated in the out-patients setting.
- A number of prediction rules to help select low risk patients have been found to be effective including the Geneva Pulmonary Embolism Severity Index among others can identify patients with an in-hospital mortality risk of < 1% *[readily available in MDCalc]*.
- Isolated calf DVT is less well studied than PE/proximal DVT in patients without severe symptoms or risks for clot extension.
- In such patients observation and repeat ultrasound in 1 weeks to look for extension has been found to be effective with rare development of proximal DVT and anticoagulation can be held.

Pulmonary Embolism Severity Index - PESI

Variable	Points
Age	1/year
Male sex	10
Cancer	30
Heart failure	10
Chronic lung disease	10
Heart rate ≥110/min	20
Systolic blood pressure <100 mmHg	30
Respiratory rate ≥30/min	20
Body temperature <36 °C	20
Disorientation, lethargy, stupor, coma	60
SaO_2 <90%	20

ESC Guidelines

European Heart Journal (2008)

Data are from reference 214.
Risk categories (30-day all-cause mortality, %): class I, <65 points (0%); class II, 66–85 points (1%); class III, 86–105 points (3.1%); class IV, 106–125 points (10.4%); class, V >125 points (24.4%). Low risk = classes I and II (0–1%).
SaO_2 = pulsoximetry.

Upper Extremity DVT Recommendations

- Upper extremity DVT involves 5-10% of all DVT's.
- 75% are related to indwelling venous catheters and 25% non-catheter related.
- Axillary and proximal clots are treated as in proximal lower extremity DVT with a minimum duration of treatment being 3 months.
- Catheter related DVT should also be treated with a standard VTE anticoagulation regimen and should continue as long as the catheter remains in place or at least 3 months.

Long-Term or Extended VTE Therapy

- **Three months** is the usual shortest duration of treatment recommended.
- Extended treatment past three months would be based on if the benefits of continued anticoagulation outweigh its risks.
- The studies comparing 3 vs. 6 months of anticoagulation have been equivocal due to small numbers of patients in the 2 major meta-analyses.
- Studies of ASA showed the risk reduction for recurrent VTE was not significant unlike the risk reduction for VKA's and the NOAC's.

Provoked VTE – Transient Risk Factor

- Transient risk factors would be those that increase the thrombotic risk for a short period of time and are **reversible**.
- Surgery would be such an example and 3 months of anticoagulation is all that is needed with the recurrence rate of <1% at one year and 3% at five years.
- A first non-surgical VTE such as pregnancy, trauma, immobilization have a higher recurrence risk of 5% in the 1st year and 15% at five years.
- Despite this increased rate of VTE it is felt 3 months of treatment is adequate.

VTE and Pregnancy

- **PE is currently the leading cause of maternal death** in the Western world with an incidence of 0.6-1.7 episodes per 1000 deliveries.
- VKA's cannot be used during pregnancy as they are teratogenic in the first trimester and can penetrate the placenta resulting in fetal ICB in the third trimester.
- As such **LMWH** are the preferred treatment with the BID regimen recommended over the q-day injection continued for 1 month and then reduced to 75% of the initial dose for the duration of the pregnancy unless delivery is imminent then a filter should be placed.
- Anticoagulation therapy should be continued for 3-6 months postpartum.

Unprovoked VTE

- A VTE without identifiable risk factor is considered unprovoked.
- Recurrence rate is substantial at 10% at 1 year and 30% in 5 years.
- Extended or even indefinite anticoagulation is recommended.
- The calculus is an estimated case fatality rate for major hemorrhage is 12%, for recurrent DVT 4%, and 8% PE.
- The recurrence risk of DVT must exceed 3x the major hemorrhage and 1.5x the PE rates and while risk prediction tools have been proposed they lack validation.
- Prediction of an individual patient's recurrent VTE rate is difficult.

Unprovoked VTE

- HERDOC2 clinical decision rule for women who have a <3% risk of recurrent VTE has been suggested but not validated and would be if no more than 1 of the following exist:
  - Signs of PTS; skin hyperpigmentation, erythema, edema.
  - D-dimer > 250 mcg/L.
  - Age > 65 years old.
  - BMI > 30.
- Other prediction factors have suggested low d-dimer level after 1 month of treatment, male sex (men have 2.2x higher risk of recurrent VTE), and residual venous occlusion but none by themselves predict a low enough recurrence rate.

Unprovoked VTE

- In one study patients with a persistently elevated antiphospholipid antibodies had a 29% vs. 14% recurrence rate compared to controls.
- The risk ratio was 2.83 is patients with a positive lupus anticoagulant.
- Patient who a second unprovoked VTE should receive indefinite anticoagulation with the caveat if that second event follows a provoked event then the risk of recurrent VTE was not elevated.
- No firm evidence is available regarding a patient who has had two VTE's during a transient risk period but the recommendation is to treat for six months.

Agents for Long-Term and Extended Therapy

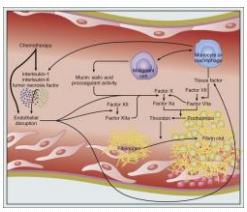
- VKA has been the standard for prolonged anticoagulation with point-of-care monitoring of INR being shown to be effective.
- Time in therapeutic range was 57% in community practice and 66% with the use of anticoagulation clinics.
- The standard recommendation is to maintain the INR at 2-3 with studies of lower intensity long-term anticoagulation at 1.5-1.9 was less effective but had a lower incidence of bleeding.

Agents for Long-Term and Extended Therapy

- The NOAC class of agents are the new anticoagulants that are being used more extensively as they do not require monitoring, are more bioavailable, have less drug and food interactions.
- Rivaroxaban and apixaban for DVT/PE was noninferior to LMWH and VKA therapy with very low rates of bleeding of 0.1-0.2%.
- Dabigatran was also shown to be as effective as VKA for VTE.
- Edoxaban has also been shown to be noninferior to VKA for recurrent VTE.

Malignancy Associated VTE

- Cancer patients have a higher incidence of recurrent VTE and bleeding complications compared to other patients with unprovoked VTE.
- Long-term use of LMWH was more effective than coumadin in patients with malignancy induced VTE.
- Patients should be treated for at least 6 months with risk of recurrence is 3x higher in cancer vs. non-cancer patients it is recommended to treat while the cancer is "active" and to continue for 6 months after cure or remission.



Summary

- Patients with VTE are divided into provoked and unprovoked groups depending on risk factors being identified and reversible or not.
- The traditional use of routine in-patient treatment with unfractionated heparin as a bridge to achieving a therapeutic INR with a VKA is changing.
- The efficacy of LMWH appears to be superior to unfractionated heparin and allows out-patient treatment in selected patients at low risk of complications and good overall general health.

Summary

- In the patient with objectively confirmed PE or DVT determine:
  - Does the patient have a PE with cardiopulmonary compromise or DVT with risk of limb loss:
    If so administer thrombolytics + heparin (LMWH or unfractionated).
  - If no cardiopulmonary compromise or risk of limb loss then determine is the patient is actively bleeding or anticoagulation is contraindicated:
    - If so arrange for IVC filter to be placed, when bleeding stops anticoagulation Tx.
    - If not determine prognostic risk.
  - Prognostic Risk:
    - DVT/PE with good prognostic risk and no renal insufficiency – out-patient treatment with LMWH or NOAC agents.
    - DVT/PE with poor prognosis and/or renal insufficiency – hospitalize, IV or subQ heparin.