

# Central venous catheters in hematological patients : risky lifelines ?

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## VALORIZATION

Central venous catheters (CVCs) are extensively used in patients with hematological malignancies undergoing intensive chemotherapy to provide cancer treatment and supportive care therapies. These CVCs improve patients' quality of life by reducing the need for venipunctures and allowing patients to receive chemotherapy, stem cell infusions, blood products, medication and parenteral nutrition. CVCs have become a 'life line' for hematological patients. The great benefits can be offset by complications. Reported complications consist of mechanical complications during or directly after the insertion (arterial puncture, hematoma and pneumothorax) and long-term complications like CVC-related infections and thrombosis. The incidence of CVC-related thrombosis varies between 1.2-18% and the incidence of CVC-related bloodstream infections varies between 0.0-40.6%. CVC-related infections and thrombosis impair CVC functioning and result in patient morbidity, may interrupt or delay administration of cancer therapy and represent a costly burden to the healthcare system. Long term complications pose hematologists with difficult questions on what anticoagulant treatment to choose in often thrombocytopenic patients and whether the CVC ('life-line') must be removed. The total annual costs of CVC-related infections in patients with cancer in the United States is estimated to exceed 18 billion dollars.

This thesis is about long term complications of central venous catheters in hematological patients undergoing intensive chemotherapy. Based on above information we can conclude that CVC-related infections and thrombosis in hematological patients undergoing intensive chemotherapy are clinically relevant problems causing morbidity, mortality and costs for the health care system. They should not be accepted as complications of modern care but must be one of the priority targets of a multidisciplinary approach emphasizing quality-of-care improvement. This thesis may help improving quality of care and thereby reducing morbidity, mortality and costs.

Many studies have addressed the incidence and associated risk factors of CVC-related thrombosis and infections in patients with solid tumors, but only limited data are available on hematological patients. This thesis focuses exclusively on hematological patients with a CVC undergoing intensive chemotherapy. Since these patients are often thrombocytopenic and leucopenic, experience mucositis and their CVC is considered a life line they deserve a specific approach. This thesis provides insight into this specific group of patients and why these patients deserve a specific approach. The ultimate target should be a multidisciplinary approach and strict adherence to an evidence based guideline. This thesis with its extensive review and studies focused specific on hematological patients provides a basis for the development of such a guideline.

Prevention of the long term complications is of utmost importance. The paradigm for dealing with these long-term complications needs to shift from treatment to

prevention. Guidelines recommend against the routine administration of pharmacologic prophylaxis to prevent CVC-related thrombosis. Since fibrin sheath formation around the external portion of the CVC and within the catheter lumen has been implicated as a major contributing factor in both occlusive and infectious events we started our randomized controlled study to determine the efficacy of concentrated citrate as a locking solution compared to heparin. No differences in CVC-related BSI were found. We did find seven times more CVC-BSI with gram negative organisms in the heparin group and a not statistically significant doubling of the incidence of CVC-related thrombosis in the heparin group. These are findings that warrant further investigation.

In this thesis elevated leukocyte count, factor VIII and plasminogen activator inhibitor-1 were found to be potential interesting biomarkers. Further investigation determining baseline clinical and laboratory parameters to help identify hematological patients at highest risk for CVC-related thrombosis and infections is needed. This will help to tailor the management of central venous catheters in hematological patients undergoing intensive chemotherapy.