Morbidity after lymph node dissection in patients with cancer: Incidence, risk factors, and prevention
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CHAPTER 1

General Introduction and Outline
The role of lymph node dissection in cancer treatment

For solid tumors, surgical intervention is still the primary curative treatment modality for many types of cancer. In patients with regional lymph node involvement, whether clinically apparent at diagnosis or established by sentinel node biopsy or by ultrasound guided fine needle biopsy, a lymph node dissection is carried out to achieve locoregional control and prevent further dissemination of the disease. In some cases, lymph node dissection is part of the standard procedure for surgical treatment with curative intent, even if there is no clinical evidence of pathological nodes. Regional lymph node dissection can also be performed as a salvage procedure after primary chemoradiation therapy in head and neck cancer. While it is an important part of surgical treatment for locally advanced cancer, lymph node dissection is also associated with both short-term and long-term morbidity.

Wound complications following inguinal lymph node dissection

As with any surgical procedure, wound complications may occur following lymph node dissection. Wound complications, such as wound infection, seroma formation, skin edge necrosis and wound breakdown, account for an important part of short-term morbidity after lymph node dissection. While wound complications can occur after lymph node dissection in any anatomical region, the inguinal lymph node dissection (ILND) as carried out in patients with established inguinal lymph node metastases of melanoma, penile- or vulvar cancer, appears to be particularly complication prone 1-4. Previous studies have addressed the risk factors associated with wound complications in ILND, but both the design and the results of these studies have not been entirely consistent (e.g., not all studies investigated the same set of risk factors; not all studies that examined any given risk factor yielded significant results) 1,4-8. Risk factors may be related to postoperative management, such as bed rest or suction drain management. Also, clinical and patient characteristics may play a role, i.e. technique and extent of the ILND, comorbidity, age or smoking behaviour.

Identifying risk factors for surgical complications may offer opportunities to reduce postoperative morbidity and improve patient outcomes for high-risk patients. The inconsistent findings of previous studies suggest the need for further research in this area. The Netherlands Cancer Institute is a specialised cancer hospital, and consequently has a high case load of patients who have undergone an inguinal lymph node dissection. Taking advantage of this high case load, two historical cohort studies were carried out to assess the incidence and risk factors of postoperative complications in patients with groin dissection for melanoma and penile carcinoma respectively. These studies are reported in Chapter 2 and 3.

Lymphoedema after lymph node dissection

With more patients surviving cancer, increasing attention is being given to long term sequelae of cancer treatment and their impact on health-related quality of life (HRQoL). The most frequently reported long term complication after lymph node dissection, and one of the most bothersome, is lymphoedema. Lymphoedema is the accumulation of interstitial fluid as a result of insufficient lymph drainage 9.

After lymph node dissection, secondary lymphoedema may occur as a result of insufficient lymph drainage due to removal of the lymphnodes. Disruption of collateral pathways due to scar tissue formation and fibroses, resulting from the surgical procedure and/ or subsequent radiotherapy
may add to the risk of developing lymphoedema. When untreated, accumulation of proteins in the lymphatic fluid will lead to increased viscosity of the lymphoedema, further impairing drainage, and ultimately to fibrosis. Lymphoedema can cause pain and discomfort, and limit activities thus impairing HRQoL 10-14.

Several criteria have been put forward for the diagnosis of clinically relevant lymphoedema, and several methods of measurement are available. Most criteria as used in research are based on quantitative changes in circumference or volume, with differing thresholds for defining the presence of lymphoedema. More sophisticated methods such as bio-impedance and ultrasound measurements are sometimes also used 15-17.

As part of usual care, several interventions can be offered to patients after lymph node dissection to reduce the risk of developing lymphoedema. There is, however, considerable practice variation. Preventive interventions may include education on risk-reduction strategies, self care and surveillance for early signs and symptoms of lymphoedema 18,19. The use of compression stockings or sleeves has been advocated 20-22. Also, manual lymph drainage is believed by some to be an effective intervention for reduction of lymphoedema risk after lymph node dissection 22-24. Strong empirical evidence on the effectiveness of these preventive interventions is scarce, with no available systematic reviews and, for some therapies, no randomized controlled trials.

Chapter 4 reports on a randomized controlled trial for prevention of lower limb lymphoedema after inguinal lymph node dissection by use of compression stockings.

Chapter 5 reports on a systematic review of randomised controlled trials on conventional interventions for prevention of lymphoedema in patients who are at risk for upper limb lymphoedema after breast cancer treatment.

The shoulder syndrome after neck dissection

Persisting lymphoedema is less well documented after neck dissection compared to axillary or inguinal lymph node dissection, although recent studies report incidence rates as high as 79% 25-27. The most important long term complication after neck dissection is related to iatrogenic damage of the eleventh cranial nerve; the accessory nerve 28-31.

Dysfunction of the accessory nerve results in paresis or paralysis of the trapezius muscle. In healthy persons, the trapezius muscle stabilizes the scapula on the thorax, during positioning and movements of the arm. While glenohumeral range of motion for abduction and forward flexion in the shoulder joint is limited to 90 degrees, the forward and lateral rotation of the scapula permits the arm to elevate up to 180 degrees in forward flexion or abduction. In these movements, the trapezius muscle is an important contributor to combined forward and lateral rotation, and elevation of the scapula. It is the sole muscle capable of lateral rotation of the scapula. Consequently, range of motion of the shoulder girdle is severely limited when the trapezius muscle is dysfunctional. Aside from limited (active) range of motion, dysfunction of the trapezius muscle may lead to changes in posture. The scapula tends to drop, rotate medially, and the shoulder girdle goes into protraction. This causes overload of the rhomboid muscles, the levator scapulae muscle, and the acromio-clavicular and sterno-clavicular joints. Secondary to these changes in anatomical position and changed scapulo-thoracic pattern of movement, patients experience shoulder joint problems such as pain and even secondary adhesive capsulitis 31,32.
In 1952, Ewing labelled the combination of shoulder drop, winging of the scapula due to inadequate stabilization, limited range of motion and changes in functional anatomy the ‘shoulder syndrome’ in patients after neck dissection. Since then, a number of elective procedures have been developed to limit postoperative morbidity by preserving non-lymphatic structures such as the accessory nerve and the sternocleidomastoid muscle. To date, such modified or selective neck dissections are the norm, and radical neck dissection with sacrifice of the accessory nerve is performed only if there is direct involvement of the nerve in the pathological process.

Still, even after nerve sparing dissections, the majority of patients experience temporary loss of function of the trapezius muscle. Although recovery of the accessory nerve typically occurs when it has not been dissected during the procedure, recovery usually does not set in before 6 months after surgery and it can take as long as 12 months for the trapezius muscle to regain its function. Chapter 6 reports on a prospective clinical study to determine incidence and recovery patterns of shoulder- and neck function after neck dissection, and to identify risk factors of shoulder disability after neck dissection in the mid-term postoperative period.

The reported incidence and prevalence of shoulder pain and disability after neck dissection varies widely, and is dependent on the type of dissection. Part of the variability in observed shoulder disability arises from the diversity of outcome measures used. This complicates the interpretation of results across studies investigating shoulder disability after neck dissection. Moreover, the patient reported outcome measures that have been used in patients after neck dissection have been insufficiently validated in this population.

Chapter 7 reports the results of a study of the psychometric properties of 3 commonly used scales to measure shoulder disability in patients after neck dissection.

Chapter 8 provides an overall summary and discussion of the research contained in this thesis.

Relevance of the studies in this thesis

Summarizing, lymph node dissection is still the de facto standard in surgical treatment of patients with regional lymph node involvement. It is associated with a variety of complications that may impact negatively on patients’ functioning, activities and quality of life. This thesis adds to the current body of knowledge by reporting on the incidence, impact, risk factors and prevention of a number of important lymph node dissection-related sequelae in patients with breast-, vulvar-, penile-, skin- and head and neck cancer.
REFERENCES


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