UNIVERSITEIT VAN AMSTERDAM

Morbidity after Lymph Node Dissection in Patients with Cancer. Incidence, Risk Factors, and Prevention

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SUMMARY

Chapter One provides a general introduction to morbidity after lymph node dissection in cancer patients. It describes the diversity of the observed morbidity in relation to the anatomical region of the lymph node dissection and provides the outline of this dissertation by identifying the knowledge gaps that are addressed in the subsequent chapters.

The aim of **Chapter two** was to assess the frequency of surgical wound complications after inguinal lymph node dissection (ILND) in patients with melanoma, and to assess the influence of potential risk factors for these complications. A chart review was carried out of all patients on whom ILND had been performed in the last ten years, and complications (infection, skin flap problems and seroma formation) were counted and graded. Previous studies had been performed to identify risk factors for surgical wound complications in melanoma patients undergoing ILND. We took this research into account when selecting the candidate-predictors for the risk model. Additionally, we studies procedure specific aspects as possible risk factors. We could not confirm most of the findings of earlier studies, and found that older age (OR 1.46, 95%CI 1.01 to 2.14) was the only siginificant predictor of grade I or higher wound complications. The predictive ability of the model was small, even in a full model containing all previously identified risk factors. This indicates that the influence of each of these factors is small, and that there may be other, yet unidentified factors at play.

In **Chapter three**, we performed a similar study among patients treated with ILND for penile cancer. In this study too, the overall complication rate was high, although the majority of complications were minor. We identified body mass index (OR 1.76, 95%CI 1.04 to 2.96) transposition of the sartorius muscle (OR 2.12, 95% IC 0.97 to 4.63) and bilateral dissection (OR 2.17, 95%CI 0.96 to 4.95) as the most important risk factors for grade 2 or higher complications in this cohort.

In **Chapter four**, we report on a randomized controlled trial on the effectiveness of graduated compression stockings for prevention of lymphoedema in the lower limb after ILND. In this trial we compared the incidence of lymphoedema in patients who used a class-II compression stocking for 6 months to the incidence in patients who did not. Additionally, we compared surgical wound complication rates, body image and HRQoL between the groups. Although patients who used stockings had a lower risk of developing lymphoedema, this difference was not statistically significant and smaller than it is generally believed to be (RR 0.80, 95%CI 0.60 to 1.07). Additionally, we found no statistically significant effect of stocking use on surgical wound complications, HRQoL, or Body Image. Approximately one-third of the patients indicated that the stocking was uncomfortable to wear.

In **Chapter five**, we performed a systematic review of conservative interventions for prevention of clinically detectable upper-limb lymphoedema after breast cancer treatment. We systematically searched the major electronic databases of medical literature. Additionally, we reviewed the reference lists of included trials and of relevant other reviews that were identified in the search.
We assessed the risk of bias in each of the included studies.

Outcome measures of interest included lymphoedema, infection, range of motion of the shoulder, pain, psychosocial morbidity, level of functioning in activities of daily life (ADL), and health related quality of life (HRQoL). We included ten trials that compared different interventions. The overall quality of the evidence was low due to risk of bias and inconsistency of results across trials.
Four of the included studies with a total of 385 patients studied the effectiveness of manual lymph drainage (MLD). In two studies MLD was added to education and/or exercises. Two studies compared MLD combined with compression or with exercise to education only. Based on these studies, no firm conclusions can be drawn about the effectiveness of physiotherapy interventions containing MLD for prevention of lymphoedema. Physiotherapy, consisting of manual lymph drainage combined with exercise, resulted in better shoulder mobility in the first weeks after breast cancer surgery, compared to exercise or education only (pooled estimate for abduction 21.8 degrees; 95%CI 13.6 to 30.1, and forward flexion 14.4 degrees; 95%CI 7.1 to 21.8). Results on longer term effects were heterogenous.
Meta-analysis of three studies did not yield a statistically significant result for lymphoedema risk reduction by delaying the onset of shoulder mobilising exercises for one week or longer, although two out of three studies showed lower lymphoedema rates in the delayed group (pooled RR 0.59, 95%CI 0.33 to 1.06). Shoulder mobility may be better at short term follow-up after early start of exercises.
Meta-analysis of two trials on progressive resistance exercise therapy showed that resistance exercises do not increase lymphoedema risk (RR 0.58, 95%CI 0.30 to 1.13), provided that symptoms are closely monitored and adequately treated if they occur. Infection, pain, level of functioning in activities of daily life, and HRQoL were scarcely used as outcome measures in the included trials, while psychosocial morbidity was not included in any of the studies. Future high quality trials are needed to further evaluate all the interventions studied in this review.

In **Chapter six**, we investigated the incidence of shoulder disfunction after neck dissection, its impact on perceived disability, and its relation to quality of life. Additionally, we aimed to identify clinical predictors for midterm shoulder disability. We found that overall, around 50% of the patients reported shoulderpain and disability. Functional loss of the Trapezius muscle due to accessory nerve damage was more prominent in patients with radical-, or modified radical neck dissection, regardless of sparing of the accessory nerve in the latter procedure. Impaired shoulder function was associated with perceived disability and with worse scores for some domains of HRQoL. We found that loss of function of the accessory nerve, scapular instability and shoulder pain were useful predictors for shoulder disability in the mid-long term, explaining 43% of the variance.

In **Chapter seven**, we assessed the psychometric properties of three commonly used scales; the Shoulder Disability Questionnaire, the Shoulder Pain and Disability Index (SPADI) and the Neck Dissection Impairment Index (NDII) in a population of patients after neck dissection. We used classical test theory to investigate reliability and validity of each of the scales. The SPADI and the NDII exhibited the highest reliability, but all scales were sufficiently reliable and valid for use in individual patients after neck dissection. We used item response theory scaling to fit a Rasch model to the combined items of the NDII and SPADI. This resulted in a better coverage of item difficulty along the continuum of self reported shoulder disability, but the ability of this combined scale to discriminate between patients with or without a self-perceived need for rehabilitation was less than that of the NDII and the SPADI as single scales, and floor effects were larger.

Finally, in **Chapter eight,** the results of each of the studies are put into a clinical perspective and recommendations for future research are made.