Carcinogenesis and treatment of adenocarcinoma of the oesophagus and gastric cardia
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In Part One the (dis)advantages of lymph node dissection for carcinoma of the oesophagus are discussed. In Chapter 1 the pattern of lymphatic dissemination in oesophageal carcinoma is described, introducing the surgical concepts of a limited transhiatal resection on the one hand and a transthoracic resection with extended two-field lymph node dissection on the other. In Chapter 2 a formal meta-analysis comparing short term and long term results of transhiatal versus transthoracic oesophageal resection is presented, covering the English literature of the last decade. This meta-analysis forms the background of the thesis.

After these introductory chapters, the clinical effects of lymphadenectomy are studied. Chapter 3 presents a retrospective study into the recurrence pattern after transhiatal resection for adenocarcinoma of the oesophagus. The recurrence pattern offers insight in the possible benefits of a more extended resection, offering the retrospective background for the main study of the thesis, which is presented in Chapter 4. Here the results of a randomised study are reported, comparing the results of limited transhiatal oesophagectomy versus transthoracic oesophagectomy with extended two-field lymphadenectomy. This is the largest ever randomised study comparing these two resection forms, more than doubling the total number of patients randomised in the literature. In this study a cost-effectiveness analysis and a study into the quality of life after both resection-forms are also included. Besides offering possible survival benefit, a more extended resection might also improve staging, which might become important for the decision for adjuvant therapy in the future. In Chapter 5, the diagnostic yield of a more extended lymphadenectomy is described, offering insight in the effects of an extended lymphadenectomy on tumour staging. The concept of stage migration is then introduced. In Chapter 6, the prognostic consequences of tumour-positive peri-truncal lymph nodes, which are considered distant metastases (M1a or M1b) for oesophageal carcinoma, are addressed. In Chapter 7, the last chapter of this part, the results of limited resection for tumours proximal to the carina are described.

In Part Two, various surgical aspects of subtotal oesophagectomy are described in more detail. Chapter 8 focuses on vocal fold paralysis, a frequent complication after subtotal oesophagectomy of which the sequelae are relatively unknown, while Chapter 9 describes the effects of injury to the trachea or main bronchi during oesophageal resection. In Chapter 10 the incidence, diagnosis and treatment of benign neo-oesophago-tracheal fistulae are discussed.

In the Netherlands, just as in many other countries, there is much debate regarding the (dis)advantages of centralisation of major surgery in centres with a wide experience. In Chapter 11 the relation between hospital volume and hospital mortality for oesophagectomy in the Netherlands is reported.

Over the last decade, much effort is put into the investigation of carcinogenesis at the molecular and genetic level. This is the subject of Part Three. To facilitate the research into the effects of duodenogastro-oesophageal reflux in vivo, an animal model for Barrett's oesophagus needs to be established.
In Chapter 12 two possible animal models for Barrett's oesophagus and possibly oesophageal carcinoma are described, and the pitfalls of these and other animal models are discussed. The understanding of the metaplasia-dysplasia-carcinoma sequence in the oesophagus lags behind when compared with the sequence occurring in the large intestine. Recently, the Wg/Wnt-pathway, a cellular signal transduction pathway, has been implied in the development of Barrett's carcinoma. In the large intestine, activation of this pathway is one of the main events leading to colorectal carcinoma, both in its familial and in its sporadic forms. In Chapter 13 the involvement of the Wg/Wnt-pathway, as indicated by the intra-nuclear presence of the β-catenin molecule and of its possible target TCF-4, is studied.

In Part Four a Summary of the preceding chapters and the major Conclusions are provided. In the Epilogue, the relevance of the results of the thesis is discussed, both in clinical perspective and at the molecular level, and recommendations for further research are provided.
In Part Two, various surgical options for lymphedema are considered. Chapter 5 focuses on vascular, lymphatic, and reconstructive techniques to address the sequelae of breast cancer, while Chapter 6 discusses the surgical options for the management of mastectomy wound healing during post mastectomy surgery. In Chapter 7, the management, treatment, and outcomes of benign mastectomy-related sequelae are discussed. In the Netherlands, as in many other countries, there is a growing concern regarding the long-term effects of mastectomy, with a focus on quality of life. In Chapter 8, the relation between psychological and hospital outcomes in post-mastectomy patients is explored.