

# SUMMARY

## Chapter 1

### **Introduction.**

Surgery is an outstanding treatment option for patients with drug resistant temporal lobe epilepsy. In practice, the decision to perform surgery is a consensus decision of a multidisciplinary team, based on a stepwise process involving complex diagnostic tests. Diagnostic research, using a multivariable approach is necessary to assess the contribution of each step of this process.

## Chapter 2

### **What is the current evidence on decision-making after referral for temporal lobe epilepsy surgery? A review of the literature.**

This chapter reviews the literature on studies assessing the independent contribution of different diagnostic tests to the decision to perform temporal lobe epilepsy surgery. Most studies studied addressed prognostic factors in operated patients only. Only ten articles met our inclusion criteria, of whom inclusion of SPECT accounted for five papers. Unbiased comparison of the results was not possible. We conclude that surprisingly little research in epilepsy surgery has focused on the decision-making process as a whole.

## Chapter 3

### **Decision-making in temporal lobe epilepsy surgery: The contribution of basic non-invasive tests.**

In chapter 3, the extent to which widely used diagnostic tests contribute to the decision whether or not to perform temporal lobe epilepsy surgery in the Netherlands was studied, using a nation-wide consecutive cohort of 201 patients referred for the presurgical work-up for temporal lobe epilepsy surgery. The individual and combined contribution of findings from patient history, routine EEG recordings, MRI, and video EEG monitoring to the consensus decision to

perform surgery was investigated using multivariable logistic regression and ROC curves. After their role in the referral to the presurgical work-up, patient history and routine EEG findings were hardly contributory to decision-making, whereas a convergence of MRI with long-term interictal and ictal EEG findings correctly identified the candidates considered eligible for surgery (25% of total) without the need for further ancillary tests. Videotaped seizure semiology contributed less than expected to the final clinical decision and basic test findings alone were insufficient to exclude patients from surgery.

## Chapter 4

### **The added value of [18F]fluor-D-deoxyglucose positron emission tomography in screening for temporal lobe epilepsy surgery.**

FDG-PET is an expensive, invasive, and not widely available technique used in the presurgical evaluation of temporal lobe epilepsy. In 469 consecutive patients referred to the national presurgical work-up, we assessed its contribution to the decision to perform temporal lobe epilepsy surgery in relation to MRI and video EEG monitoring, comparing documented decisions concerning surgery before and after FDG-PET results. FDG-PET was performed in 110 patients (23%); in 78 (71%) FDG-PET findings led clinicians to change the decision based on MRI and video-EEG monitoring findings. In 17% of all referred patients, the decision regarding surgical candidacy was based on FDG-PET findings. FDG-PET was most useful when previous MRI results were normal or did not show unilateral temporal abnormalities, or when ictal EEG results were not consistent with MRI findings or videotaped seizure semiology. We conclude that in patients referred for the presurgical work-up for temporal lobe epilepsy surgery, FDG-PET findings can form the basis for deciding whether a patient is eligible for surgery, especially when MRI or video-EEG monitoring are nonlocalizing.

## Chapter 5

### **The intracarotid amobarbital or Wada test: unilateral or bilateral?**

The intracarotid amobarbital procedure (IAP or Wada test) is part of the presurgical work-up for temporal lobe epilepsy in the Netherlands. The Wada test includes two consecutive injections of amobarbital, ipsilateral and contralateral to the epileptic focus. We studied whether a bilateral procedure has added value to a unilateral, ipsilateral procedure. Using multivariable modeling, we assessed the added value of bilateral IAP on the decision for surgery, resection size, amygdalohippocampectomy, postoperative seizure freedom, memory performance, and IQ change in 183 consecutive patients referred for the presurgical work-up for temporal lobe epilepsy surgery who underwent bilateral IAP. We conclude that a bilateral IAP has added value in predicting postoperative verbal memory and IQ. A bilateral IAP is currently not used to guide surgical strategy, but may be used for this purpose when verbal capacity is of particular concern in patients with a left-sided focus. In all other cases, IAP should be performed unilaterally.

## Chapter 6

### **Prognosis after temporal lobe epilepsy surgery:**

#### **The value of combining predictors.**

Many independent predictors of seizure freedom after temporal lobe epilepsy surgery have been identified. However, the combined predictive value of these predictors is largely unknown. In 484 operated patients referred for drug resistant temporal lobe epilepsy, we assessed the combined predictive value of a multivariable model including known independent predictors. Good outcome was defined as Engel class 1, one year after surgery. All known predictors from literature were assessed and included as independent predictor when the multivariable p-value was below 0.20. The final multivariable model included

independent predictors from history (absence of tonic-clonic seizures, absence of status epilepticus), MRI (ipsilateral MTS, space occupying lesion), video EEG (absence of ictal dystonic posturing, concordance between MRI and ictal EEG), and FDG-PET (unilateral temporal abnormalities), and had an expected ROC area of 0.63 (95% confidence interval 0.57 to 0.68) for new patient populations, which means that the model has a moderate ability to discriminate between becoming seizure free or not. Furthermore, it is particularly difficult to predict not becoming seizure free after surgery.

## Chapter 7

### Is epilepsy surgery utilized to its full extent?

It has been stated that there is a world-wide underutilization of epilepsy surgery. We established how many patients should have been and were actually referred to the Dutch national taskforce for presurgical evaluation using two random samples of patients, one from a secondary and one from a tertiary epilepsy facility. Using international guidelines, presurgical evaluation should have been considered in 95 of 578 evaluated patients (16%), but only 22 (4%) were actually referred. An expert panel evaluated clinical data from the 73 cases who were not referred and thought that 4 of these patients (5%) were potential candidates for presurgical evaluation and diagnostic testing was insufficient in another 12 (16%). Our results show that in the Netherlands 1.3 to 2.4 times more patients treated in secondary care should be referred to presurgical evaluation and 1.1 to 1.4 times more in tertiary care. Therefore, we confirm an underutilization of epilepsy surgery in the Netherlands and conclude that treating neurologists should be more aware of current guidelines, make better use of available noninvasive diagnostic techniques, and discuss surgery with their drug resistant epilepsy patients.

## Chapter 8

### General discussion.

In chapter 8, the findings in preceding chapters are discussed. Diagnostic test results that contribute to the decision for or against surgery do not necessarily contribute to the prediction of postoperative seizure freedom and vice versa. The Dutch presurgical work-up is only partly comparable to international programs. The use of ancillary tests may differ considerably between programs and countries. The Dutch presurgical work-up is a nation-wide program focused on reaching an accurate decision using the least invasive diagnostic tests. The differences between presurgical work-up programs across countries limit the possibilities of international comparison and of obtaining an international consensus on the decision for or against temporal lobe epilepsy surgery. Based on the findings from this thesis, a protocol for the presurgical work-up can be suggested, which should be evaluated in a randomized study, comparing the current Dutch work-up to the suggested protocol, with seizure outcome and quality of life after surgery and after the decision not to perform surgery as outcome variables.