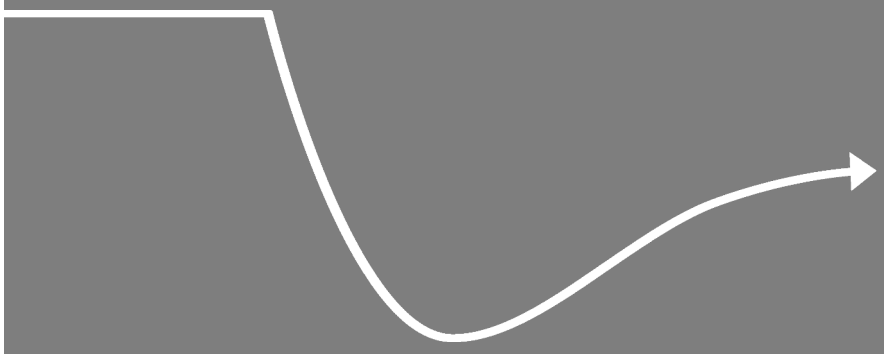

1

Introduction

The focus of healthcare is increasingly on preventive care,[1] and this is also true for perioperative hospital care. Several aspects of preventive care are already being implemented during the preoperative phase, such as assessment of the patient's health, evaluation of the operative risk, and, where necessary, optimization of the patient's mental and physical condition. Perioperative hospital care is mainly focused on frail patients, who are typically aged 60 years or older and suffer from multiple medical conditions. In an increasing number of Dutch hospitals, the preoperative consultation is now common practice,[2] with anaesthetists having a coordinating role in the interdisciplinary management strategy for individual patients.

Role of preoperative functional status

The studies described in this thesis reflect this development, with emphasis on the preoperative functional status of older patients (>60 years) scheduled for abdominal or thoracic surgery, which are major surgical procedures.[3] Patients' preoperative functional status is considered in relation to surgery-related side effects, such as postoperative complications, functional decline, and mortality. The current outpatient preoperative evaluation aims to identify patients at risk of postoperative complications, by evaluating the presence of well-known demographic and/or medical factors such as age, sex, diabetes, chronic obstructive pulmonary disease (COPD), and heart failure.[4-9] This preoperative evaluation, however, pays little attention to the possible impact of the patients' preoperative functional status on postoperative outcomes even though the literature provides several reasons to do so.[10-12] For this reason, functional status should be further investigated as part of the preoperative work-up in the future.

In the studies described here, functional status is investigated both as a predictor and as a prominent determinant of change (preferably improvement) during recovery from elective major surgery.

Relevance

It is essential to prevent a complicated postoperative course and to ensure that patients can perform activities of daily living (ADL) and instrumental activities of daily living (IADL) adequately after discharge from hospital, and this is especially true for older patients, in order to maintain quality of life and independent functioning and to limit the direct costs of care and additional costs, especially if home care or admission to a nursing home is

necessary. In 2011, 15.6% of the Dutch population was older than 65 years (CBS, Statistics Netherlands, 2011), but this proportion will increase the coming decades by about 2% every 5 years. In 2040 more than a quarter of the population will be older than 65 years (CBS, Statistics Netherlands, 2011), and these individuals will account for a sizable part of healthcare costs. Although the level of physical activity of the Dutch population has increased over the last decade, in 2009, 52.8% (95% CI 49.5–56.1%) of people older than 65 years met the requirements for the Dutch Standard for Healthy Exercise.[13] This affects the functional status of patients, putting older patients at a disadvantage when hospitalization is necessary.

Effects of hospitalization and surgery in older patients

Functional decline is a common side effect during and after hospitalization and major abdominal and thoracic surgery.[14,15] It is mainly due to a low level of physical activity after surgery, which leads to loss of physical condition, and to the physiological side effects of surgery and medication. Decreased physical activity is common during the perioperative period and can only in part be explained by mandatory bed rest as a result of manifest pathology and the type of surgery scheduled.[16] During hospitalization, patients stay in bed most of the day, even though there is usually no medical reason for this.[16] Bed rest leads to a loss of lower extremity strength, power, and aerobic capacity. Even young and healthy people lose about 100–200 g lean body mass per week when hospitalized, and older people have a 3-to 6-fold greater rate of muscle loss.[17] Kortebein reported that healthy older people lost 1 kg of lean body mass after 10 days' bed rest, mainly from the ambulatory and postural muscles of the lower extremities, which are important for mobility.[18] In addition, older patients do not usually return to their previous level of physical activity after a period of inactivity, leading to a protracted functional decline.[18]

Functional decline is also caused by major surgery which is a challenge to the physiological system. The surgical stress response encompasses a wide range of physiological effects which seriously and directly impair cardiopulmonary and muscle function.[19] Hormonal dysregulation and an inflammatory response to surgery contribute to an accelerated loss of lean tissue.[20] Muscle mass is lost at a 3-fold higher rate during hospitalization secondary to surgery and medical treatment than during bed rest at home.[21]

Special attention should be paid to the perioperative decline in respiratory muscle function, and in particular diaphragm function, in patients scheduled for abdominal

and thoracic surgery. Besides a deterioration of muscle function due to anaesthesia (even during surgery), surgery close to the diaphragm can cause reflex inhibition of phrenic nerve output, further exacerbating the decline in diaphragm function.[22] Mechanical ventilation can also result in a further decline in respiratory muscle function in this patient group.[23]

The above-mentioned consequences of surgery could lead to functional decline, which can be considered an iatrogenic event in old (>60 year) patients as it leads to a higher risk of postoperative complications and mortality, a longer hospital stay, and a protracted and sometimes permanent loss of mobility and ADL.[4,24,25] Theoretically, a good preoperative functional status could positively influence these outcomes. Recently, Malani and Covinsky emphasized the importance of the functional status in surgery.[26,27] Figure 1.1 summarizes the described phenomena and serves as the central model in this thesis.

Conceptual frame

Functional status is not a well-defined concept, which hampers its use in research.28 In this thesis, functional status is operationalized as part of patients' health, as stated by Huber et al.,[29] who consider health as a dynamic property. Thus a physically healthy person has the capacity to cope with physiological stress (among which surgical stress) and to restore the physiological balance, a process called allostasis.[30] This is consistent with the WHO International Classification of Functioning, Disability, and Health (ICF),[31] which distinguishes between performance and capacity as qualifiers of reality and potential

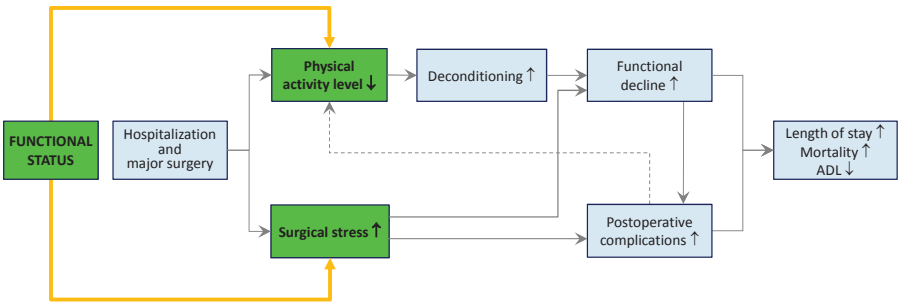

Figure 1.1 Visualization of possible effects of surgery and hospitalization in older patients and the role of preoperative functional status.

in daily life, respectively. A combination of specific performance- and capacity-based measures might provide prognostic information[32] to predict the postoperative course.

The studies described in this thesis focus on performance and capacity measures of physical determinants of functional status, operationalizing them as physical activity and physical fitness, respectively. Physical activity is defined as 'any bodily movement produced by skeletal muscles that results in caloric expenditure'.[33] Physical fitness is considered as a set of attributes that people have or achieve relating to their ability to perform physical activity.[34]

Frailty

Frail people often lack the adaptive capacity to cope with events that put various physiological systems under pressure. Bortz related adaptive capacity and allostasis to the redundant structure and function of organ systems. In this view, excess capacity provides organ systems with a high level of resilience to environmental perturbation of the physiological system.[35] Review of a wide range of body systems consistently reveals that 30% of maximal function represents a threshold for adequate function.[35] This implies that most organ systems can sustain a 70% of loss of function before manifest system failure occurs, which is termed frailty. A decline in organ function approaching or even crossing the threshold of 30% will have serious consequences for an adequate functional status, as visualized in Figure 1.2; for example, difficulties with walking and other daily activities

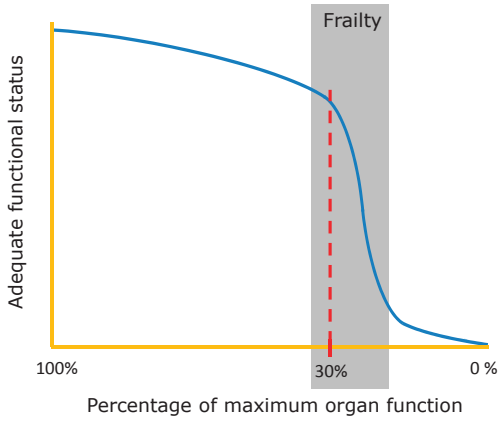

Figure 1.2 Relation between organ function and functional status showing that frailty occurs at 30% of the maximal function.

such as getting out of a chair and climbing stairs. Muscle strength, anaerobic and aerobic power, and coordination are considered biomarkers of frailty and the cause of decreased physical activity. The reverse is also true: frailty can lead to diminished physical activity.

Model of preoperative and postoperative course

We used a modification of the model of Topp[36] to visualize functional decline and recovery after hospitalization (including the preoperative period) and surgery (see Figure 1.3). Many patients show a satisfactory functional recovery during the postoperative period because they have an adequate stress response and regain their pre-hospitalization level of functioning (see Figure 1.3a). These patients are able to withstand the allostatic load, whereas some patients do not recover fully. Figure 1.3b shows the situation of a patient with a poorer preoperative physical condition (partly due to a decline during the waiting

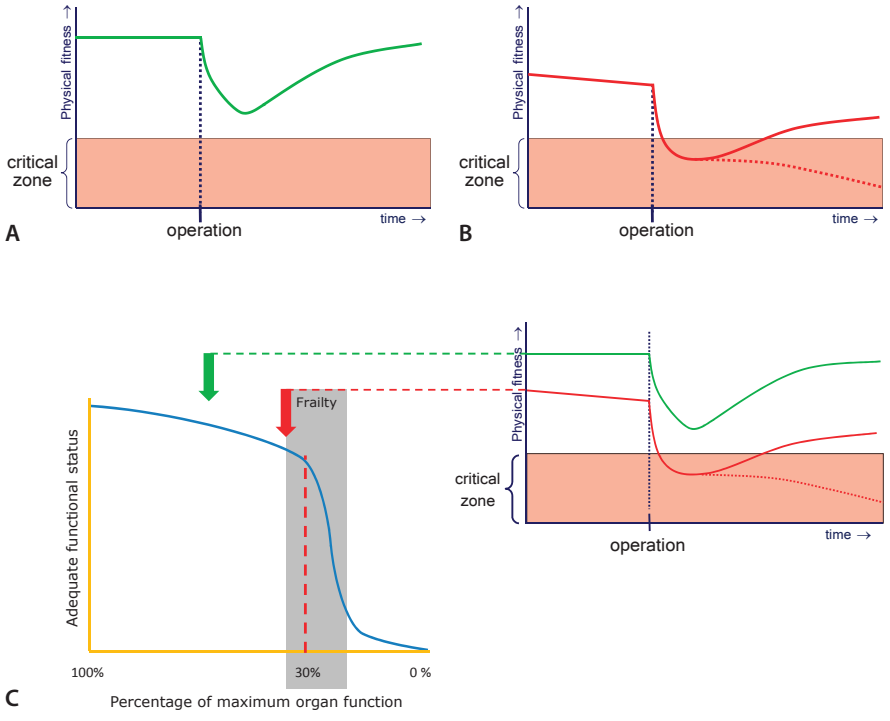

Figure 1.3 Preoperative physical condition and postoperative course (based on Topp et al.[36]). **(A)** Good preoperative physical condition and postoperative recovery keeping the patient away from the critical zone. **(B)** Poor preoperative physical condition puts the patient in the critical zone with limited recovery. **(C)** Preoperative physical condition related to frailty.

period) who is not able to respond to the physical stress of surgery, which leads to a poor postoperative course and brings that patient into the critical zone. Functional recovery is limited, making the patient susceptible to postoperative complications and even death. This type of patient is characteristic of a group that can be termed the "frail elderly" – older patients who are unable to successfully cope with surgery and hospitalization. Figure 1.3c combines the visualization of the frailty model with the concept of Topp et al. and shows frail patients at high risk of postoperative complications.

Risk stratification

The first step in preoperative care is to identify frail patients, patients who are at high risk of functional decline into the critical zone (red arrow on the curve in Figure 1.3C). Evidence shows that the preoperative physical condition of patients awaiting surgery is an independent risk factor for postoperative complications, functional recovery, and mortality after major abdominal and thoracic surgery[37-39] although the specific determinants responsible for this increased risk have not yet been identified.

Preoperative exercise training

Risk stratification enables physiotherapists to identify patients eligible for preoperative exercises to optimize their physical condition prior to elective surgery. Long-term training appears to be beneficial in older individuals.[40,41] It improves their preoperative condition, possibly making them better able to withstand the consequences of surgery and hospitalization, as represented in Figure 1.4. In this figure, these patients are less susceptible to complications and functional decline in the postoperative period. However, the time available for training before elective surgery is often limited, especially with

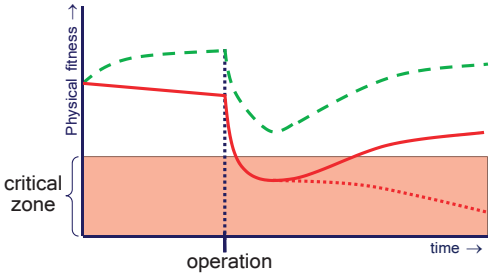

Figure 1.4 Assumed effect of preoperative exercise training (in the model based on Topp[36]).

oncological abdominal and thoracic surgery. Little research is available on the effect of short-term training for older patients in the preoperative period.[42] To date, inspiratory muscle training has been shown to decrease the incidence of postoperative pulmonary complications.[42,43] High-intensity training for other muscles and aerobic exercise training are possible in older patients; however, potential adverse effects of very strenuous training (such as musculoskeletal injuries, cardiac events and temporary reduced immunity) should be taken into account.[44-46]

Aim and outline of the thesis

The aim of the studies reported in this thesis was to investigate the role of physical fitness and physical activity in recovery after major surgery (specifically abdominal and non-cardiac thoracic surgery). In the following chapters, we investigate the following research questions:

- What is the relationship between determinants of physical fitness / physical activity and recovery from elective abdominal and thoracic surgery in older patients (chapters 2–4).
- What is the effect of a short course of physical training given preoperatively on preoperative physical fitness and on the postoperative course (i.e., recovery of respiratory function, postoperative pulmonary complications, and length of hospital stay) (chapters 5–6).

The study described in Chapter 2 reviews the predictive value of the determinants of physical fitness on postoperative cardiopulmonary complications. The prospective cohort study reported in Chapter 3 investigates the association between determinants of physical fitness and physical activity in older patients and postoperative recovery (mortality, length of stay, and discharge destination). The explorative study presented in Chapter 4 focuses on preoperative respiratory fitness and addresses the appropriateness of using concepts such as 'complexity' and 'variability' when determining the postoperative recovery of respiratory function, and thereby the appropriateness of stratifying the risk of postoperative complications. The study described in Chapter 5 investigates the feasibility and preliminary effect of preoperative training of respiratory fitness (i.e., the inspiratory muscles) on postoperative pulmonary complications in older patients scheduled for elective abdominal surgery, and that reported in Chapter 6 investigates the feasibility and preliminary effect of a broad preoperative therapeutic exercise programme for

older patients scheduled for elective abdominal surgery. The results of the studies are summarized and discussed with reference to the current literature in Chapter 7. The chapter closes with a discussion of the clinical relevance of findings and suggestions for future research.

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