



# 7

General discussion

Surgery is increasingly common in older patients,<sup>1</sup> and advances in anaesthetic and surgical techniques have enabled surgery to be performed even in the oldest old.<sup>2</sup> The incidence of major abdominal surgery in the Netherlands is about 80, 150, and 120 per 10,000 inhabitants in the age groups 40–65, 65–80, and 80 years and older, respectively. In total, 35,000 major abdominal surgical procedures are performed annually in people aged 65 years and older (source, Kiwa Prismant, 2012). As the population is ageing, it is anticipated that the number of operations will continue to increase in the future. However, the incidence of adverse postoperative outcomes is still higher in older patients than in younger patients.<sup>3</sup> This may complicate successful surgery, if success is defined as an improvement in the medical condition, recovery without postoperative complications, and a good postoperative functional status. Successful postoperative recovery depends on the ability of patients to cope with the physiological changes induced by surgery and its immediate aftermath. The research described in this thesis focused on the preoperative functional status of patients as a modifiable predictor of postoperative outcomes such as mortality and functional recovery. On the basis of our findings and in agreement with fellow researchers in this field, we conclude that patients' preoperative functional status is a potential modifiable factor that is substantially associated with postoperative recovery. Short-term, high-intensity exercise programmes might be one way to improve preoperative functional status.

### **Current developments**

The studies reported in this thesis reflect the increased interest in the functional status of the patient beyond the pathology or illness that makes hospitalization and surgery necessary. This new focus is illustrated by the switch to more functional parameters as performance indicators for the quality of hospital care.<sup>4</sup> Recovery of nutritional status is already considered an indicator of the quality of hospital care, and it is expected that the recovery of functional status will also become an indicator. A lack of recovery is considered an adverse outcome, an iatrogenic complication that deserves serious attention. Dutch hospitals have devoted themselves to reducing 'avoidable damage' in a 'safety management system' (VMS Safety programme) for hospitalized patients. 'Frail elderly' is one theme and aims to prevent functional decline due to hospitalization in patients aged 70 years and older. While these performance indicators focus on the functional status as clinical outcome measure, this thesis focuses on the preoperative functional status as a potential complicating/risk factor for the postoperative period, a factor that is modifiable in the preoperative period.

This concern about hospital-associated functional decline is international. Malani et al. and Covinsky et al. called for recognition of the importance of the functional status in relation to hospitalization and surgery in articles published in the Journal of the American Medical Association (JAMA), a highly influential journal in health care.<sup>5,6</sup> A number of articles have been published on the role of preoperative functional status, including the development of training programmes (also called prehabilitation).<sup>7-14</sup> All these developments reflect a shift from a solely medical to a more functional health-based paradigm both before and during hospitalization and surgical care. More knowledge is needed in this area. The studies described in this thesis contribute to this knowledge base, focusing on the preoperative setting.

### **Thesis research**

The research described in this thesis is consistent with the concept of health recently proposed by the WHO,<sup>15</sup> in which health is defined as ‘the ability to adapt and to self-manage’. The studies focused on physical aspects of health, defined as the ability of a person to mount a protective response, to reduce the potential for harm, and to restore an equilibrium when confronted with physiological stress.<sup>15</sup> In other words, the ability of patients to adapt to the physiological stress of an operation. An important aspect of preoperative care is the assessment and optimization of patients’ adaptive capacity as a component of functional status.

Methodologically, the thesis can be divided in two distinct parts, each of them answering a specific research question, as stated in Chapter 1. The first part consists of *observational* research that provided convincing evidence that preoperative physical fitness and physical activity are associated with postoperative recovery after elective abdominal and thoracic surgery in older patients (Chapters 2–4). A review of the literature (meta-analysis) demonstrated a significant association between preoperative physical fitness and postoperative outcomes. Most of the studies included in this meta-analysis involved patients due to undergo lung surgery and were based on the rationale that a loss of lung tissue in lung surgery could give rise to a postoperative decline in  $VO_{2max}$ . Consequently, the convincing results were limited to preoperative maximal cardiorespiratory fitness in lung surgery patients and did not apply to other components of physical fitness or other types of surgery.

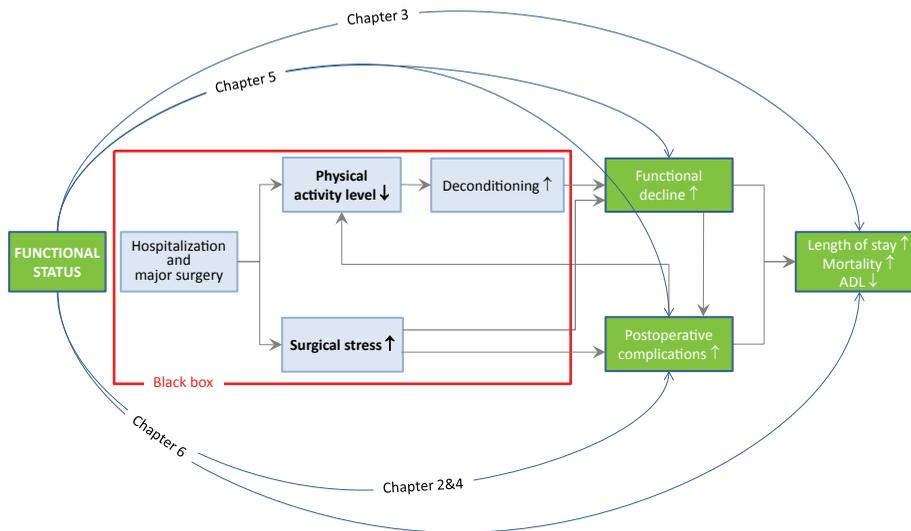
To complement these results for abdominal surgery and for a broader range of determinants of physical fitness and physical activity, a prospective cohort study was performed involving older patients scheduled to undergo abdominal, or more specifically oncological colorectal, surgery. The frailty concept explained in the introduction of this thesis (Chapter 1) formed the theoretical basis for this study. Findings revealed that physical activity (as measured with an activity questionnaire) and physical fitness (as measured with muscle strength/endurance and functional mobility) were significantly and strongly associated with the postoperative outcomes mortality, length of stay, and recovery of functional mobility. This was particularly true for physical activity and strength and endurance of the inspiratory muscles. The addition of these variables to prediction models involving conventional factors significantly improved the prediction of mortality, discharge destination, and length of stay. These observational studies ended with an exploratory study evaluating an alternative and new way to assess the preoperative adaptive capacity of the respiratory system, which is based on the assumption that the respiratory system has an adequate internal network of multiple control systems with the capacity to maintain an existing equilibrium (homeostasis) or to achieve a new equilibrium (allostasis) after perturbation of the system.<sup>16</sup> The shape of the breathing pattern, established by recording air flow and pressure, reflects the complex output of this network. Evaluation of these recordings with the help of non-linear measures proved to be an innovative and promising tool in the preoperative respiratory work-up.

Observational research does not provide answers to cause–effect relationships. This requires experimental research, which in this case addressed the second research question of this thesis. Two pilot RCTs showed that older patients (>60 years of age) can be trained in a relatively short time (2–3 weeks) to improve their physical condition and revealed a trend effect of preoperative inspiratory muscle training on the incidence of postoperative (pulmonary) complications. The feasibility of preoperative training was further underlined by the appreciation of patients, their high compliance with the training programme, and the lack of adverse events among the patients studied (Chapters 5 and 6). The first experimental pilot study investigated the effect of preoperative training on inspiratory muscle endurance and strength. These muscles were investigated because there is a neurogenic decline in the function of the diaphragm muscles during and after abdominal (and also thoracic) surgery, a decline which is regarded as a major cause of postoperative pulmonary complications.<sup>17</sup> In addition, the above-mentioned observational studies showed respiratory function to be significantly associated with postoperative outcomes

(mortality and length of stay). Although the RCT was conducted as a pilot and feasibility study only, it nevertheless revealed a borderline effect on the incidence of postoperative complications. This study was included in a recent meta-analysis by Valkenet et al., which revealed a significant overall effect of inspiratory muscle training on postoperative pulmonary complications.<sup>18</sup> Other components of physical fitness identified in the observational study justified a second pilot RCT investigating the feasibility and effect of a more general physical fitness training programme on postoperative complications, length of stay, mortality, and functional recovery. Unfortunately, this short-term training programme did not significantly affect preoperative and postoperative outcomes. The study was included in a systematic review by Jack et al.,<sup>8</sup> which concluded that a short-term, preoperative exercise programme can influence physical fitness, also in older patients, even if it is uncertain that this approach has a positive effect on the surgical outcome. These results highlighted the need for a well-powered, high-quality RCT to clarify the postoperative effects of preoperative training.

The research studies described in this thesis were conceived and carried out by health professionals in the real-life healthcare setting of a community hospital. The studies directly addressed clinical questions and made use of usual care measurements. An advantage of this approach is that results can readily be applied to day-to-day clinical practice. For example, the predictors of postoperative recovery identified in the observational study are feasible and can be relatively easily incorporated into clinical practice. Also the use of limited exclusion criteria increased the external validity of findings, improving their generalization. According to the idea of comparative effectiveness research that refers to 'real world' settings, our experience is that accurately recorded routine clinical treatment data are an important source of information for applied scientific research. However, clinical practice research has its limitations: comprehensive and expensive equipment is usually not available, so that usual care measures have to be used, and study populations are limited in terms of the number of patients available. That is why two RCTs were performed to address the feasibility and preliminary effects of a preoperative training programme. Adequately powered studies require multicentre trials.

Figure 7.1 shows the position of the study findings in the model presented in the first chapter. The studies provided information about the association between the beginning (functional status) and end (postoperative outcome measures) of the process. The 'black box' in the middle refers to knowledge of the interaction between functional status, surgical stress, activity level, and postoperative outcome, knowledge that is relevant to



**Figure 7.1** Position of study findings in a scheme visualizing possible effects of surgery and hospitalization in older patients and the role of preoperative functional status.

designing appropriate exercise training programmes. For example, an adequate functional status could be considered a requirement for early postoperative ambulation, which in turn prevents functional decline and postoperative complications. Preoperative training should be aimed at the level of fitness required to perform activities of daily living (ADL). Because lower leg muscle function is closely related to functional mobility and ADL,<sup>19</sup> preoperative training should focus on the strength of these muscles. Another more physiologically based rationale refers to the immune system. The immune response is also a part of the adaptive capacity, with a person's level of immunity appearing to be associated with their level of physical activity.<sup>20</sup> This is consistent with the importance of the level of physical activity as predictor of postoperative recovery, as found in the observational study described in Chapter 3.

### Recommendations for future research

As the studies of this thesis and the literature have found preoperative functional status to be associated with the postoperative course, future research should focus on functional status as a modifiable factor. If a cause–effect relationship exists, patients will benefit from preoperative interventions to improve their functional status. In the absence of a rationale,

as indicated in the above section, current preoperative interventions use general training programmes for elderly patients that focus on strength, aerobic, and functional training, which is neither cost effective nor a targeted approach. Instead, research should identify which aspects of training programmes (strength, (an)aerobic capacity, or functional mobility<sup>21</sup>) are appropriate for individual or specific groups of patients, as recommended by Hoozeboom et al.<sup>22</sup> Future research on the effects of preoperative exercise training should also address the optimization of training parameters, among which intensity. High-intensity training is necessary to achieve improvements given the often short time available before surgery. Frail older patients can tolerate high intensities<sup>23</sup> but overtraining is always possible and should be avoided because this puts the patient in an even worse preoperative condition than without training.<sup>24</sup> The challenge is to optimize the training parameters, aiming a maximal improvement without overtraining, which is a real hazard in older people.<sup>25</sup>

Neither our or other studies provided RCT-strength evidence that preoperative training of general physical fitness parameters affects patients' postoperative outcomes. From a methodological point of view, a well-powered RCT should provide this missing evidence. However, it can be questioned whether this is an ethically sound approach. The strong evidence for the relationship between preoperative physical activity and physical fitness and the postoperative course, together with the biological plausibility of this approach (showing a relationship between the physical condition and the adaptive capacity of the body system), raises the question whether new RCT research with the use of a control group without any form of intervention can be justified. This issue addresses the therapeutic obligations of clinicians to their patients and makes the distinction between a research and treatment approach apparent.<sup>26</sup> Literature proposes 'clinical equipoise' as a requirement for the random assignment of patients. It is defined as a state of professional uncertainty about the relative therapeutic merits of treatments and is a much-debated issue.<sup>27,28</sup> According to de Graaf et al.,<sup>29</sup> we should find out whether there is a lack of agreement among expert clinicians about the relative merits of alternatives to preoperative training. In addition, research designs other than RCTs are possible, such as a stepped wedge design and comparative effectiveness research.

Besides intervention studies, the exploratory study that evaluated complex breathing patterns using non-linear measures should be extended, for instance, by investigating whether non-linear measures distinguish between older people at risk or not at risk of postoperative complications and whether these measures can help guide physiotherapists

implementing, monitoring, and evaluating the progress of preoperative inspiratory muscle training.

### **Recommendations for clinical practice**

The results reported in this thesis and in the literature support the recommendation that physical activity and physical fitness factors be incorporated into the preoperative work-up. A cut-off point of 15 ml/kg/min for  $\text{VO}_{2\text{max}}$  for physical fitness, as found in de meta-analysis, implies that patients have to be able to walk briskly or cycle at moderate speed.<sup>30</sup> The activity level determined with the activity questionnaire corresponds to light household activities and/ or walking for 1–2 hours a day. This suggests that a moderate level of physical activity should enable patients to undergo surgery successfully. This is in accordance with Dutch Standard for Healthy Physical Activity Behaviour and other research prescribing moderate physical activity for health.<sup>31</sup> For cost-effective care, patients should be asked a few questions about their level of physical activity, to identify those at risk of postoperative problems, because it is time-consuming and expensive to test the physical activity and fitness of all patients, when only a few might have a poor physical condition.

The function of waiting time in relation to the patients' preoperative condition should be reconsidered. Waiting time is currently considered idle time that has to be kept as short as possible. Indeed, the waiting period is used as a performance indicator for the quality of hospital care. Given the lack of RCT evidence and budgetary restrictions, doctors are not motivated to delay surgery in order to optimize the physical condition of their patients. This, in turn, prevents research to provide evidence, creating a vicious circle. We think that the time between the decision to operate and actual surgery should be used to optimize the physical condition of frail and elderly patients and be included as a standard part of the preoperative protocol. Depending on a patients' medical status and preoperative physical condition, the duration of the preoperative period should be adjusted to ensure that the patient has the physical condition necessary to undergo surgery.

Physical activity status was found to be a robust predictor of the postoperative course, consistent with the literature showing a strong association between physical activity and health outcomes such as disability<sup>32</sup> and life expectancy.<sup>33</sup> This association also highlights the decrease in habitual physical activity in Western society.<sup>34</sup> To achieve a more adequate level of physical activity, there needs to be a change in the mind-set of patients, their

family, and healthcare and social workers.<sup>35,36</sup> Being in an adequate physical condition gives patients an advantage should they need surgery, as it promotes a successful recovery from surgery and successful ageing.<sup>37</sup>

In conclusion, the studies described in this thesis highlight the role of physical activity and physical fitness in patients scheduled for abdominal and thoracic surgery. We hope that our findings will be implemented in the preoperative care setting and contribute to a more functional health-based approach to hospital and surgical care, with as goal to ensure that patients leave hospital in the same, if not better, functional condition as when they were admitted: it's a question of 'the better in, the better out'.

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