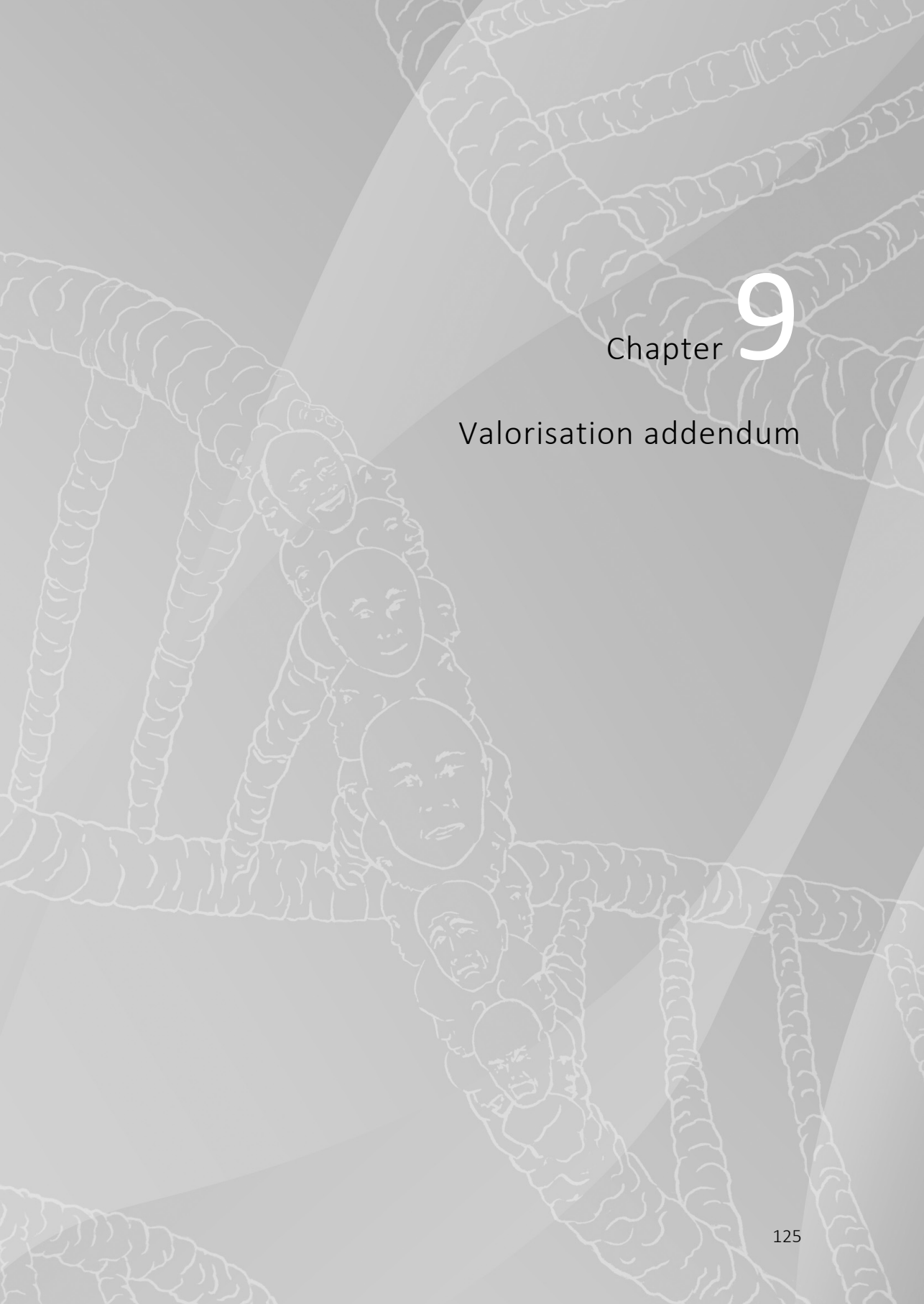
The way to understanding Chronic Postsurgical Pain



Chapter 9

Valorisation addendum

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The goal of this thesis is to contribute to the scientific knowledge and understanding of the pathologic processes involved in the human body with regard to pain; but also to find approaches to improve and optimize healthcare in the perioperative setting in order to decrease the prevalence and severity of chronic postsurgical pain (CPSP). The goal of this paragraph is to highlight the societal and economic importance of the research aims in this thesis; both on the voluminous group of surgical patients, as well as on society in general.

We will start by explaining the impact of pain on the individual patient and on society. Second, we will explain the importance of developing prediction models for CPSP. We will end this paragraph by highlighting the future research directions that are necessary to develop methods for preventing CPSP as adequately as possible.

Personal and societal impact of pain

Pain is an important and widely prevalent health problem, especially in the developed world. Pain causes discomfort and suffering, and research has demonstrated that pain severity is an important determinant of quality of life.[1-3] Aiming to prevent and treat pain as adequately as possible therefore has a substantial moral ground, and is considered an essential part of optimal patient care.[4] In addition to this, research has also demonstrated that pain, especially acute postsurgical pain (APSP), is associated with increased morbidity and mortality. Patients who suffer from APSP are prone to cardiac morbidity (e.g. myocardial infarction), pulmonary morbidity (e.g. pulmonary infections), stroke and postoperative delirium.[5-7] It has also been demonstrated that pain has a negative impact on other organ systems, such as the gastrointestinal system, the renal system, blood coagulation and the immune system.[8]

In addition to the negative consequences of pain for the individual patient, research has shown that pain can have an important negative impact on society in general. Multiple studies have shown that chronic pain is associated with increased consumption of health care resources, absenteeism from work and a substantial associated economic burden.[9-13] More specifically, moderate to severe acute postsurgical pain has been clearly demonstrated to be associated with delayed hospital discharge and, in case of ambulatory surgery, with unanticipated hospital admission and contact with the general practitioner or other health care professionals.[5, 14] Since it is estimated that over 80% of all surgical patients experience inadequately managed pain during the acute postoperative phase, it is easy to imagine that APSP leads to a substantial increase in health care costs and a negative impact on society.[5] This is especially true for societies which are based on a system of solidarity, and in which health care costs are thus considered a shared individual and governmental responsibility.

The societal consequences of CPSP have been less extensively studied. A small study has demonstrated that patients with severe neuropathic CPSP or neuropathic post-trauma pain visit physicians more frequently and use more prescription medication than patients with less severe pain.[15] Another study demonstrated an increase in health care utilization of patients with CPSP after kidney transplantation.[16]

The described negative consequences of acute and chronic postsurgical pain on the individual patient (e.g. discomfort and suffering, increased morbidity and mortality) and on society in general (e.g. increased health care costs, absenteeism from work and increased economic burden) are important reasons to make every attempt to reduce the prevalence and severity of APSP and CPSP. As mentioned before, adequate treatment of APSP and CPSP is very important in order to reduce the prevalence and severity of these pain problems, and should be part of optimal patient care. However, prevention will be far more effective in reducing the negative consequences for the individual patient and society. In order to prevent the development of CPSP in postsurgical patients, it is of paramount importance that we first understand the risk factors for the development of CPSP. Only then will we be able to focus research on identifying strategies to prevent the development of moderate to severe CPSP.

Importance of prediction of CPSP

During the last decade many researchers have attempted to develop tools to identify patients at risk for the development of moderate to severe CPSP. Until recently, the focus has been on demographic, clinical and psychological risk factors. These risk factors can be easily identified with the use of questionnaires and do not require invasive testing. One of the most important risk factors seems to be the presence of moderate to severe preoperative pain.[17-20] Other risk factors are the presence of moderate to severe acute postoperative pain, preoperative analgesic use, surgical fear, lack of optimism and pain catastrophizing.[2, 17, 21, 22] However, clinical and psychological risk factors have only been able to explain part of the observed variance in the prevalence and severity of CPSP. For this reason, genetic factors have recently become of interest. Our own studies, as well as several others, have been able to identify genetic polymorphisms as possible predictors for CPSP.[23, 24] Especially polymorphisms within the COMT gene, opioid receptor genes, potassium channel genes, GCH1, CACNG, CHRNA6, P2X7R, cytokine-associated genes, human leukocyte antigens, DRD2 and ATXN1 seem to be promising predictors for CPSP.

Defining the risk factors for CPSP is the first step towards reduction and prevention of CPSP. It will create possibilities for an individual approach, which is paramount in the time of personalized medicine. It could help identify the predictors for CPSP on an individual level during the preoperative phase, after which a personalized plan can be made. It will allow patients to be informed of their individual risk at CPSP, which might lead to an informed decision of the treatment plan. In some cases patients might decide

not to undergo the planned surgery at all. This could be the case for patients with a high risk at developing CPSP, who are about to undergo surgery that is not strictly necessary (e.g. cosmetic procedures), or procedures for which non-surgical alternatives exist. In other cases, a preoperative tailor-made treatment plan might be offered to the patient, in order to try to influence the present risk factors (e.g. treatment of preoperative pain or psychological factors).

Future research will hopefully make us gain even more insight into the predictors for the development of CPSP. In order to further clarify this, future research should not only focus on the intensity of the reported pain (e.g. NRS or VAS), but also on the characteristics of the pain (e.g. neuropathic, inflammatory, etc.), as well as the location of the reported pain. This is important because various types of pain can have a different origin and can therefore be associated with various risk profiles. Future research should also try to further reveal the genetic risk factors for the development of CPSP. Most studies have so far focused on genetic polymorphisms that have been associated with other types of pain, as well as psychiatric diseases. This type of genetic research is also known as hypothesis-driven research. A different approach, in the form of genome-wide associated studies (GWAS) will hopefully lead to the identification of other promising polymorphisms associated with CPSP.[25, 26] Ones GWAS have identified promising polymorphisms, and these data have been validated in large patient cohorts, these polymorphisms can be tested in smaller procedure-specific cohorts, and can be incorporated into clinical and psychological prediction models.

Towards prevention of CPSP

Our research has demonstrated that the prevalence of CPSP is at least 10-15% after several types of surgical procedures.[17, 24, 27] Several studies have demonstrated that the presence of CPSP is associated with an increase in health care costs and societal economic burden.[15, 16] Our own research found an association between preoperative pain, one of the most important predictors of CPSP, and the amount of hospital-based health care costs as well as absenteeism from paid work.[28] All these data suggest that adequate prevention of moderate to severe CPSP will be able to reduce health care costs and societal economic burden significantly.

Even though the research in this thesis does not describe preventative methods with regards to CPSP, the importance of adequate prevention in society does warrant a short summary of possible methods for prevention. Future research will have to demonstrate whether these methods will actually be able to reduce the prevalence and severity of CPSP.

Small studies have already suggested that the prevalence of CPSP can be reduced by treating acute postoperative wound pain and neuropathic pain.[29, 30] However, our own studies, as well as several others, have demonstrated that preoperative pain appears to be an even stronger predictor for the development of CPSP.[17, 18, 20] It would therefore be

interesting to know if treatment of preoperative pain is able to reduce the prevalence and severity of CPSP even further. In order to be successful, treatment of preoperative pain will probably have to be as timely and as effective as possible, in order to limit preoperative sensitization of the peripheral and central nervous system.

Furthermore, research has also demonstrated that preoperative anxiety, pain catastrophizing and pessimism are important risk factors in the development of CPSP.[2, 17, 21, 22] The role of targeting these psychological risk factors should also be clarified by future research. More research in the field of genetics and CPSP might lead to new perioperative pharmacologic targets for the prevention and treatment of CPSP.

Summary

Defining the predictive factors for the development of CPSP after several types of surgery is the first step towards the prevention of CPSP. A decreased prevalence and severity of CPSP will in turn lead to a reduction of health care costs, work absenteeism and societal economic burden.

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