Prediction of outcome following mild traumatic brain injury

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General discussion
GENERAL DISCUSSION

This dissertation on mild traumatic brain injury aimed to study the role of posttraumatic complaints, psychological distress and the provided aftercare on general outcome and specifically return to work the first year after injury. All presented studies were part of a multicenter cohort study (UPFRONT) conducted between 2013 and 2015 in the Netherlands. In the following paragraphs, an integrated discussion of results and future perspectives is presented suggesting a different perspective on mTBI aftercare.

As can be observed from the cover of this thesis, mild traumatic brain injury encompasses a wide range of patients and causes of injury. For example the affected population comprises young healthy students falling off their bicycle in an intoxicated state, frail elderly stumbling on a slippery sidewalk, road traffic victims with extra-cranial injuries, and those with various recreational and sporting accidents. The heterogeneity the group impedes attempts of defining the specifics of necessary care in the different stages of recovery. Therefore a personalized approach of mTBI seems more fitting. Especially the subset of patients comprising up to 20% – occasionally referred to as the miserable minority – that report persistent complaints and struggle with resumption of pre-injury activities are the ones that should be targeted for interventions in an earlier stage. However, timely identification of these patients who are in need for follow-up and determining the appropriate aftercare is notoriously challenging.

As discussed in chapters 3 and 4 of this dissertation, opting to provide patients with a form of aftercare is currently primarily based on the mere fact whether patients were or were not admitted to a hospital following injury.\textsuperscript{1} It is remarkable to note that many studies do not report on their included patients in terms of hospitalization rates,\textsuperscript{2-4} and those that do report admittance rates varying from 11 up to 45%.\textsuperscript{5-8} In chapter 3, we showed that 60% of patients in the UPFRONT-cohort were admitted to the hospital, but guidelines for admission were not always followed as many cases of admission depended on the clinical presentation at hand. We zoomed in on the consulted medical specialists in the aftercare and found that 60% of hospitalized patients visit a neurologist in the first six months after injury, while according to guidelines all admitted patients should be followed-up. Other specialists involved in aftercare for all mTBI patients were those related to physical injuries (i.e. surgeons and physical therapists), rehabilitation physicians, psychologists and psychiatrists. Apparently, outpatient follow-up outside of the scope of the neurologist is relatively common, which raises questions whether comparable (after)care is provided by these specialists and if a more interdisciplinary approach might be more effective.

We were surprised to find that 25% of the non-hospitalized patients returned to the outpatient neurology clinic within 6 months after injury and chose to study this relatively unin-
vestigated group further in chapter 4. Initially, we hypothesized that non-hospitalized patients who did return to the outpatient clinic (OFU) were probably more severely injured when compared to their nOFU counterparts. Although characteristics related to injury severity have weak predictive value in terms of outcome, it could be argued that premature discharge (either initiated by the patient or physician) might be related to unfavorable outcome and manifested by return to the outpatient clinic. Strikingly, we were unable to identify differences in any of the patient demographics or injury characteristics between OFU and nOFU patients. Two weeks after injury, however, a differentiation was discernible with regard to experienced psychological distress; symptoms of anxiety or depression early after injury were associated with higher odds of returning to the outpatient clinic. Signs of psychological distress such as anxiety or depression are associated with persistent posttraumatic complaints (PTC), which tend to develop due to a combination of factors. The first being occurrence of brain injury itself as a trigger, with predisposing factors (e.g. maladaptive coping style) and post-injury stressors (e.g. anxiety and depression) explaining why in some patients complaints persist up to months after injury. These pre-injury personality factors and post-injury stressors might also explain why uninjured individuals and non-head injured trauma patients also occasionally report complaints that are often attributed to brain injury. In these cases, a non-head trauma or major life event may serve as a trigger for the development of complaints, resembling those of brain injury.

Due to these aforementioned reasons, we aimed to investigate whether complaints reported after mTBI may be distinguished from trauma control patients regarding the nature (i.e. which specific complaints) and frequency in relation to anxiety and depression. We demonstrated in chapter 5 that complaints reported after mTBI are also reported after orthopedic traumas. However, patients with mTBI not only reported more complaints than the control group, but also in a completely different pattern. Factor analyses yielded 3 factors, the biggest comprising cognitive and somatic complaints such as headache, poor concentration, and fatigue. This factor, which we summarized and labeled as mental distress, also showed the strongest correlation with depression and anxiety. This was especially the case for the mTBI group suggesting that the development of complaints – although variable in nature – could be seen as a manifestation of psychological distress. Our findings imply that the influence of psychological distress is more important after sustaining brain injury when compared to an orthopedic trauma. Injury to the head apparently causes an acute stress response, prompting the patient to adapt with the consequences of injury. Supported by the finding that an acute problem-focused coping style is related to better outcome when compared to a passive coping style, it is concluded that some patients are better equipped to regulate the stress response after trauma leading to a better outcome.
In this regard, an interesting subgroup of mTBI patients are those with an acute alcohol intoxication (AAI), whom account for up to 30-50% of all mTBIs. Given that an AAI may affect the stress response after injury by a dampened experience of trauma, and thereby possibly influence outcome, we studied this subgroup in chapter 6. Approximately 30% of the UPFRONT-cohort was severely intoxicated during injury, mostly young males. When compared to the patients who sustained an injury while being sober, intoxicated patients reported a lower number of complaints and less symptoms of depression after two weeks, and they had a better outcome 6 months after injury. Furthermore, intoxicated patients were more often admitted to the hospital, but mostly just for one day of observation to “sleep it off”. In chapter 4, we plead that the dichotomization for outpatient follow-up based on hospital admission is rather ambiguous and unfit for the heterogeneity of mTBI. Signs of psychological distress the first weeks after injury are probably more suitable for selecting patients in need of aftercare, as they are indications of adaptive disorders irrespective of the cause (e.g. structural abnormalities related to the injury or predisposing factors related to for instance maladaptive coping style).

When focusing on the societal consequences, persistent posttraumatic complaints after mTBI are the largest contributors of costs, due to loss of work productivity and sick leave. Several studies have focused on finding predictors for return to work (RTW), with inconclusive results. Although it would be intuitive to assume that the nature, load and satisfaction of employment are of influence in the process of work resumption after mTBI, prognostic models have mainly been focused on patient demographics and injury characteristics. Furthermore, the levels of work resumption as defined by absent, partial or complete RTW are often unacknowledged and long-term work resumption (or sustainability of work) is largely understudied. In chapter 7, we aimed to address these issues by studying three levels of RTW (complete, partial, and no RTW) throughout the first year after injury. Interestingly, a lot of shifting took place in terms of the aforementioned status of RTW in the course of time – even after six months – indicating that a decline or improvement of functioning may take place outside the scope of most outcome studies. In the developed multifactorial prediction model we identified a substantial role of occupational factors on work resumption after 6 months, apart from the well-known predictors (e.g. age, cause of injury and extra-cranial injuries). Both occupational category and workload in hours/week were predictive for return to work. Occupations requiring manual labor had the lowest odds of RTW after six months, when compared to those of skilled or professional functions. Furthermore, the workload in hours per week showed a U-shaped effect, with the lowest odds of RTW on a 32-hour workweek. All physicians involved in the treatment of mTBI patients – which we studied in chapter 3 – should be aware of these effects when advising patients on their recovery. In both the model for 6 and 12 months RTW, reporting of complaints and depression after 2 weeks were...
related to lower odds of work resumption. It might be argued that the first measurement moment of the UPFRONT-study (after 2 weeks) is a relatively late interval to identify and possibly treat maladaptive disorders and predicting problems with RTW on the longer term. In a clinical setting, screening for problems at one week after injury might more fitting. However, an outpatient clinic visit one week after injury for all mTBI patients is not feasible. Studies have pointed out that telephonic follow-up could be effective in the prevention of persistent complaints after mTBI.\textsuperscript{26} Therefore, mTBI might be a very suitable population for telephonic screening. The development of a personalized approach to assess whether and in which manner screening for maladaptive disorders is necessary, depending on patients’ demographics, occupation, workload and adaptive capacities should therefore be a future goal for the mTBI field.

It seems applicable to propose an approach in which patients at-risk of unfavorable outcome based on signs of psychological distress are screened, including those who are without complaints early after injury; the fortunate few from chapter 8. In this chapter, we approached recovery of mTBI from a new perspective. Instead of focusing on the so-called miserable minority we studied patients that seem to recover very soon without impairments. Our ambition was to find characteristics in this subgroup that were protective of unfavorable outcome. However, our selected group of fortunate few was even smaller than we had anticipated. We were surprised to find that half of these supposedly fully recovered patients in an early stage developed secondary complaints in a later stage, affecting quality of life one year after injury. Patients developing secondary complaints reported more symptoms of anxiety and depression already 2 weeks after injury, showing the possibility of early identification even in those patients who would not meet the criteria for many interventions, since they are mostly based on the presence of posttraumatic complaints.\textsuperscript{27}

The question remains whether this suggested change in practice to screen all mTBI patients for signs of maladaptation will lead to better outcomes. The key is early identification of at-risk patients to prevent instead of treat persistent complaints and unfavorable outcome. The first step is education as it has been shown that a reduction in posttraumatic complaints may be accomplished by providing information.\textsuperscript{26,28} Adequately informing patients on recovery might recondition symptom expectation and illness perception of patients, both of which are known to influence psychological wellbeing.\textsuperscript{29,30} Screening patients for psychological distress and adequately informing and reassuring them creates a threefold benefit of this approach: first, unnecessary consultation may be avoided for patients who were admitted to the hospital but recover without impairments. Second, non-hospitalized patients who feel the need to ask additional questions are provided with this opportunity during a telephonic follow-up, preventing negative symptom expectation.
Third, when deemed necessary patients are able to visit the outpatient clinic in an early phase after injury, thereby possibly preventing the development of chronic complaints and problems that limit the resumption of activities.

**Future perspectives**

As discussed throughout this dissertation, outcome following mTBI is a multifactorial process, on which we are gaining knowledge that provides new research angles as future perspectives on the mTBI research field.

For several decades, research has been focused on explanations for unfavorable outcome after mTBI. First endeavors for prediction models aimed to look at injury and patient characteristics such as GCS, CT-abnormalities, age and gender. When these models proved to be of insufficient accuracy, personality traits as coping style and psychological factors as anxiety and depression became an important scope. The bio-psychosocial model in combination with occupational factors has provided us with a good prediction model for RTW, leading to additional knowledge on recovery of mTBI. In the preceding paragraphs, we touched upon the suggestion that the provided care might also influence outcome. In case of a heterogenic disorder such as mTBI, guidelines are often unspecified for individual cases and the adherence varies.\textsuperscript{31,32} Comparative Effectiveness Research (CER) is a way of identifying factors related to care that influence outcome. While conducting the UPFRONT-study we signaled differences in provided care between the three participating centers. Although all centers comply to the same guideline,\textsuperscript{33} considerable differences were present in guideline adherence, clinical care, and follow-up. It is in our believe that the future of mTBI research should therefore not only focus on finding predictors in characteristics on a patient level, but also on differences and effectiveness of care systems.

In a time of globally rising health care costs, important questions pertain to the economic burden of disease and cost-effectiveness of treatments. The Dutch health care system, with its nationwide insurance and accessibility is consistently graded as among of best in the world.\textsuperscript{34} The important role of general practitioners (GPs), who refer only 5-10% of their patients to in-hospital medical specialists, is one of the reasons for affordable healthcare. Most patients are treated within the GP practice, as probably also goes for a substantial part of the mTBI population. The advises for recovery, as provided by GPs are probably as important as those of the neurologists at the ED or at outpatient clinics. Even more so, since GPs are often better informed about a patients’ background in terms of for instance family life and occupation. Little is known about how GPs assess and treat mTBI, for instance when they choose refer to either ED or outpatient clinic and how they advise patients in terms of recovery. The investigation of effectiveness of care systems should therefore not only focus on in-hospital treatment but also on the characteristics of the GP population and treatment.
Over the last decades, the ageing population has led to a shift towards older mTBI patients visiting the ED. Although the economic consequences in terms of work resumption do not apply to the elderly, it is easy to imagine the economic effects related to healthcare costs within this population. Since higher age is associated with comorbidity and poly-pharmacy, more diagnostic procedures (e.g. CT-scans) are performed, hospital admittance and longer length of stays are common, and concurrent injuries requiring surgical intervention and/or inpatient rehabilitation cause a rise in direct healthcare costs. Furthermore, although relatively new as a subject of TBI research, some associations between mTBI and the development of mild cognitive impairment and dementias have been proposed. A recent publication on the late-life effects of TBI at older age combined three large prospective cohort studies and reported that TBI is related to Lewy body accumulation, progression of Parkinsonian features, and the risk of developing Parkinson disease. The shift in the mTBI population and its effects on society urges an important task for governments and physicians related to fall prevention and long-term care solutions.

These aforementioned suggestions for futures scopes on mTBI research will add to the increasing insights of the factors that are related to outcome after mTBI, leading eventually to the most effective care towards complete recovery after mild traumatic brain injury.

CONCLUSION

In this dissertation we studied factors influencing general outcome and specifically return to work following mTBI. By investigating posttraumatic complaints, psychological distress and aftercare, and accounting for pre-injury adaptive capacities and occupational factors we contributed to the current body of work on the specifics of recovery after mTBI. Our findings indicate that adaptive disorders could and should be signaled early after injury, to ensure proper aftercare for the broad spectrum of mTBI patients that the heterogenic disorder entails.
REFERENCES


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