Complications in abdominal surgery: Assessment, prediction and prevention
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SUMMARY AND PERSPECTIVES

In this chapter we summarize the main findings of this thesis and put them into a broader context of surgical research. Despite several attempts the assessment of surgical outcomes is not standardized and reporting of post-operative complications is still incomplete. Often, only complications judged to be important are selectively reported while ignoring minor and the occurrence of multiple complications. To address this lack of a standardized and comprehensive assessment, we developed and validated the comprehensive complication index (CCI) that summarizes the entire postoperative experience of the patient with respect to complications.

Extended Summary of the Studies

The development of the CCI was based on a first study (Chapter two), in which we compared perceptions of the severity of post-operative complications by patients, nurses and physicians. Six hundred and fifteen patients, nurses and physicians estimated the severity of post-operative complications, as described by scenarios, in a fully structured and validated questionnaire, on a numerical analogue scale from 0 (not severe at all) to 100 (extremely severe). We found that the severity of post-operative complications was perceived similarly by patients, nurses and physicians. All participants graded the complication scenarios similarly across all grades of the Clavien-Dindo classification (from grade I to IVb). The data provided additional support for the validity of the Clavien-Dindo classification from the perspective of patients and health care professionals. We observed that not only health care professionals but also patients classified the severity of complications according to the need for treatment and the grades of severity of the Clavien-Dindo classification, respectively. Moreover, the results suggested that the perception of the severity of complications by nurses, who often have a closer relationship with patients than physicians, is in between the perception of physicians and patients.

In the study reported in Chapter three we developed the comprehensive complication index (CCI) which summarizes all complications and their respective severities on a single continuous scale ranging from 0 (none) -100 (death). For the development of the CCI, we used the established Clavien-Dindo classification system for complications, adopting methods from operation-risk-index analysis in marketing research and developed a formula that considers any combination of complications. Validations from four different perspectives showed that the CCI discriminates well between patients with different numbers and severity of complications, and that the CCI is more responsive to treatment effects than commonly used ways to classify complications. In addition, the validity of the CCI was supported through expected negative correlation with the postoperative health. In a fourth validation, patients were asked to evaluate different complication scenarios that included one or more different types of complications. In a conjoint analysis we tested different attributes by rating each attribute on a score and finally, the conjoint analysis was used to determine how patients valued and favored...
different attributes. The CCI showed a high correlation with the ratings from this conjoint analysis. This analysis supported our assumption that minor complications would receive less weight if additional and more severe complications occur. It also supports the notion that complications of less severity still have an impact on overall morbidity and must not be ignored.

We believe the potential benefit of this comprehensive complication index may be substantial. For the first time a tool is available which summarizes all postoperative complications and their severities in one single number. The CCI has the potential to become a standardized outcome measure in randomized trials, observational studies and benchmarking.

In a number of additional studies we focused on acute renal failure as a major post-operative outcome after liver surgery (chapter four and five)\(^7,\,8\). Acute renal failure (ARF) is a frequent and life-threatening complication after abdominal surgery, associated with substantial mortality, morbidity and costs\(^7\). Therefore it is relevant to identify those patients at increased risk for ARF and develop prevention strategies. In the study reported in Chapter four, an easily applicable score was developed and validated to estimate the risk of ARF in patients scheduled for liver resection\(^7\). The score includes only parameters that can be collected pre-operatively and covers a risk spectrum for ARF from 4.1\% to 87.3\%. We then developed a more parsimonious score based on the four strongest predictors (pre-existing cardiovascular disease, chronic renal failure, diabetes and high levels of ALT) which predicted ARF nearly as accurately as the full score. Depending on the trade-off between user friendliness and accuracy, clinicians and investigators can choose between the full and the parsimonious risk score. While the full score provides a more precise and nuanced prediction of the risk for ARF, the parsimonious score is simpler, and more likely to be used in clinical practice.

In Chapter five we showed that the previously developed prediction score (chapter four) could be improved by adding intra-operative parameters such blood transfusions, hepatico-jejunostomy and oliguria\(^8\). The resulting score is superior in identifying patients who could benefit from admission to a special care unit for ARF, and may prevent unnecessary admissions to such a unit following liver resection, in patients at lower risk of ARF. Discrimination represented by the area under the curve, calibration by the Hosmer-Lemeshow test and the five-fold cross validation indicated a good validity and accuracy of the updated prediction model.

In Chapter six we described a trial protocol for a strategy to prevent ARF after liver resection. This will be the first randomized trial investigating the preventive effect of terlipressin on post-operative ARF following liver resection. Since terlipressin is associated with harms, only patients at moderate to high risk for ARF will be included since we found in a formal benefit harm analysis that terlipressin is likely to provide overall benefit if the risk for ARF after liver surgery is moderate high\(^7\). The prediction model developed in chapter four will be used to determine the risk for ARF and select
those patients for the randomized trial that are at least moderate risk for ARF.

In Chapter seven we showed that the continuous application of the volatile anesthetic sevoflurane does not protect patients from ischemia-reperfusion injury in liver surgery. Use of sevoflurane resulted in similar clinical outcomes compared with continuous application of intravenous anesthetic propofol. These results may indicate that volatile anesthetic-induced liver protection is triggered by an on-off mechanism, such as pre- or postconditioning, with no preventive and protected effect in a setup of continuous application of volatile anesthetics. Chapter seven shows the importance of further research to find the best strategies for preventing ischemia-reperfusion injury in liver surgery.

Taken together, the results of the research reported in this thesis could improve the quality of care in abdominal surgery, to the benefit of patients, health professionals, and society in general.

Implication for Future Research and Clinical Practice

Validation studies of prediction models are necessary because the original model may be too optimistic. An external validation study investigates if a model developed in a particular population provides accurate predictions in a different patient population. Conventional measures of model performance include calibration and discrimination but approaches for judging the clinical usefulness should also be explored. There is a growing methodological literature on these novel approaches and it would be important to apply them in more validation studies.

Future research may address if the perceptions of postoperative complications is different in other patient and physician populations from other countries and if it’s possible to generalize the reference values. For this reason, we already initialized another study at McGill University in Montreal, Canada.

Even though the CCI was developed and validated on a broad patient population in general surgery, it should also be tested for generalisability and validity in different fields of surgery such as urology, neurosurgery, cardiac surgery and/or gynecology. Only if the CCI is successfully externally validated, it will be widely adopted and may become the standard outcome measure in surgery or even interventional medicine such as e.g. invasive cardiology.

A standardized assessment of complications is important for comparability of results across future studies. Thereby, the quality of evidence summarized by systematic reviews and meta-analyses is likely to improve. The CCI may also offer a more precise tool in clinical research such as clinical trials or databases and registries. For example, clinical trials may be able to more easily detect clinically relevant differences, which would in turn decrease sample size requirements and potentially reduce the number of false-negative surgical trials.

In addition, the CCI may become a standard outcome in clinical practice and used to compare the risks associated with different surgical procedures but also to compare the performance across surgeons and even hospitals. The CCI may be implemented in clinical information systems to serve as
a quality control and even benchmarking tool, although for this later use, risk adjustment must be included for proper comparison of CCI values across patients and hospitals. The incorporation of the CCI in clinical information systems may allow for the first time a systematic 90-days assessment of the overall morbidity by regular clinical controls in the outpatient clinic. This may have an important implication in the clinical practice and will give essentially more information about the burden and course of postoperative complications. Until now, only in-hospital morbidity has been reported. In some surgical fields such as cardiac surgery 90-days mortality is used to be reported but so far, it is unusual to report 90-days morbidity. An increased CCI after 90 days compared to the CCI at the day of discharge may change the postoperative course of patients and improve the follow-up in quantity as well as quality, so that an early identification or even a prevention of possible complications is possible. This may also have an implication on the health-care costs and the quality of life of patients.

Further research could also focus on external validation of both prediction scores (chapter four and five) to determine the extent to which an update is necessary and the clinical usefulness and potential consequences of such using the risk scores*. Additionally, further preventive strategies and treatments should be investigated in trials to offer protection and/or prevention of postoperative complications. The trial on described in chapter six will show if terlipressin is a promising preventive treatment strategy to reduce specific postoperative complications such as acute renal failure. Reducing postoperative complications is likely to increase the quality of life of patients significantly and has the potential to reduce costs.

Concluding Remarks

In the last twenty years, there has been a debate about the best outcome measure for surgical procedures. There have been too many different definitions for postoperative complications. It has become evident that a standardized assessment, prediction and prevention of postoperative complications are important to improve the surgical quality. The current thesis presents some important tools to improve the quality of surgical research. The CCI seems to be a very promising outcome measure to contribute to that goal. Also, preventive treatment strategies as well as risk-adapted decision making models are potentially useful approaches to reduce postoperative complications and to improve the surgical quality.

References:


