Surgical site infections of orthopaedic implants

Chapter X

Summary

Because orthopaedic procedures with total joint prosthesis and instrumented spinal fusion have shown good results, with an increase of quality of life, a further increase of these procedures in the coming decades is expected, with more aged patients, more revision procedures, but also more younger patients who will undergo these procedures.

Unfortunately, orthopaedic implants have a risk for bacterial infection. In literature the incidence of surgical site infection (SSI) after spinal surgery ranges from 2 to 12%, depending on diagnosis, surgical approach, use of spinal instrumentation, and the complexity of the procedure. The incidence of prosthetic joint infection ranges between 1-2% in literature, and may be increasing just as the incidence of SSI after spinal surgery.

Even if the incidence rate of implant infections remains unchanged, the prevalence of implant infections will increase, with the increasing number and more complex orthopaedic implants procedures. It has been predicted that infection will become the most frequent mode of failure of total knee and hip arthroplasty.
Deep postoperative and hematogenous prosthesis infections may be treated with retention of the prosthesis, if the prosthesis is stable. How long the infection may be present to not exclude a good result is unclear.
In the second chapter we studied retrospectively 89 deep infected stable prostheses: 69 total hip and 20 total knee replacements; 83 early or delayed postoperative infections and 6 hematogenous. In postoperative infections, treatment started 12 days to 2 years after implantation, in hematogenous infections symptoms were present for 6-9 days. Patients were treated by debridement, prosthesis retention, systemic antibiotics and local antibiotics: gentamicin-PMMA beads or gentamicin-collagen fleeces. The minimum follow-up was 1.5 years. We analyzed how the result of the treatment was influenced by the length of the period the infection was present, and by other variables as host characteristics, infection stage and type of bacteria.
In postoperative infections the risk for failure increased with a longer postoperative interval: from 0.2 (CI 0.1-0.3) if the treatment started ≤4 weeks postoperative, to 0.5 (CI 0.2-0.8) if started ≤ 8 weeks. The relative risk for success was 0.6 (CI 0.3-1.0) if the treatment started ≤ 8 weeks. In the hematogenous group, 5 of 6 infections were treated successfully.

A longer delay before the start of the treatment causes an increased failure rate, but this must be weighed to the advantage of keeping the prosthesis. We consider a failure rate of < 50% as acceptable and therefore advocate to keep the prosthesis up to 8 weeks postoperatively, as well as in hematogenous infection with short duration of symptoms.

A 2-stage revision is the most common treatment for late deep prosthesis infections and in all cases of infected loosening. However there is no consensus about the optimal interval between the 2 stages.
In the third chapter we retrospectively studied 120 deep infected total hip (n=95) and knee (n=25) prostheses, treated during 24 years. The mean follow-up was 5 (2-20) years. All infections were treated with extraction, 1 or more debridements and with systemic and local antibiotics (gentamicin-PMMA beads). There were different intervals between extraction and reimplantation: median 14 (11-47) days in short term treatment with uninterrupted hospital stay, and 7 (3-22) months in long term treatment with temporary discharge. We analysed the outcome regarding infection healing and clinical results.
88% (105/120) of the infections healed, with no difference between short and long term treatment, 82 prostheses were reimplanted. In the last decade we treated patients more often with a long term treatment,

but reduced the discharge interval between the extraction and reimplantation. In long term treatments more reimplantations were performed compared with short term treatments, despite more difficult-to-treat infections with worse soft tissue condition.

Patient, wound and infection characteristics resulted in an individualized treatment with different intervals between stages. The 2-stage revision treatment in combination with local gentamicin PMMA beads resulted in good results in even difficult prosthesis infections and gentamicin resistant germs.
In contrast to knee and hip prosthesis infection there is no generally established treatment algorithm for the management of surgical site infection (SSI) and non-union after instrumented spinal surgery. In contrast to infected hip- and knee- arthroplasties, the use of a local gentamicin impregnated carrier in spinal surgery has not been widely reported in literature.

In the fourth chapter we described 48 deep SSI and non-union patients after instrumented spine surgery, treated between 1999 and 2016. The minimum follow-up was 1.5 years. All infections were treated with a treatment-regimen consisting of systemic antibiotics and repetitive surgical debridement, supplemented with local gentamicin releasing carriers.

We analysed the outcome of this treatment regimen with regard to healing of the infection, as well as patient- and surgery-characteristics of failed and successfully treated patients. 42 of the 48 (87.5%) patients showed successful resolution of the SSI without recurrence with a stable spine at the end of treatment. 36 patients' SSI were treated with debridement, local antibiotics, and retention or eventual restabilization of the instrumentation in case of loosening. 3 patients were treated without local antibiotics because of very mild infection signs during the revision operation. 3 patients were treated with debridement, local antibiotics and removal of instrumentation, of which one of these patients was restabilized in a second procedure. Infection persisted or recurred in 6 patients. These patients had a worse physical status with a higher ASA-score. *Staphylococcus aureus* was the most frequent causative microorganism.

We see that debridement and retention of the instrumentation, in combination with systemic antibiotics and the addition of local antibiotics provided a successful treatment for SSI and non-union after instrumented spinal fusion.

The rate of a surgical infection is relatively high after instrumented spine surgery. The availability of an easy-to-use prediction model would be of great help to select those patients that are at highest risk and probably prevent the devastating consequences of an infection.

After literature search in spine surgery, one prediction model was found that used only few predictors to estimate an individual's probability of a surgical site infection. Lee et al. developed a prediction model for SSI after spine surgery that was derived from a surgical spine register of the USA (The Spine End Result Registry).

In the fifth chapter we external validate this previously published prediction model for surgical site infection after spine surgery in our patient population, a Western European cohort of patients that underwent instrumented thoracolumbar spine surgery in a university hospital.

We included 898 consecutive patients who underwent instrumented thoracolumbar spine surgery. To quantify overall performance using Nagelkerke's R^2 statistic, the discriminative ability was quantified as the area under

the receiver operating characteristic curve (AUC). We computed the calibration slope of the calibration plot, to judge prediction accuracy.
Sixty patients developed an SSI. The overall performance of the prediction model in our population was poor: Nagelkerke's R^2 was 0.01. The AUC was 0.61 (95% confidence interval (CI): 0.54 – 0.68). The estimated slope of the calibration plot was 0.52.
Our conclusion was that the previously published prediction model showed poor performance in our academic external validation cohort. To predict SSI after instrumented thoracolumbar spine surgery for the present population, a better fitting prediction model should be developed.

In the sixth chapter we described the development including internal validation of a multivariable model for accurate prediction of surgical site infection (SSI) after instrumented spine surgery using a large cohort of a Western European academic center.

Data of potential predictor variables was collected in 898 adult patients who underwent instrumented posterior fusion of the thoracolumbar spine.
We used logistic regression analysis to develop the prediction model for SSI.
The ability to discriminate between those who developed SSI and those who did not was quantified as the area under the receiver operating characteristic curve (AUC). Model calibration was evaluated by visual inspection of the calibration plot, and by computing the Hosmer and Lemeshow goodness-of-fit test.

*S*ixty patients (6.7%) were diagnosed with an SSI. After backward stepwise elimination of predictor variables we formulated a model in which an individual's risk of an SSI can be computed. Age, body mass index, ASA score, degenerative or revision surgery and NSAID use appeared to be independent predictor variables for the risk of SSI.
The (AUC) was 0.72 (95% CI: 0.65 – 0.79), indicating reasonable discriminative ability.

The new developed prediction model for SSI after instrumented thoracolumbar spine surgery showed reasonable discriminative ability and calibration. Identification of patients at risk for SSI allows for individualized patient risk assessment with better patient-specific counseling, and may accelerate the implementation of multi-disciplinary strategies for reduction of SSI.

In the seventh chapter we determine *in vitro* and *in vivo* pharmacokinetic release profile of antibiotics from PMMA spacers and PMMA beads we used in aforementioned studies.
For the *in vitro* experiment the PMMA spacers or beads were submerged in phosphate-buffered saline and gentamicin concentrations were determined from collected specimen at several times points, measured with ELISA.

To assess the *in vivo* antibiotic release profile of different spacers, wound drainage fluid samples were collected after implantation of a spacer over a period of maximum 14 days.
After 48 hours the burst gentamicin concentration elution was 9,862 ± 1,782 ng/ml (mean ± SD) from spacers vs. 38,394 ± 7,071 ng/ml (mean ± SD) for beads. Over 35 days, spacers had eluted a cumulative mean concentration of 13,812 ± 3,548 ng/ml vs. 55,048 ± 12,006 ng/ml for beads (P<0.001).
Clinical samples of patients with a Vancogenx® spacer showed higher gentamicin release than Refobacin™ spacers (P<0.001).

Our study was the first that measured the release data of local antibiotics with ELISA. Compare to spacers, the exact release values of gentamicin from PMMA beads are more than 10 times higher and reached a maximum much later than spacers. This makes the use of PMMA beads more preferable to use for treatment of the infection itself.