

Supplementary article data

The “true” incidence of surgically treated deep prosthetic joint infection after 32,896 primary total hip arthroplasties

A prospective cohort study

Per Hviid GUNDTOLT^{1,2,3}, Søren OVERGAARD^{2,3}, Henrik Carl SCHØNHEYDER^{4,5}, Jens Kjølseth MØLLER^{6,7}, Per KJÆRSGAARD-ANDERSEN⁸, and Alma Becic PEDERSEN⁹

¹ Department of Orthopedics, Kolding Hospital, Kolding; ² Department of Orthopaedic Surgery and Traumatology, Odense University Hospital, Odense; ³ Institute of Clinical Research, University of Southern Denmark, ⁴ Department of Clinical Microbiology, Aalborg University Hospital; ⁵ Department of Clinical Medicine, Aalborg University, Aalborg; ⁶ Department of Clinical Microbiology, Vejle Hospital, Vejle; ⁷ Institute of Regional Health Research, University of Southern Denmark; ⁸ Department of Orthopedics, Vejle Hospital, Vejle; ⁹ Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark.

Correspondence: per.hviid.gundtoft@rsyd.dk

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Appendix A. List of antibiotics redeemed by patients. These Anatomic Therapeutic Chemical Classification System codes were used in identification of antibiotics

ATC-Code	Generic name	DDD ^a	Unit
J01AA07	tTetracyclin	1,000	mg
J01CA02	Pivampicillin	1,050	mg
J01CA04	Amoxicillin	1,000 + 250	mg
J01CA08	Pivmecillinam	600	mg
J01CE02	Phenoxyethylpenicillin	2,000	mg
J01CF01	Dicloxacillin	2,000	mg
J01CF05	Flucloxacillin	2,000	mg
J01CR02	Amoxicil/Clavulanic acid	1,500	mg
J01EA01	Trimethoprim	400	mg
J01EB02	Sulfamethizol	4,000	mg
J01FA01	Erythromycin	1,000	mg
J01FA06	Roxithromycin	300	mg
J01FA09	Clarithromycin	500	mg
J01FA10	Azithromycin	300	mg
J01FF01	Clindamycin	1,200	mg
J01MA02	Ciprofloxacin	1,000	mg

^a Defined daily dose

Appendix B. Background to algorithm

A: Kamme and Lindberg (1981) described the procedure for obtaining and culturing prosthetic biopsies in 1980. They concluded that one or 2 positive prosthetic cultures was a strong indicator of contamination, while growth in 5 out of 5 cultures was a strong indicator of an infection. Atkins et al. (1998) later showed that growth in 3 out of 5 biopsies was highly predictive for infection, while 2 out of 5 was not. Mikkelsen et al. confirmed these findings by showing that using a cutoff of 3 positive prosthetic cultures proved to have high specificity but low sensitivity (Mikkelsen et al. 2006).

Some bacteria distinguish themselves by their virulence, and the isolation of these increases the likelihood of infection as opposed to isolation of less virulent and spore-forming bacteria, which can be of more questionable significance. We therefore grouped bacterial species and yeasts into groups A, B, and C according to their perceived virulence. Based on the studies of prosthetic cultures and the grouping of bacteria, we used 3 or more positive cultures with growth of the same group A or B microorganisms as definite confirmation of a prosthetic joint infection.

B: No previous studies have directly investigated the negative predictive value of no positive prosthetic cultures in a sample of 5, but based on the studies of Trampuz et al. and Atkins et al., this result has a high likelihood ratio for no

infection (Atkins et al. 1998, Trampuz et al. 2007). However, Trampuz et al. and Malekzadeth et al. showed that antibiotic treatment within 14 days prior to revisions had an effect on the sensitivity of prosthetic cultures (Trampuz et al. 2007, Malekzadeh et al. 2010). Based on this, we decided to classify revisions as having been performed for causes other than infection if 5 or more prosthetic cultures were negative. When the patient had not been treated with antibiotics prior to the revision, the indication for revision was not reported as infection in the DHR and NRP, and no positive aspiration of synovial fluid was found.

- C: A sinus tract reaching from the skin to the prosthesis is an indisputable clinical sign of infection (Zimmerli et al. 2004, Parvizi and Gehrke 2013). In the review of the medical records, a sinus tract was defined as observed if the physician specifically described a fistula, a sinus tract, or communication between skin and the prosthesis. A suppurating wound was not defined as a sinus tract.
- D: An audit was performed to avoid misclassification of revisions with a large number of prosthetic cultures, as this may increase the risk of growth by chance. All the authors were involved in the audit, which was based on the results of prosthetic cultures and/or aspirations, prior to use of antimicrobial therapy, CRP level, and observed purulence. Unanimous agreement was required for classification.
- E: Numerous studies have shown that a normal CRP (< 10 mg/L) is a good predictor for ruling out of a prosthetic joint infection (Bernard et al. 2004, Savarino et al. 2004, Schinsky et al. 2008, Yi et al. 2014). As CRP is elevated in the first weeks after primary THA, it was determined by the International Consensus Meeting on Periprosthetic Joint Infection that a cutoff value of 100 mg/L would apply if the test had been obtained less than 6 weeks from the most recent surgery and 10 mg/L would be used if the test had been obtained more than 6 weeks from surgery (Parvizi and Gehrke 2013). In this study, CRP was used to rule out infection, which is why we regarded a CRP value of < 10 mg/L as being definitive for a revision to be classified as having been performed for causes other than infection. If a CRP measurement had not been performed, the revision was classified as having been performed for causes other

than infection, as most surgeons would request a CRP before revision if there was any doubt regarding aseptic loosening or infection. An example where CRP is not used would be a patient with dislocation of the THA.

- F: Few studies have analyzed the diagnostic specificity and sensitivity of 2 positive prosthetic cultures with the same microorganism, as judged by phenotypic characteristics. The specificity is reported to be lower than that obtained with ≥ 3 positive prosthetic cultures (Atkins et al. 1998, Mikkelsen et al. 2006, Trampuz et al. 2007, Schafer et al. 2008). When the CRP was elevated and there were 2 positive prosthetic cultures with growth of microorganisms of the same phenotype, we defined the revision as having been performed due to infection. A single positive culture or 2 positive cultures of different microorganisms (or different phenotypes) have low specificity (Atkins et al. 1998, Trampuz et al. 2007, Schafer et al. 2008); therefore, we required additional supportive evidence—such as elevated CRP and either purulence or positive aspiration—to be able to classify the revisions as having been performed due to infection. Previous studies have shown that aspirations of synovial fluid have low to moderate sensitivity and high specificity (Lachiewicz et al. 1996, Malhotra and Morgan 2004, Williams et al. 2004). Based on these studies, we considered a positive aspiration as a good “rule in” measurement, while a negative aspiration was given less weight in classifying the revisions.
- G: In previous and present definitions of prosthetic infection, the presence of purulence has been a definitive sign of infection (Zimmerli et al. 2004, Parvizi et al. 2011), but this is a subjective measurement and a number of case reports have described purulence in revisions that were not infected (Biant et al. 2010, Blumenfeld et al. 2010, Molvik et al. 2010). In the algorithm, purulence was only definitive if the CRP was elevated and the result of microbiology was inconclusive, e.g. due to antibiotic treatment. In a review of the medical records, “presence of purulence” was defined as having been observed only if the purulence was described. Descriptions of inflammatory tissue or blurred synovial fluid etc. were not considered to be “purulence”.