Editor's Spotlight/Take 5

Editor's Spotlight/Take 5: Increased Mortality After Prosthetic Joint Infection in Primary THA

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No one who cares for patients with infected THAs would mistake prosthetic joint infection (PJI) of the hip for a minor complication. Neither does anyone assume that every patient treated for PJI will be restored to full health, or even that all of these patients' infections can be eradicated. But most of us probably would not imagine that the risk of death within a year of surgery for PJI is more than twice the risk of patients who undergo no revision at all—and nearly twice that of patients

who undergo major THA revisions for aseptic causes.

Yet that seems to be exactly the case. Why do those findings, published this month in *Clinical Orthopaedics and Related Research*® by Dr. Søren Overgaard and his team from Denmark, seem so discordant? And why should this matter to all readers—even those who do not do revision hip arthroplasty?

The reason the findings seem surprising is the event in question is sufficiently rare that neither of our usual sources of information—personal experience and prior research—is sufficiently reliable in the setting of such an uncommon event. If a busy surgeon treats a few dozen patients a year with PJI of the hip (or even a couple hundred), it would be all-but-impossible for her to discern reliably a doubling or even a tripling of an event that happens to only a few percent of her patients. And even large

studies are susceptible to drawing discordant conclusions about rare events [1, 3, 4], since event-rate estimates in this setting often are beset by wide confidence intervals.

These facts, and this exceptional paper, remind us just how important well-conducted registry research can be. Because of this, readers who never expect to revise an infected THA should pay attention. Registries exist for sports injuries, spine surgery, tumors, and other conditions that orthopaedic surgeons treat; large-insurance databases and big-data sources of other kinds can help practicing surgeons answer questions that otherwise would be inaccessible [2].

Dr. Overgaard's remarkable synthesis evaluated nearly 70,000 patients' experiences with infections after primary THA, and drew not just from the Danish Hip Arthroplasty Register, but from three other massive, national data sources during a 10-year period. And their team resisted what must have been a tremendous temptation to limit the study to a high-level look at mortality; they drilled deep into the bacteriology of PJI, and identified that patients with infections caused by *Enterococcus* species were at much greater risk of death within one year of surgery than others. I have not seen a

A note from the Editor-In-Chief:

In "Editor's Spotlight," one of our editors provides brief commentary on a paper we believe is especially important and worthy of general interest. Following the explanation of our choice, we present "Take Five," in which the editor goes behind the discovery with a one-on-one interview with an author of the article featured in "Editor's Spotlight."

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study present this risk quite so convincingly before.

It is difficult to do this kind of work well, but the answers to our biggest questions may come no other way. This work should inspire similar approaches in all orthopaedic subspecialties, and the Take-5 interview with Dr. Overgaard that follows will likewise be of interest equally to those who treat PJI and those who do not.

Take Five Interview with Søren Overgaard, MD, DMSc, senior author of “Increased Mortality After Prosthetic Joint Infection in Primary THA”

Seth S. Leopold MD: *Congratulations on this remarkable study. I see this as one that can inspire analogous efforts far outside of arthroplasty. What nonarthroplasty-related “big questions” do you think are most amenable to research from national registries or large databases in the short-term future?*

Søren Overgaard MD, DMSc: Traditionally, arthroplasty registries have focused on long-term revision risk, including identifying those implants that are at increased risk for revision. However, patients are susceptible to a number of other complications like thromboembolic events, bleeding, kidney injury, and infections. Registers

might help inform us about these endpoints. In addition, reconstructive success is defined by more than simply an implant remaining in situ; patient-reported outcomes (PRO) matter tremendously. Finally, the influence of comorbidities is important; for example, patients with diabetes who have an increased risk of infection.

I believe that arthroplasty registers can be generalized to other databases like those used in trauma, spine surgery, and even in more-general health-insurance sources. Additionally, the kinds of topics I mentioned above would also be of major interest. A focus on short-term complications and other outcomes will be important. Simply knowing the real complication rates may be an eye-opener for many, and could help identify patients who will not benefit from surgery.

Dr. Leopold: *Your paper has four authors; among them are nine advanced degrees (four MDs, three PhDs, and two master's degrees). I take it that this speaks to the many skillsets it takes to do this kind of work well. What advice do you have to young clinician-scientists who want to develop teams that can answer important questions using large datasets?*

Dr. Overgaard: Indeed, the team of authors behind this paper all have

Søren Overgaard MD, DMSc

more than one advanced academic degree. But what may be more important for a successful team is that it consists of researchers with complementary skills who trust each other.

A young clinician-scientist who wants to develop a team within large datasets or registries should consider the following:

- One cannot do this kind of research alone. The team is the key to successful register research.
- The research question must be important, and it should focus on benefits to the patient. Thus, having a clinician on the team who has extensive knowledge within the

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field of interest and with the database to be used is important.

- The team must have in-depth information about the database. One must be mindful of pitfalls associated with this kind of work, such as changes of the register's definitions, or inclusion of new variables over time. Moreover, bigger is not better—or at least it's not enough. Verification of completeness and data validity is essential.
- The team needs a statistician and epidemiologist with a good understanding of the methods to be used.
- There are benefits to joining networks and participating in congresses that focus on register research; the International Society of Arthroplasty Registries (<http://www.isarhome.org>) is one good example.

Dr. Leopold: *Your study didn't just take a high-level look at mortality; you made a number of important observations about bacteriology. Enterococci don't just infect arthroplasties; how do you think spine and tumor surgeons should consider your findings, particularly as resistant Enterococcus species become more prominent?*

Dr. Overgaard: Enterococcal infection is associated with high mortality in many settings, including cardiology and intensive care units. There is no reason to believe that spine and tumor

surgery should have a different risk profile than hip revision surgery regarding *Enterococcus* species.

One of the factors that may contribute to the high mortality rate was that we found that 75% of the patients with enterococcal THA infections were treated with a prophylactic antibiotic that *Enterococcus* is resistant to (such as cefuroxime). Among other kinds of bacteria, resistance may be acquired over time, which underlines the worldwide problem of increasing antimicrobial resistance. Therefore, unfortunately, we can expect mortality from this problem to increase in the future.

Furthermore, we must presume that the antibiotic type used before surgery was continued after surgery until the results of the intraoperative cultures were known. This emphasizes the need for faster diagnostic procedures and a close collaboration in the multidisciplinary team consisting of an orthopaedic surgeon and microbiologist, regardless of specialty.

Dr. Leopold: *What are you and your colleagues in this work doing differently in your practices based on your findings? The 8% 1-year mortality you found is dramatic; in other diagnoses, this might mandate extensive and sustained multidisciplinary care, yet many of these patients are managed by an orthopaedic surgeon in isolation or*

perhaps with help from an infectious diseases consultant. What kinds of more-systematic approaches to the ongoing care of these patients—which perhaps might also apply to other orthopaedic patients with serious infections—should we consider?

Dr. Overgaard: These data are also new for us. We have to interpret them with caution and make new strategies where required. Certainly the patient group with deep infection runs the risk of severe complications. However, we have to put the results into context. Based on the findings in our paper, we can estimate that approximately 1% will get a deep infection after a primary THA and 8% of these patients will die within 1 year. This means that the mortality risk associated with infection in primary THA is eight in 10,000.

I believe that we have to tailor antibiotic prophylaxis much better in the future, and identify patients before surgery who are at high risk for deep infection. Those at risk should be counseled.

Some may decline the surgery. A multidisciplinary team should be involved in the care of these patients, as well as those having revision surgery, and the latter group should be evaluated specifically for the possibility of deep infection. The multidisciplinary team working with

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these patients may need to include radiologists. It may be worth considering dedicating specialized wards to the care of these patients to detect and treat complications early.

Dr. Leopold: *About half of the revisions for PJI in this paper were performed in 90 minutes or less; might some of these have been simple exchanges of modular polyethylene bearings and femoral heads or even simple incision and drainage procedures? If so, this makes the mortality findings even more intriguing. Do you know what proportion of the procedures in this dataset were simple bearing exchanges, single-stage exchanges of all components (as is more common in Europe than in the United States), and two-stage exchanges?*

Dr. Overgaard: We did not have extract data on the type of revision

done, as this was not a part of our research question, although they are available in the register. For our study, the number of different PJI revisions would most likely be too small for effective statistical comparisons.

It is my impression that most centers in Denmark will perform modular-bearing exchanges for infections within the first 2 months after primary surgery, and patients presenting later than that with PJI will undergo two-stage revision. My best estimate is that around one-third may have had bearing exchanges alone. We do not know if there is difference in mortality risk between one- and two-stage procedures. Currently, randomized control trials on one- versus two-stage revisions are being performed. It will be interesting to see the results both on rerevisions and also on mortality risk.

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